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Epidemiological investigation of enteric canine coronaviruses in domestic dogs: A systematic review and meta-analysis

Amienwanlen Eugene Odigie [1], Paolo Capozza [1], Maria Tempesta, Nicola Decaro, Annamaria Pratelli [*]

Department of Veterinary Medicine, University of Bari, Valenzano, Bari, Italy

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ABSTRACT

Canine enteric coronavirus (CeCoV) is a globally distributed enteric pathogen that causes significant harm to canines. The objective of this systematic review was to examine the global dissemination of CeCoV and assess the potential for infected canines to be exposed to various CeCoV genotypes and subtypes. With an aggregated prevalence of 18.8%, the study predicted regional variations, indicating that CeCoV is an exceptionally prevalent disease. The increased likelihood that infected canines will be asymptomatic is a significant cause for concern, as undetected cases of CeCoV infection could persist and spread the disease. This underscores the significance of ongoing surveillance of CeCoV in order to avert its transmission. Nevertheless, further investigation is necessary in order to ascertain the moderators that significantly impact the prevalence and distribution of distinct subtypes and genotypes of CeCoV. Hence, it is imperative to undertake randomized clinical trials in order to acquire a more accurate understanding of the variables that influence the prevalence of CeCoV. By conducting ongoing surveillance, regional variations in the prevalence of CeCoV in canines can be accounted for, thereby enhancing our comprehension of the illness and ultimately impeding its transmission.

1. Introduction

Coronaviruses (CoVs) (subfamily *Orthocoronavirinae*, family *Coronaviridae*, order *Nidovirales*) are enveloped, single-stranded, positive-sense RNA viruses, composed of four major structural proteins, spike (S), small envelope (E), membrane (M), and nucleocapsid (N). The S glycoprotein is a major antigenic determinant and is also responsible for host cell receptor binding and viral entry (Decaro and Lorusso, 2020). Currently, CoVs are classified in four different genera, including *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus* and *Deltacoronavirus* (Decaro and Lorusso, 2020).

Three CoVs are known in dogs, i.e., two *Alphacoronaviruses* of the subgenus *Tegacovirus*, namely canine coronavirus type-I (CeCoV-I) and canine coronavirus type-II (CeCoV-II), and one *Betacoronavirus* of the subgenus *Embecovirus*, namely canine respiratory coronavirus (CRCoV). CeCoVs (species *Alphacoronavirus-1*) are commonly responsible for mild, self-limiting enteritis in pups (Decaro and Buonavoglia, 2011; Pratelli, 2011). Although they are neglected viruses and vaccination is not recommended, two independent studies have demonstrated their significant involvement in the onset of acute canine enteritis (Dowgier et al., 2017; Duijvestijn et al., 2016).

CeCoV was first recognized in an outbreak of gastroenteritis among dogs in 1971 (Binn et al., 1974). Since then, several CeCoV outbreaks have been reported worldwide, showing that CeCoV is an important entero-pathogen of dog (Decaro and Buonavoglia, 2008). Serological and virological investigations have demonstrated that dogs of all age and breed are susceptible to infection and that the virus is widely spread in the dog population, mainly in kennels and animal shelters (Bandai et al., 1999; Naylor et al., 2001; Pratelli, 2011; Rimmelzwaan et al., 1991; Schulz et al., 2008; Tennant et al., 1993; Yesilbag et al., 2004).

Genetic and phylogenetic analysis carried out on multiple regions of several CeCoVs revealed that CeCoV-I and feline coronavirus type I (FCoV-I) originated from a common ancestor, while CeCoV-II arose from multiple recombination events with an unidentified genetic source (Lorusso et al., 2008; Pratelli et al., 2003). Several pieces of evidence have shown that CeCoV-II is genetically related to with transmissible gastroenteritis virus (TGEV) of swine and FCoV-II (Decaro et al., 2007; Herrewegh et al., 1998).

* Corresponding author.
E-mail address: annamaria.pratelli@uniba.it (A. Pratelli).
[1] These authors contributed equally to this work.

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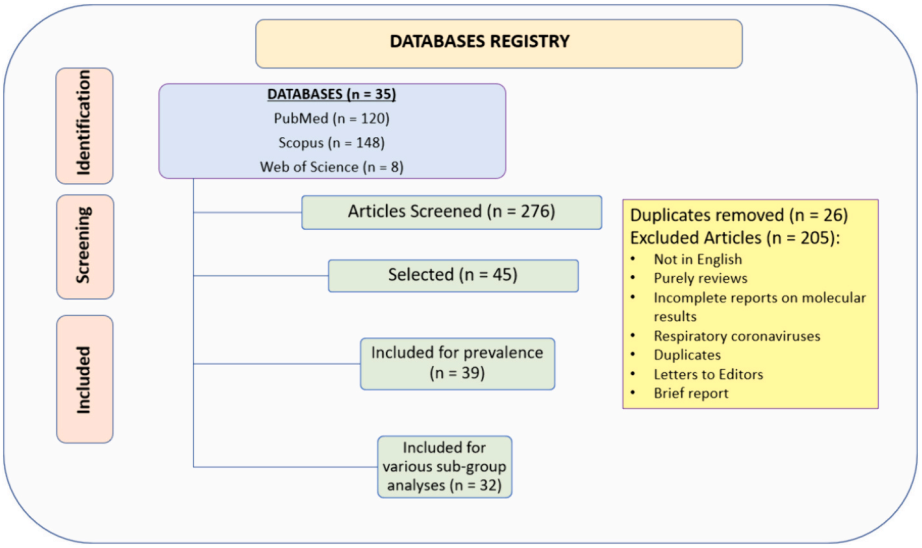

Fig. 1. Flow chart of the article selection process (PRISMA flow diagram).

Table 1
Overwiew of the studies included in the qualitative synthesis of canine enteric coronavirus (CeCoV) prevalence in dogs.

Reference	Country	Study period	Sample	Assay	Total	Postive (%)
Schulz et al. (2008)	Germany	1991–2001	Faecies	Electron microscopy	1136	450 (39.6)
Sakulwira et al. (2003)	Thailand	1999–2001	Faecies	RT-PCR	70	9 (12.9)
Yesilbag et al. (2004)	Turkey	2004	Faecies	RT-PCR	90	14 (15.6)
Jeoung et al. (2014)	Korea	2003–2007	Faecies	RT-PCR	67	22 (32.8)
Godsall et al. (2010)	United Kingdom	2006–2008	Faecies	RT-PCR	355	28 (7.9)
Decaro et al. (2010)	Europe	2001–2008	Faecies	RT-PCR	1172	493 (42.1)
Soma et al. (2011)	Japan	2007–2009	Rectal swab	RT-PCR	109	55 (50.5)
Decaro and Buonavoglia (2011)	Europe	2008–2009	Faecies	RT-PCR	156	60 (38.5)
Tupler et al. (2012)	Florida, USA	2009	Faecies	RT-PCR	100	10 (10.0)
Stavisky et al. (2010)	United Kingdom	NA	Faecies	RT-PCR	249	7 (2.8)
Duijvestijn et al. (2016)	Netherlands	2009–2011	Faecies	RT-PCR	161	51 (31.7)
Castanheira et al. (2014)	Cape Verde	2010–2011	Rectal swab	qPCR	146	2 (1.4)
Decaro et al. (2013)	Europe	2009–2011	Carcasses	RT-PCR	345	124 (35.0)
Di Martino et al. (2013)	Italy	2008–2011	Faecies	RT-PCR	256	35 (13.7)
Costa et al. (2014)	Brazil	2006–2012	Faecies	RT-PCR	250	30 (12.0)
Stavisky et al. (2010)	United Kingdom	cross-section	Faecies	RT-PCR	219	41 (18.7)
Cavalli et al. (2014)	Albania	2011–2013	Faecies	RT-PCR	57	31 (54.4)
Licitra et al. (2014a); Licitra et al. (2014b)	USA	2008–2013	Intestine	RT-PCR	11	9 (81.8)
van Nguyen et al. (2017)	Vietnam	2013–2015	Faecies	RT-PCR	80	7 (8.8)
Zobba et al. (2021)	Sardinia, Italy	2013–2014	Faecies	RT-PCR	39	11 (28.2)
Takano et al. (2016)	Japan	2011–2014	Rectal swab	RT-PCR	101	27 (26.7)
Gizzi et al. (2014)	Brazil, USA, Australia, Canada, United Kingdom	2014	Faecies	RT-PCR	147	15 (10.2)
Wang et al. (2016)	China	2014–2015	Faecies	RT-PCR	201	57 (28.4)
Li et al. (2016)	China	2014–2015	Faecies	RT-PCR	201	21 (10.4)
Navarro et al. (2017)	St. Kitts and Nevis, West Indies	2015–2016	Faecies	RT-PCR	104	5 (4.8)
Dowgier et al. (2017)	Italy	2013–2016	Faecies, rectal swabs	RT-PCR	286	55 (19.2)
Cardillo et al. (2020)	Italy	2015–2017	Carcasses	RT-PCR	138	43 (31.2)
Li et al. (2018)	China	2018	Faecies	RT-PCR	42	34 (81.0)
Santana-Clavijo et al. (2020)	Colombia	2014–2018	Faecies	RT-PCR	43	12 (27.9)
Awad et al. (2019)	Egypt	2016–2018	Faecies, blood	PCR and qRT-PCR	86	45 (52.3)
He et al., 2020	China	2018–2019	Faecies	RT-PCR	213	51 (23.9)
Sulehria et al. (2020)	Pakistan	2018–2019	Faecies	RT-PCR	450	107 (23.8)
Chen et al. (2021)	Taiwan	2015–2019	Rectal swab, blood	RT-Semi nested PCR	52	3 (5.8)
Alfano et al. (2020b)	Italy	2014–2019	Guts, internal organs	RT-PCR	352	76 (21.6)
Wang et al. (2020b)	Tangshan, China	2019	Faecies	RT-PCR	82	6 (7.3)
Wang et al. (2020a)	China	cross-section	Faecies, rectal swab	multiplex TaqMan RT-PCR	82	7 (8.5)
Rosa et al. (2020)	Portugal	1995–2011	Carcasses	RT-PCR	62	20 (32.3)
Radford et al. (2021)	United Kingdom	2020	Faecies, rectal swabs, vomit	RT-PCR	71	17 (23.9)
Hossain et al. (2021)	Bangladesh	2009–2016	Oropharyngeal and rectal swabs	RT-PCR	69	3 (4.3)

