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SARS-CoV-2 in domestic and big cats: a narrative review

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Abbreviations

DPI	Days post infection
ELISA	Enzyme-linked immunosorbent assay
MIA	Multiplex microsphere immunoassay
MNT	Microneutralization test
PCR	Polymerase chain reaction
PRNT	Plaque reduction neutralization tests
RBD	Receptor-binding-domain
RNA	Ribonucleic acid
SARS-CoV-2	Severe acute respiratory syndrome – Coronavirus - 2
TMPRSS2	Transmembrane serine protease 2
(s)VNT	(Surrogate) Virus neutralization test
VOC	Variant of concern

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly transmissible zoonotic pathogen mostly affecting humans but that was also detected in domestic and big cats. The close interaction between humans and domestic cats has sparked scientific interest due to its potential for transmission, resulting in numerous scientific studies. Additionally, there have been reports of infections occurring in captive wild feline individuals, further highlighting the importance of investigating the host capacity, clinical aspects, and transmission potential of SARS-CoV-2 in cats. The objective of this review was to present a comprehensive overview of the characteristics and patterns of both experimental and naturally occurring SARS-CoV-2 infections in domestic cats and (wild and captive) big cats. A literature search, primarily using the PubMed search engine, was conducted between 23/03/2022 and 04/05/2023. The publications were screened according to defined inclusion/exclusion criteria. Selected publications were then organised and labelled with keywords related to the main topic they covered via the reference manager Mendeley. Ultimately, 116 peer-reviewed articles were included in the review. This review addresses the current knowledge about infection sources, transmission routes, risk factors for infection, clinical manifestations in infected cats, and immunity. The risk of interspecies transmission is also considered. Furthermore, I provide a global overview of the results of (sero)prevalence studies and cover the viral and serological laboratory methods used to detect infections with SARS-CoV-2 in cats. Notably, this work presents a list of SARS-CoV-2 variants detected in both domestic and big cats and outlines the incubation periods and duration of infection in these species. This review identified research and data gap regarding SARS-CoV-2 infection in cats, in particular, the need for comparable studies. This calls for more research in obtaining standardised data on a global scale, which is one of the key elements to evaluate the risk SARS-CoV-2 poses to domestic and big cats as well as the spillover risk at human-cat interfaces.

Zusammenfassung

Das Schwere-akute-respiratorische-Atemwegssyndrom-Coronavirus Typ 2 (SARS-CoV-2) ist ein hochgradig übertragbarer, zoonotischer Krankheitserreger, der vor allem Menschen befällt, aber auch bei Haus- und Großkatzen nachgewiesen wurde. Der enge Kontakt zwischen Menschen und Katzen hat aufgrund des Übertragungspotenzials wissenschaftliches Interesse geweckt und zu zahlreichen wissenschaftlichen Studien geführt. Darüber hinaus gibt es Berichte über Infektionen bei in Gefangenschaft lebenden Wildkatzen, wodurch die Bedeutung der Untersuchung der Wirtskapazität, der klinischen Aspekte und des Übertragungspotenzials von SARS-CoV-2 bei Katzen noch deutlicher wird. Ziel dieser Übersichtsarbeit war es, einen umfassenden Überblick über die Merkmale und Muster sowohl experimenteller als auch natürlich auftretender SARS-CoV-2-Infektionen bei Hauskatzen und (wildlebenden und in Gefangenschaft lebenden) Großkatzen zu geben. Zwischen dem 23/03/2022 und 04/05/2023 wurde eine Literaturrecherche, hauptsächlich mit der Suchmaschine PubMed, durchgeführt. Die Publikationen wurden nach definierten Ein- und Ausschlusskriterien gefiltert. Ausgewählte Publikationen wurden dann mit Hilfe des Referenzmanagers Mendeley organisiert und mit Schlüsselwörtern zum Hauptthema, das sie behandeln, versehen. Letztendlich wurden 116 peer-reviewed Artikel in die Untersuchung einbezogen. Die Arbeit befasst sich mit dem aktuellen Wissensstand über die Übertragungsquellen, die Infektionswege, die Risikofaktoren für eine Infektion, die klinischen Symptome bei infizierten Katzen und die Immunität. Zudem wird auch das Risiko einer Übertragung von der Katze auf den Menschen berücksichtigt und ein globaler Überblick über die Ergebnisse von (Sero-)Prävalenzstudien gegeben sowie auf die viralen und serologischen Labormethoden, die zum Nachweis einer Infektion mit SARS-CoV-2 bei Katzen verwendet werden, eingegangen. Insbesondere enthält diese Arbeit eine Liste von SARS-CoV-2-Varianten, die sowohl bei Haus- als auch bei Großkatzen nachgewiesen wurden und gibt einen Überblick über die Inkubationszeiten und die Dauer der Infektion bei diesen Arten. Bei dieser Überprüfung wurden Forschungs- und Datenlücken in Bezug auf SARS-CoV-2-Infektionen bei Katzen festgestellt, insbesondere der Bedarf an vergleichbaren Studien. Dies erfordert weitere Forschungsarbeiten zur Beschaffung standardisierter Daten auf globaler Ebene, die eines der Schlüsselelemente zur Bewertung des Risikos von SARS-CoV-2 für Haus- und Großkatzen sowie des Spillover-Risikos an den Schnittstellen zwischen Menschen und Katzen darstellen.