CeCoV-I possesses a divergent spike protein and the intact form of an additional gene, ORF3, whose remnants are present in CeCoV-II and, to a lesser extent, in TGEV. Therefore, CeCoV-II likely emerged following a recombination event between the original CeCoV-I and an unknown CoV at the S gene level and the progressive loss of ORF3 (Decaro and Lorusso, 2020; Lorusso et al., 2008; Pellegrini et al., 2022; Pratelli et al., 2021; Pratelli et al., 2003; Pratelli et al., 2022). Further recombination occurred in the 5′ end of the S gene between CeCoV-II and TGEV, giving rise to back recombinant CeCoV-II strains, also known as TGEV-like CCoVs, having a spike protein N-terminus of TGEV in a CeCoV-II backbone (Decaro et al., 2009; Decaro et al., 2010; Pellegrini et al., 2022; Pratelli et al., 2021; Pratelli et al., 2022). Consequently, the CeCoV taxonomy was revised, with classical and TGEV-like strains being referred to as CeCoV-IIa and CeCoV-IIb, respectively (Decaro and Lorusso, 2020; Smith et al., 2022).

While CeCoVs are usually involved in mild forms of diarrhea, there are some hypervirulent CeCoV-IIa strains, designated pantropic CeCoV, that are associated with severe, hemorrhagic, sometimes fatal gastroenteritis (Decaro and Lorusso, 2020). Pantropic CeCoV strains, have been reported in Italy (Alfano et al., 2020a; Buonavoglia et al., 2006), in other European countries (Decaro et al., 2013) and in South America (Pinto et al., 2014).

Recombination or mutation events of S the gene can result in the ability to spread between species, as observed in some *Betacoronaviruses (*Forni et al., 2020*)*, such as severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003 (Bolles et al., 2011), Middle Est respiratory coronavirus (MERS-CoV) in 2014 (Azhar et al., 2014), and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which may have originated from horseshoe bats and have infected so far >100 million people worldwide (Singh and Yi, 2021; Zhou et al., 2020).

Domestic carnivores, i.e. dogs (*Canis lupus familiaris*) and cats (*felis catus*), are considered the most popular pets worldwide (Weber et al., 2018; Zhang et al., 2014). They share their habitat with humans, increasing the potential risk of transmission of zoonotic pathogens (De Grazia et al., 2007; Lackay et al., 2008; Matthijnssens et al., 2011; Tsugawa and Hoshino, 2008; Wu et al., 2012). Furthermore, some viruses that infect these animal species are genetically closely related to human viruses, such as feline astrovirus (FeAstV), strain 1637F (Lau et al., 2013), and *Felis domesticus* papillomavirus type 1 (FdPV-1) (Tachezy et al., 2002). SARS-COV-2 has swept the globe, causing high prevalence. Although dogs have not been reported as a source of infection, studies have shown that dogs can be infected with this virus (Barroso-Arevalo et al., 2022; Barroso-Arevalo et al., 2021; Shi et al., 2020; Sit et al., 2020). More recently a novel canine-feline recombinant alphacoronavirus, CCoV-HuPn-2018, was isolated from child patients with pneumonia (Vlasova et al., 2022). The ability of CeCoVs to evolve raises several questions on the biology of these viruses, focusing important epidemiological outcomes in the field, both regarding virus evolution and prophylaxis (Pratelli et al., 2022).

Viral surveillance in wild and domestic animals, such as dogs and cats that are in close contact with humans, through the combined use of well-described conventional and molecular methods, could be a crucial

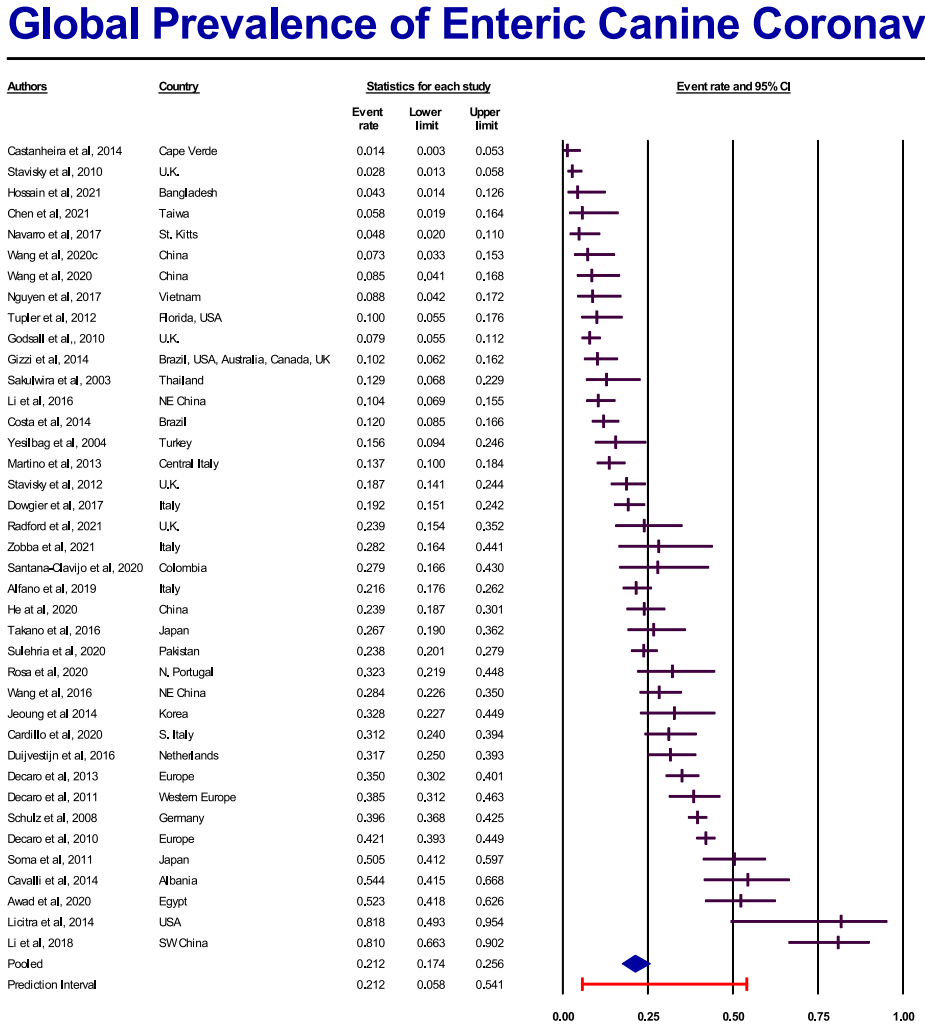

Fig. 2. Meta-analysis for the pooled effect size (prevalence) of canine enteric coronavirus among the selected studies.

A

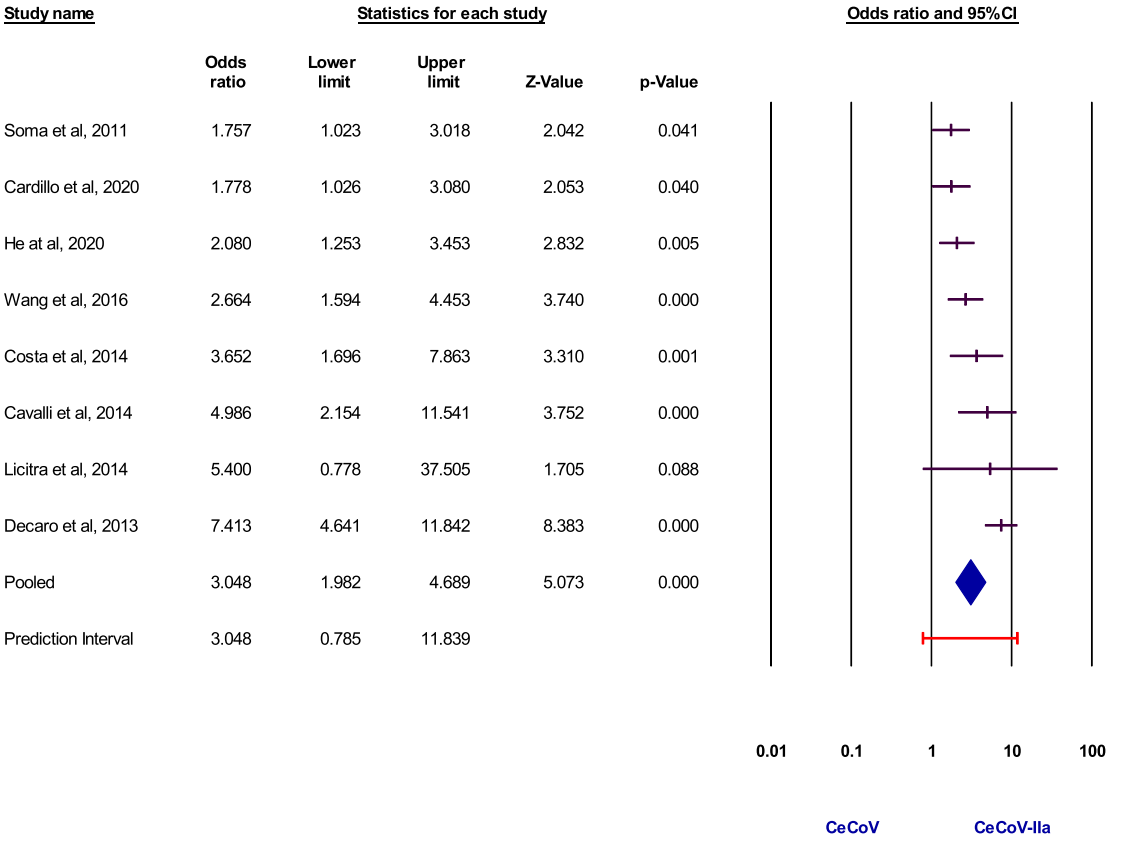

Fig. 3. (A, B, C, and D): Assessment of exposure risk to canine enteric coronavirus and the prevalence of the various types and subtypes.

B

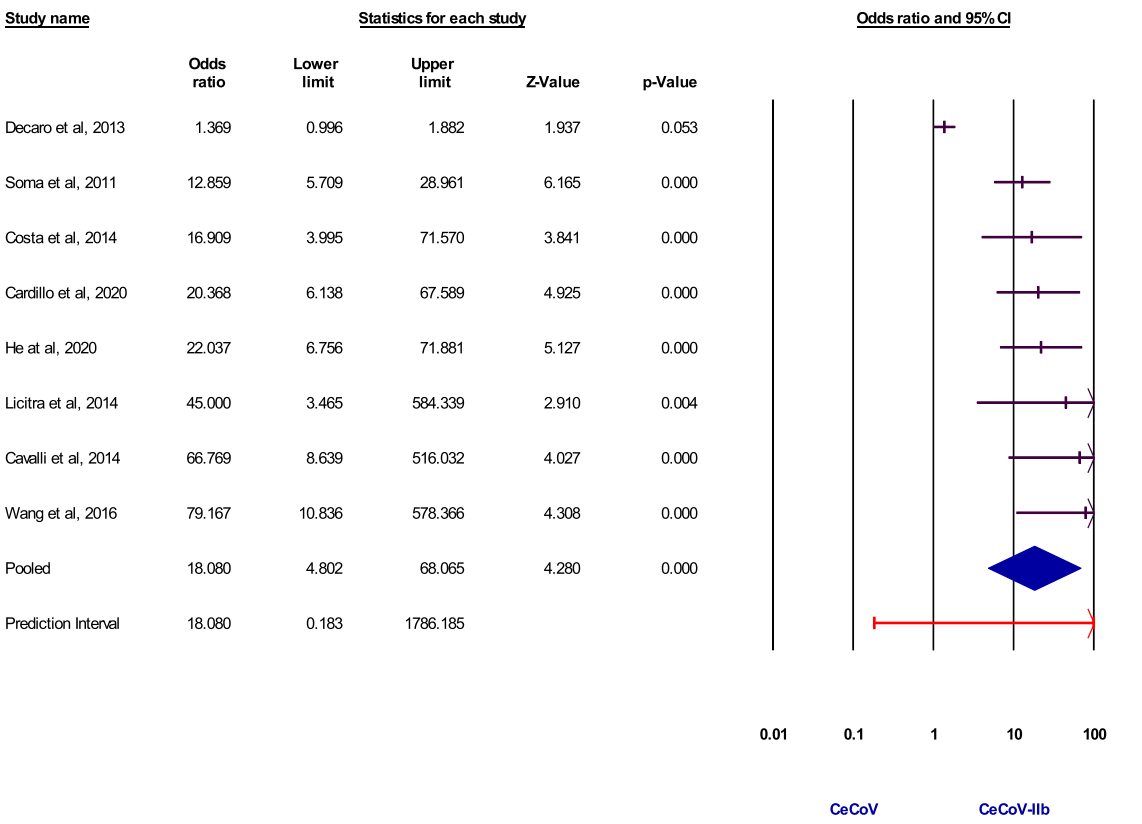

Fig. 3. (*continued*).

C

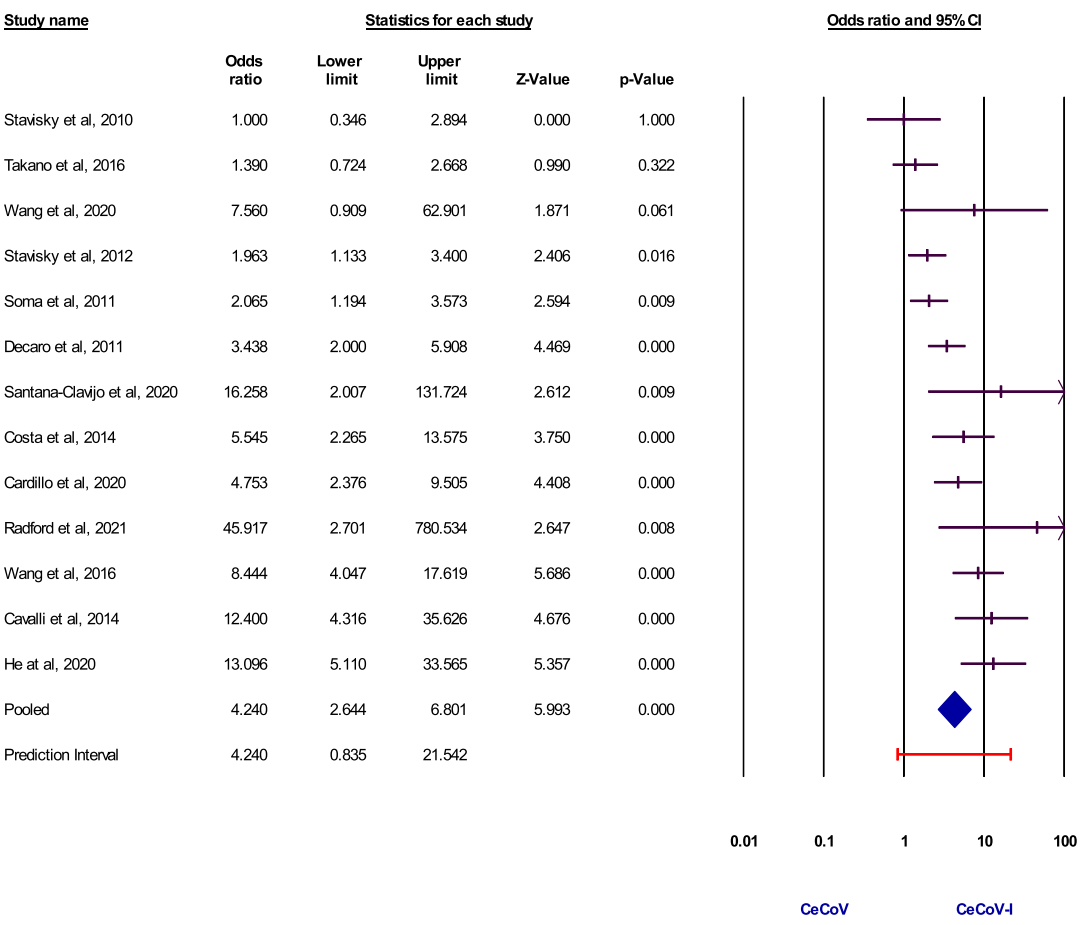

Fig. 3. (*continued*).

D **Odds ratio of CeCoV exposure risk and presence of CeCoV-II**

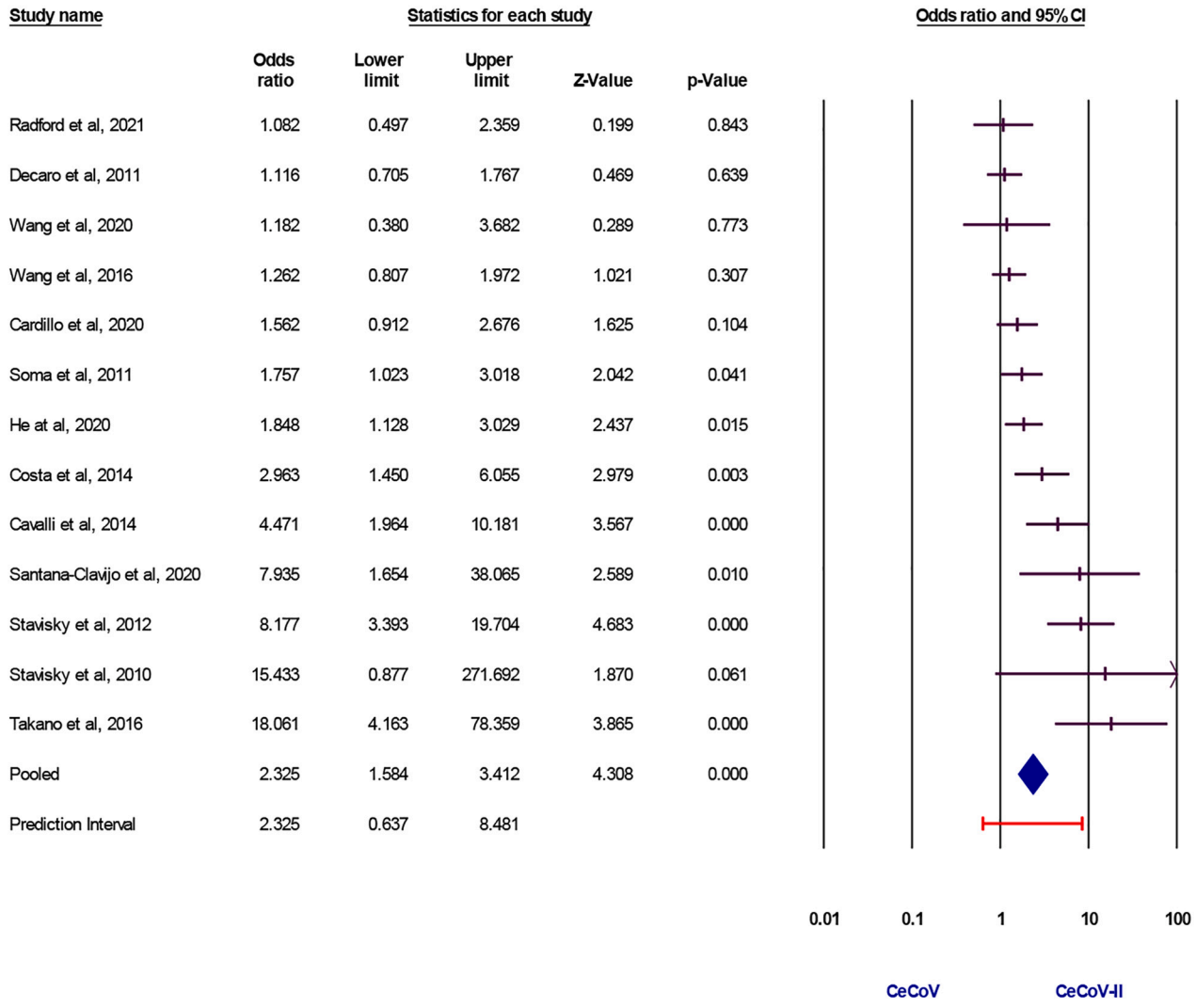

Fig. 3. (*continued*).

tool to promptly monitor and characterize emerging and re-emerging zoonotic viruses, providing a baseline of the virus diversity and circulation, useful for dealing with future infectious emergencies.

This systematic review and meta-analysis study was conducted to determine the global distribution of different CeCoV types as well as their occurrence with respect to demographics (sex, breed, ownership), and clinical signs (diarrhea). The risk of exposure to classical CeCoV-IIa and TGEV-like CeCoV-IIb was also assessed and the research questions were formulated using the PICO format for observational case-control studies. Most cases of CeCoV infection result in mild forms of enteritis associated with diarrhea, which are often self-limiting. However, in some cases, particularly in puppies or dogs with weakened immune systems, the infection can result in more serious clinical conditions, occasionally with multi-systemic spread and fatal outcome, always confirmed in the laboratory by molecular techniques (i.e. Polymerase Chain Reaction-PCR and his applications).

2. Materials and methods

2.1. Study selection

A comprehensive search of relevant literature was conducted, and studies were retrieved from three electronic databases: SCOPUS (https://www.scopus.com/), PubMed (https://pubmed.ncbi.nlm.nih.gov/), and Web of Science (https://apps.webofknowledge.com/) between May and October 2022 (last accessed in March 2023). The search strategy included the MeSH (Medical Subject Headings) using the following string: “canine coronavirus” OR “canine enteric coronavirus” AND “prevalence” OR “global distribution”. Initially, articles screening involved independent assessment of titles and abstracts to exclude irrelevant studies and full text articles were subsequently retrieved and assessed based on predefined inclusion and exclusion criteria. In cases of disagreement, consensus was reached through discussion among authors. The risk of bias for all enrolled studies was assessed using the “Newcastle-Ottawa Quality Assessment Scale for Case-Control Studies”. The effect size index calculated for included publications was the odds ratio in the random-effects model.

2.2. Inclusion and exclusion criteria

The criteria for inclusion in this systematic review were studies published in English, and in which CeCoV was identified and confirmed with molecular investigations. Studies were screened for accuracy of variable estimates of interest before final inclusion for meta-analysis.

In contrast, brief reports, letters to Editors, non-English studies, and research primarily focused on respiratory rather than CeCoV were excluded. Studies that used only serology or other non-confirmatory results to detect CeCoVs, were also discarded. Investigations with the same sampling group used in more than one publication, and studies in which the data necessary for meta-analysis were missing were also discarded.

2.3. Research question

The PICO (population, intervention, comparison, and outcome) format was used to formulate the research question. The population was represented by global laboratory-confirmed cases of CeCoV; no intervention was carried out as only observational studies were found; the comparison was for CeCoV-infected dogs with respect to demographics, CeCoV genotypes and subtypes, and coinfection status, while the outcome was the presence or absence of CeCoV. Hence the formulated PICO question was to investigate the determinants of the global distribution of CeCoV and the exposure risk among dogs infected with different CeCoV genotypes and subtypes.

2.4. Effect size

The effect size index computed for included studies was the odds ratio under the random-effects model. The random-effects model is robust to both sampling variability and true heterogeneity in effects sizes across all studies and hence incorporates adjustments for both within-study variability (sampling error) and between study variability (heterogeneity). Therefore, the results of the meta-analysis under this model selection are generalizable to a universe of potential studies. The Q-statistic provided a test of the null hypothesis that all studies in the analysis shared a common effect size, and where all studies shared the same true effect size, the expected value of Q was equal to the degrees of freedom (the number of studies minus 1). The tau-squared (τ^2) and tau (τ) estimated the variance and standard deviation of the true effect sizes respectively in log units. The prediction interval was computed based on the random effect model taking as parameters the pooled effect size, the 95% upper confidence limit, and tau squared. The interval obtained represented the range of values within which we expected future observations to fall with 95% confidence.

2.5. Moderator analysis

The potential risk of exposure of dogs to CeCoV were investigated

A

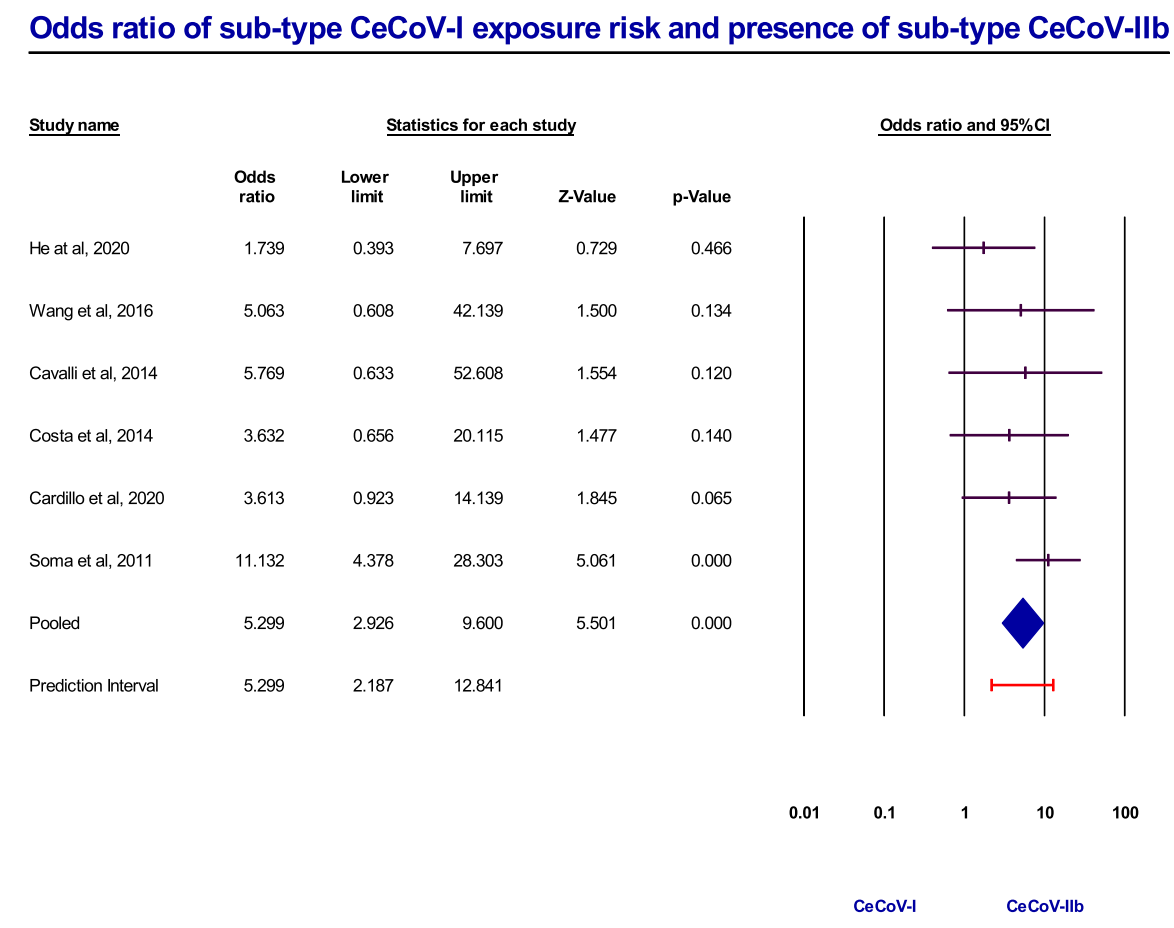

Fig. 4. (A and B): Assessment of exposure risk to canine enteric coronavirus (CeCoV) type I in comparison to the CeCoV-II subtypes.

B

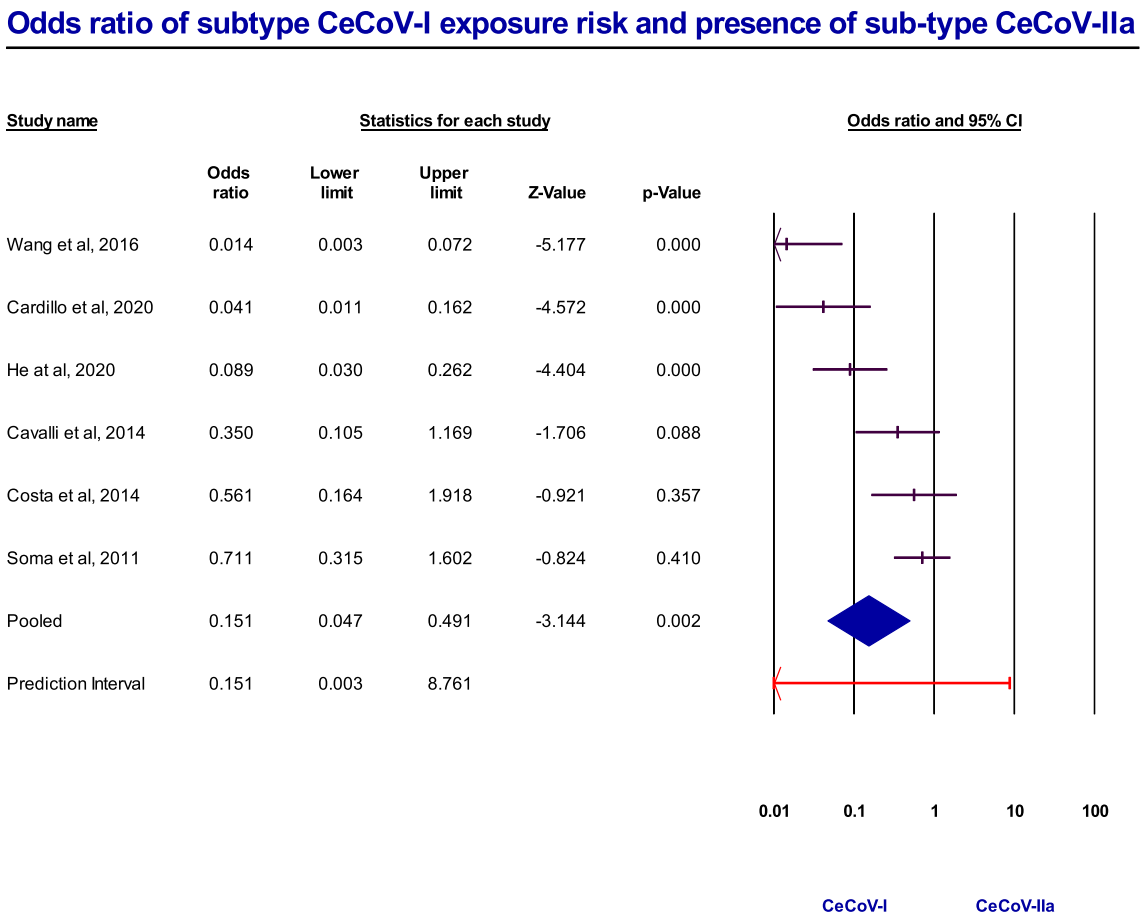

Fig. 4. (*continued*).

using subgroup analyses (sex, presence or absence of clinical signs, and circulation of CeCoV types and subtypes). Only a subset of all included studies which provided sufficient details on variables for specific subgroup analysis were further analyzed.

2.6. Limitation

In general, estimates of heterogeneity based on fewer than ten studies have less power and are less likely to be reliable. In addition, no randomized clinical studies were found which impacted on the risk of bias assessment. Where no data on moderators were available, meta-regression analysis could not be performed to account for cases where high heterogeneity was observed. However, where high heterogeneity was observed, the One-study-removed analysis was computed to identify studies shown to significantly influence the estimated odds ratio.

3. Results

3.1. Included studies

The summary of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram, shown in Fig. 1, describes the study selection process. Following initial search on SCOPUS, PubMed, and Web of Science, a total of 276 records were obtained, and among these, 43 studies were included for meta-analysis. (See Table 1.)

3.2. The pooled effect size of all studies

The analysis of pooled effect size was based on 39 studies and the effect size index were the prevalence or event rate (Fig. 2). The pooled effect size was 0.212 with a 95% confidence interval of 0.174 to 0.256%, and no individual study received a relative weight >2.99. The Q-value was 675.451 with 38 degrees of freedom and $p < 0.001$ while the I^2 statistic was 94.374 with the calculated variance of effect size (τ^2) as 0.518. The estimated prediction range was 0.058 to 0.541, meaning that the true effect size in 95% of all comparable populations fell within this interval.

Distribution of CeCoV across the continents (Supplementary Fig. 1) showed that the highest prevalence occurred in Europe (prevalence = 24.4%, lower limit = 19.2%, upper limit = 30.6%) while the least was reported in Africa (prevalence = 11.5%, lower limit = 0.2%, upper limit = 90.4%). The wide variability in prevalence recorded in Africa indicated a lower prediction accuracy as seen in the calculated prediction intervals. When assessing the distribution of CeCoV across the continents (Supplementary Fig. 1), the tau-squared was computed based on the assumption that there was no common variance component across study using the fixed effects model, and hence the tau-squared estimates within group were not pooled. The estimated prevalence with the prevalence interval (PI) was highest for Europe (prevalence = 24.4%%, PI = 19.2–30.6) than Africa (prevalence = 7.5%, PI = 0.2–90.4), Asia (prevalence = 19.8%, PI = 13.7–27.8), North America (prevalence = 20.6%, 95% = 3.5–64.8) and South America (prevalence = 18.1%, PI = 7.4–38.0).

A

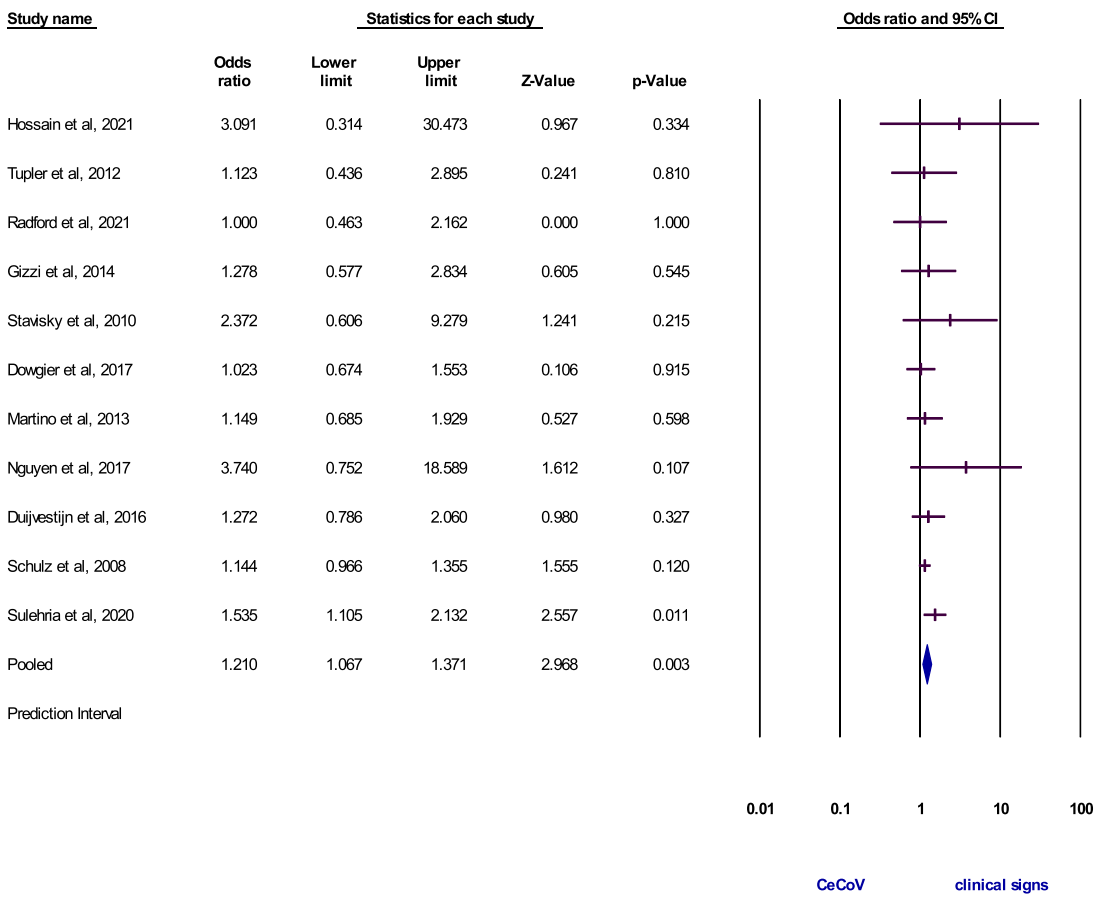

Fig. 5. (A and B): Assessment of exposure risk to canine enteric coronavirus (CeCoV) in comparison to presence or absence of clinical signs in infected dogs.

B

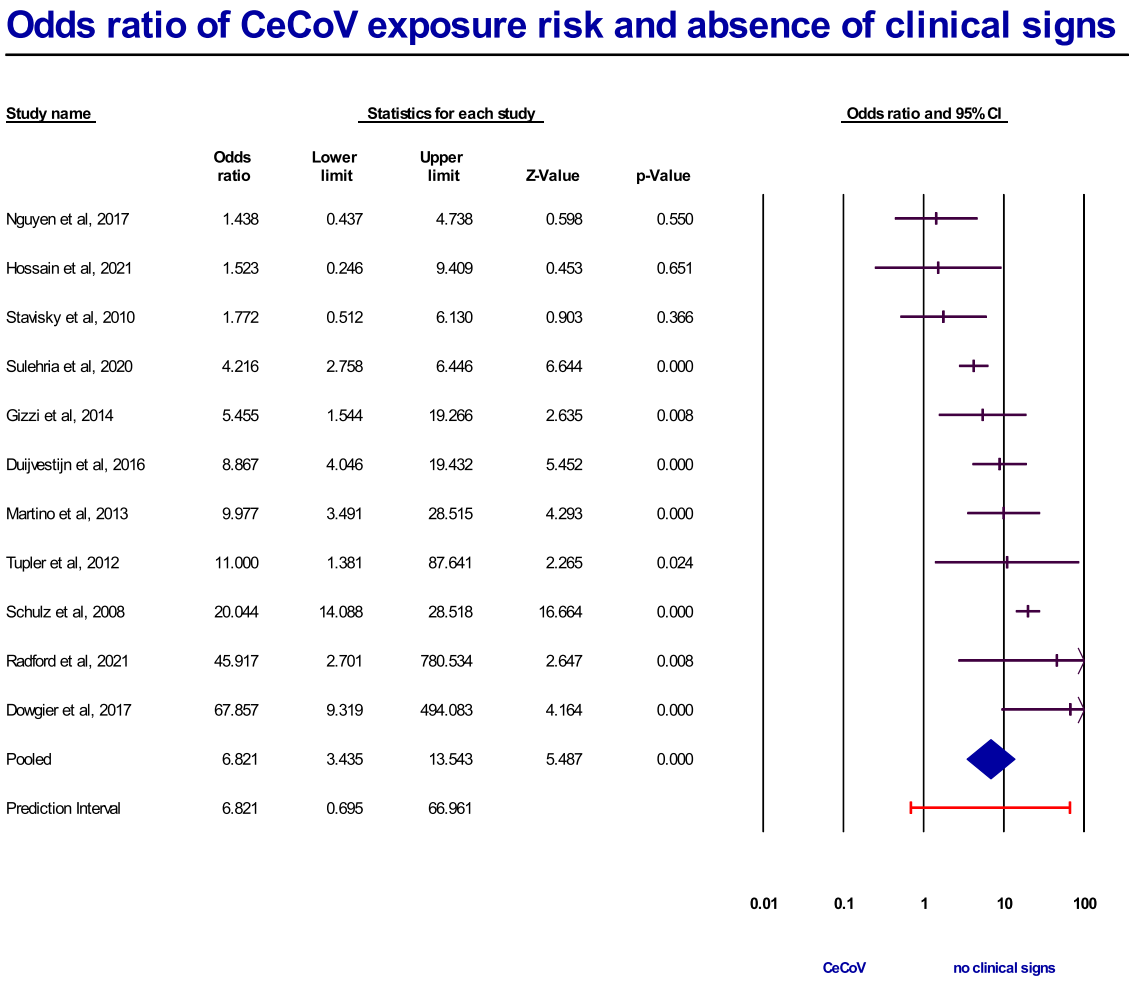

Fig. 5. (*continued*).

3.3. Subtypes disparity

Compared to the general prevalence of CeCoV among infected dogs, the mean effect size for CeCoV-I, CeCoV-II, CeCoV-IIa, and CeCoV-IIb were 4.240 (95% CI = 2.644 to 6.801, z = 5.993, $P < 0.0001$), 2.325 (95% CI = 1.584 to 3.412, z = 4.308, $P < 0.0001$), 3.048 (95% CI = 1.982 to 4.698, z = 5.073, $P < 0.0001$), and 18.08 (95% CI = 4.802 to 68.068, z = 4.280, $P < 0.0001$) respectively. (Fig. 3 A, B, C and D). The estimate for the Q statistics, degree of freedom and corresponding *P*-value for this and other comparisons is summarized in the supplementary table (Supplementary Table 1).

In contrast, as shown in Fig. 4 A and B, the analysis assessing the risk of exposure across subtypes revealed that dogs were more likely to be CeCoV-IIb positive with an estimated odds ratio of 5.299 with intervals range of 2.926 to 9.60 at 95% confidence (z = 5.501, $p < 0.001$) in comparison to CeCoV-I exposure risk. The Q statistics obtained was 5.083 with 5 degrees of freedom and an I^2-value of 1.625 ($\tau^2 = 0.01$, $P \leq 0.0001$). In the universe of comparable studies, the prediction interval fell between 2.187 and 12.841. In contrast, there was a lower probability of infection with CeCoV-IIa than with CeCoV-I (odds ratio = 0.151, 95% CI = 0.047 to 0.0491, z = −3.144, $P = 0.055$). In addition, significantly higher heterogeneity was observed (Q = 30.308, df = 5, $p < 0.0001$, $I^2 = 83.503$, $\tau^2 = 1.776$), with a prediction interval of 0.003 to 8.761, in 95% of all comparable populations.

3.3.1. Clinical presentation

Infected dogs were more likely to show no clinical signs (odds ratio = 3.835, 95% CI = 2.566- 5.731, z = 6.556, P ≤0.0001) (Fig. 5 A and B). Likewise, low heterogeneity was observed with a Q statistic of 15.505 with 10 degrees of freedom, I^2 of 35.506. The prediction interval in 95% of all comparable populations was 1.509 to 9.743. However, a higher odds ratio (6.821, $P < 0.0001$) was found among dogs not showing any clinical signs prior to CeCoV diagnoses in contrast with those showing clinical illness prior to laboratory confirmation (odds ratio = 3.293, P < 0.0001) (Supplementary Table 1).

3.3.2. Auto-coinfection and multiple infections

As indicated in Fig. 6 A and B, there were three times the odds to develop a state of autoinfection compared to exposure risk with CeCoV (odds ratio = 3.293, 95% CI = 2.124–5.106, Z = 5.325, and P ≤0.0001). A significantly high heterogeneity was observed among the included studies (Q = 67.284, df = 12, p < 0.001, $I^2 = 82.165$, and $\tau = 0.656$). The true effect size in 95% of all comparable populations fell in the range of 0.716 to 15.139. Similarly, dogs in the population at risk of CeCoV exposure, were 2.625 times more likely to have multiple undiagnosed viral infections (95% CI = 1.355–5.087, Z = 2.860, $P = 0.004$). High heterogeneity was demonstrated by a Q-value of 138.475 with 12 degrees of freedom (P < 0.0001) and an I^2 of 91.334 having a variance of 1.147. The prediction interval was found to be 0.189 to 36.459.

A

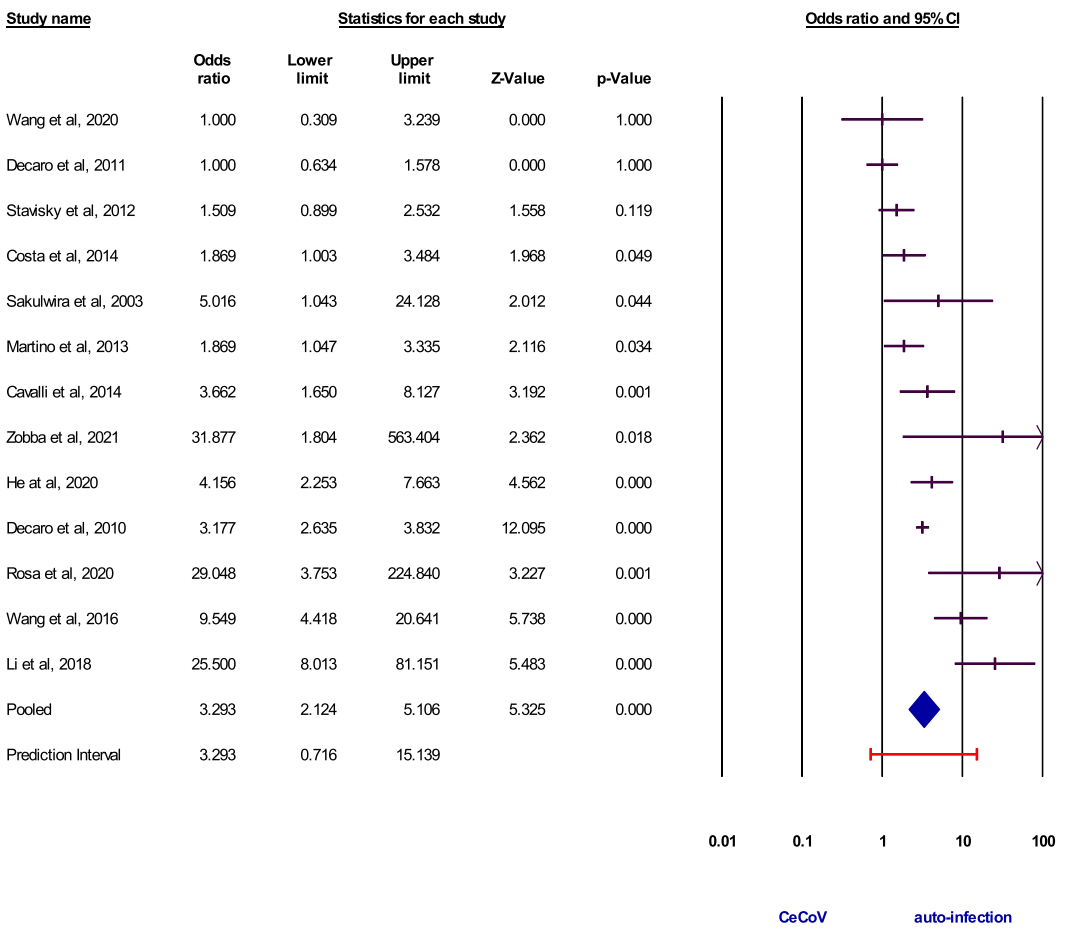

Fig. 6. (A and B): Assessment of exposure risk to canine enteric coronavirus (CeCoV) in comparison to auto-coinfection or multiply infection in infected dogs.

B

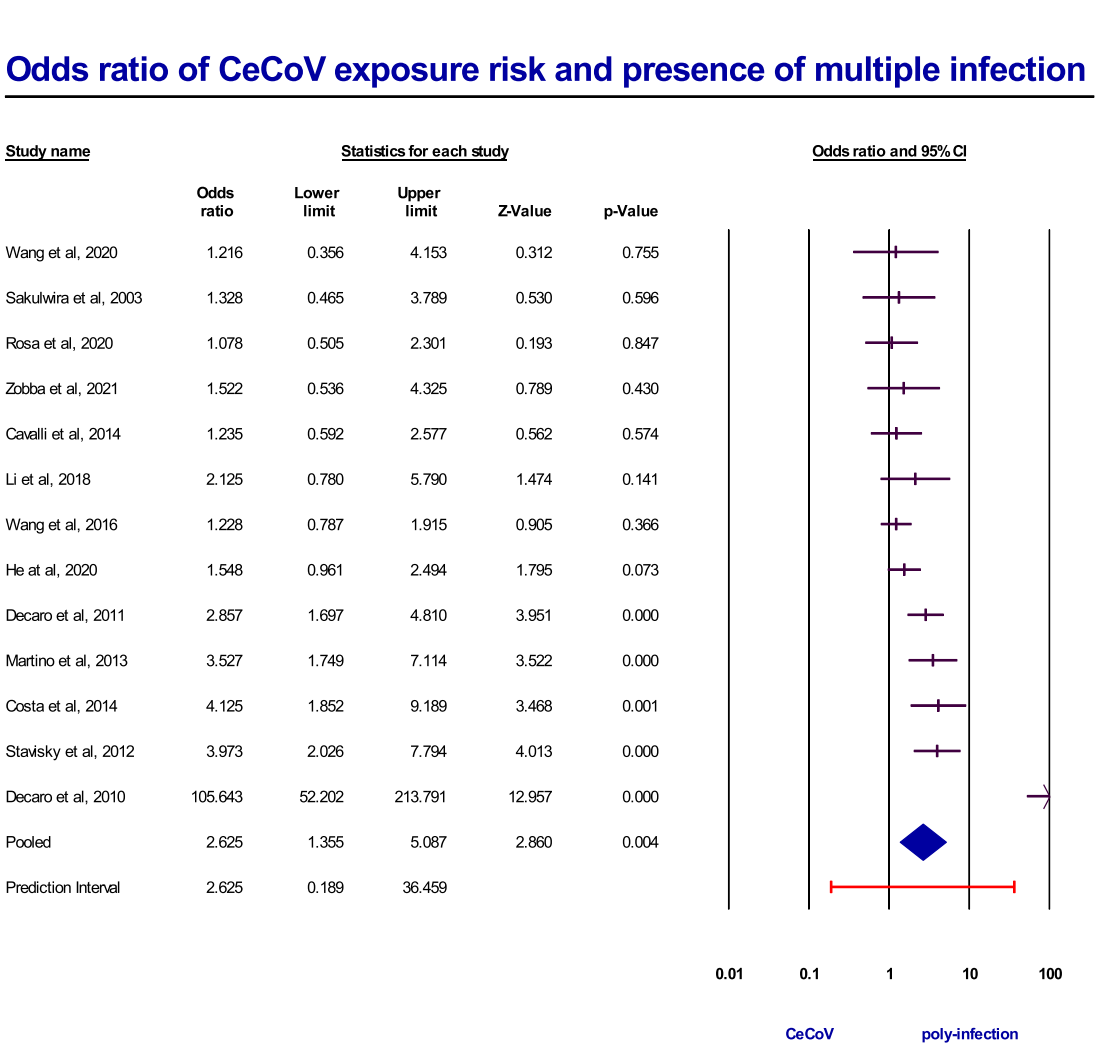

Fig. 6. (*continued*).

3.3.3. *Other moderator variables*

Figure 7 A, B and C revealed that probabilities obtained for other variables of sex, virus subtypes, and clinical signs.

Among CeCoV-infected dogs, the odds of infection in males were 1.328 higher than infection in females (95% CI = 0.797–2.212, z = 1.087 and $P = 0.277$). However, both males and females had approximately equal odds of being infected with CeCoV in undiagnosed dog populations.

4. Discussion

The global prevalence of CeCoV was remarkably variable, with an overall prevalence of 21.2% and a wide prediction interval ranging from 17.4% to 25.6%, thus indicating that CeCoV prevalence varies significantly across regions and across dog populations.

Other studies support this variability in the prevalence rate of CeCoV in the global dog population. An investigation conducted in the United Kingdom in 2010 (Stavisky et al., 2010) on 249 dogs visited in veterinary practices found a prevalence (2.8%) slightly lower than expected for Europe (3.9% to 58%). On the other hand, a systematic review conducted on CeCoV prevalence in mainland China (Dong et al., 2022) revealed a much higher prevalence of CeCoV (33%), falling within the expected prevalence range for Asia (6.4% to 54.6%).

The results of this investigation showed that the observed regional differences are predictable and can be attributed to the ability to detect infected dogs in the absence of obvious symptoms. CeCoV infection is known to manifest in several ways, from asymptomatic to severe disease being influenced by host-dependent factors such as breed, age, and immune status (Haake et al., 2020).

Furthermore, the study results are particularly noteworthy, as they indicate that the prevalence of CeCoV infection may be much higher than previously thought (Dong et al., 2022; Stavisky et al., 2010).

The meta-analysis demonstrated that infected dogs were twice as likely to be asymptomatic, suggesting that many cases of CeCoV infection may go undetected. This has implications for disease management and control, as undiagnosed cases can lead to the persistence and circulation of the virus, making it more difficult to control and prevent spread. Therefore, it is crucial to consider these factors when investigating and interpreting regional differences in canine infection rates. The study also suggests that traditional diagnostic methods, such as veterinary clinic investigations, may not be sufficient to accurately assess the prevalence of the disease. Hence, it is essential to employ reliable diagnostic tools and protocols to accurately detect asymptomatic carriers. Overall, more accurate and comprehensive studies of both the epidemiology of CeCoV infections and the role played by asymptomatic dogs in the spread of the infection are needed to define effective prevention and control measures.

In addition, the study provides important insights on the prevalence and distribution of CeCoV genotypes and subtypes globally. The results revealed that CeCoV -IIb was the most commonly circulating genotype

A

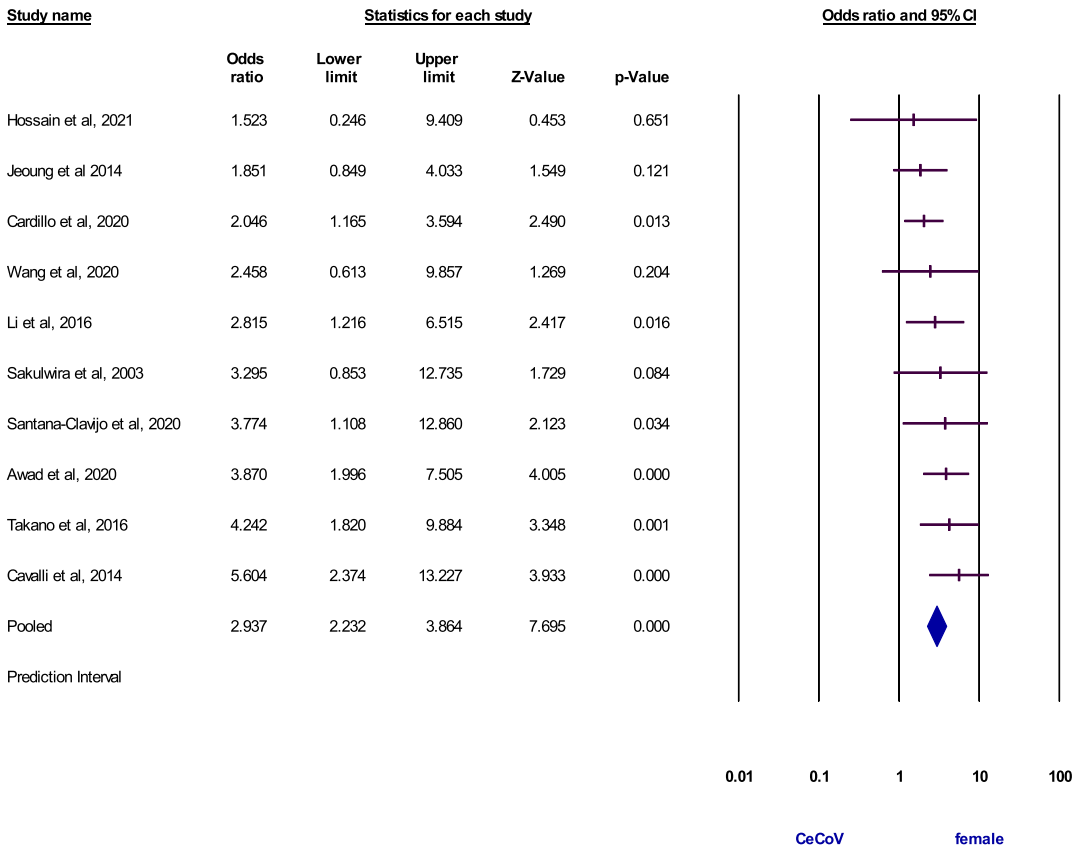

Fig. 7. (A, B and C): Meta-analysis of disparities in exposure risks to canine enteric coronavirus with respect to sex.

B

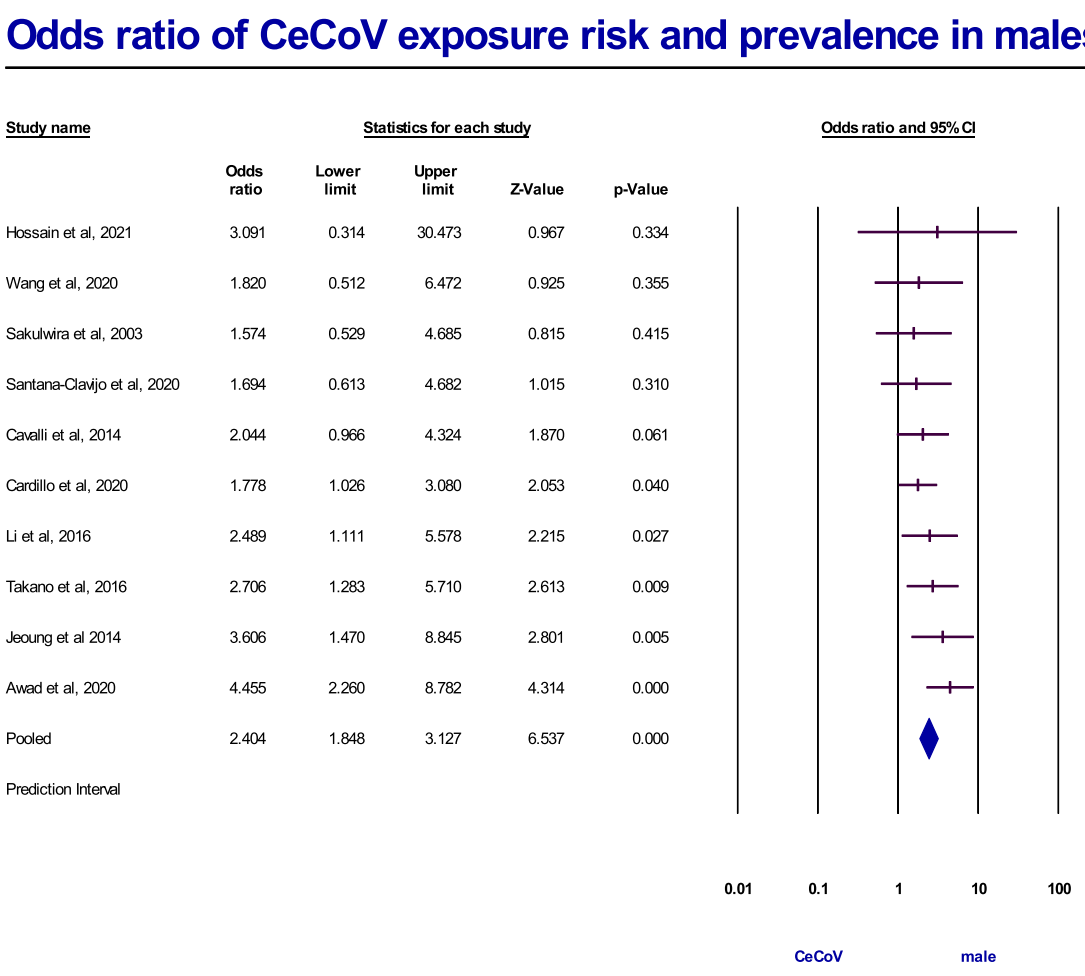

Fig. 7. (*continued*).

C

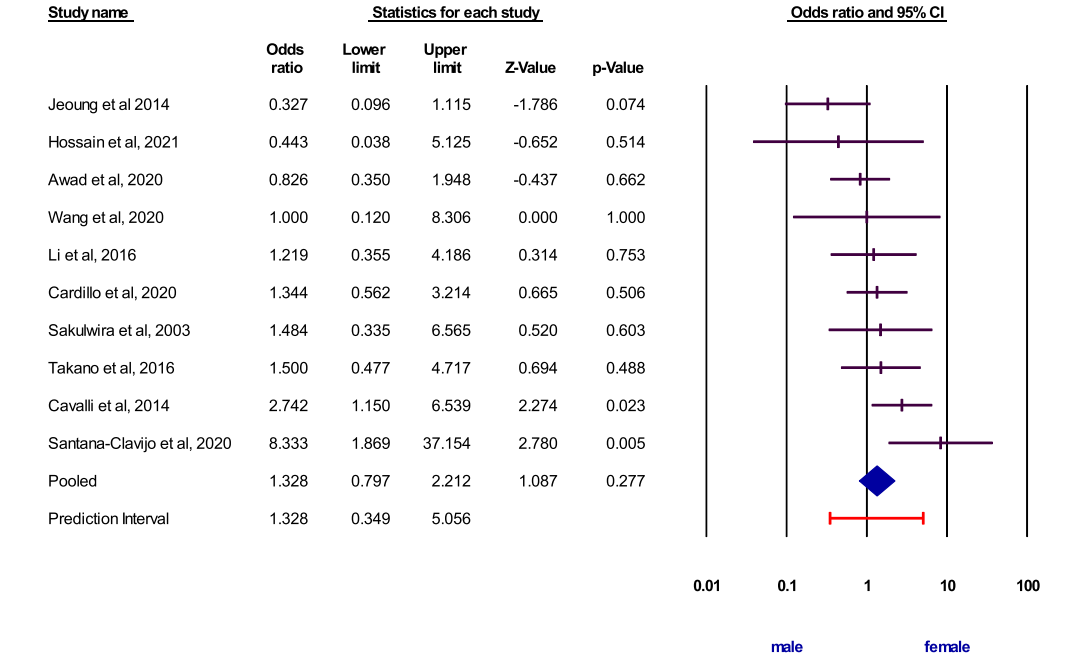

Fig. 7. (*continued*).

among dogs with an odds ratio of approximately 5, which is significantly higher than that of CeCoV-I, with an odds ratio of about 1. Although Dong et al. (2022) supported the conclusion that CeCoV-II was likely the predominant CeCoV subtype in Chinese dogs, our investigation identified the specific subtypes implicated in the global occurrence of the disease. Furthermore, the current study indicated a higher probability of coinfection with two CeCoV genotypes in the same host compared to coinfection with other virus species (i.e. parvovirus, astrovirus and kobuvirus). However, there remains a lack of information on randomized clinical studies that will be necessary for a more accurate determination of moderators which significantly influence the prevalence and distribution of the various CeCoV genotypes and subtypes.

In conclusion, this investigation highlights the need for continuous monitoring of CeCoVs considering regional differences in assessing its prevalence. These findings have implications for improving dogs' health and guiding CeCoV control and preventive strategies.

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CRediT authorship contribution statement

Amienwanlen Eugene Odigie: Writing – original draft, Investigation, Formal analysis, Data curation. **Paolo Capozza:** Writing – review & editing, Writing – original draft, Software, Resources, Methodology, Investigation, Funding acquisition, Formal analysis. **Maria Tempesta:** Writing – review & editing, Supervision, Conceptualization. **Nicola Decaro:** Writing – review & editing, Validation, Supervision, Conceptualization. **Annamaria Pratelli:** Writing – review & editing, Visualization, Validation, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that there is no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rvsc.2024.105289.

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