1. Introduction

The severe acute respiratory syndrome coronavirus 1 (SARS-CoV), the first known zoonotic-origin coronavirus with pandemic potential, emerged in late 2002 in China, and resulted in 8,096 reported cases including 774 deaths across 29 countries (1,2). A laboratory study showed that cats (*Felis catus*) (3) and ferrets (*Mustela putorius furo)* (3) were susceptible to experimental infections with SARS-CoV and both species can efficiently transmit the virus to co-housed healthy cats. The study reported that cats could shed the virus for more than 10 days while virus-neutralising antibodies could be retrieved by day 28 after infection (4).

In 2012, the Middle East respiratory syndrome (MERS) a new zoonotic viral respiratory disease caused by a coronavirus (MERS-CoV) emerged in Saudi Arabia (5). Outbreaks in humans are still regularly reported, with the last human case reported from Saudi Arabia on 09/11/2022 (6). To date, 2,603 confirmed cases have been reported to the World Health Organization (WHO) worldwide, including 935 associated deaths (7). The virus is endemic in dromedary camel populations of East Africa and the Middle East, which serve as viral reservoir and from which zoonotic spillover events (i. e., animal-to-human transmissions) occur (8,9).

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in December 2019 in Wuhan, Hubei province, China, as a pneumonia of unknown origin in humans (10). The origin of SARS-CoV-2 has sparked considerable debates and, despite the presence of related viruses in bats (11), the specific intermediate animal host responsible for the transmission to humans remains unknown (12). The Wuhan Huanan Seafood Wholesale Market in China is thought to be the source of the outbreak because investigations into the early cases revealed an epidemiological association between the market and the first individuals who tested positive for SARS-CoV-2 (13,14). After the disease rapidly spread worldwide, the WHO declared the COVID-19 a global pandemic on 11 March 2020 (15). As of 17 February 2023, 756,581,850 confirmed cases of COVID-19, including 6,844,267 deaths, have been reported to the WHO worldwide (16).

SARS-CoV, MERS-CoV, and SARS-CoV-2 belong to the genus Betacoronavirus, family Coronaviridae, and subfamily Coronavirinae. Coronaviruses are enveloped viruses with a single-stranded positive-sense ribonucleic acid (RNA) of roughly 30 kilobases (kb). Therefore, coronaviruses present one of the largest known RNA genomes among all RNA viruses. The genome encodes for four main structural proteins including a nucleocapsid protein (N), a membrane protein (M), an envelope protein (E), and a surface spike protein (S) that helps in attachment of the virus to the host cells´ ACE-2 receptors (17,18).

After the first report of natural SARS-CoV-2 infection in a cat by the media in the early phase of the pandemic (19), the susceptibility of cats to SARS-CoV-2 received more scientific and media attention (20). Early in 2020, the first positive case in a cat, living in a household with a positive owner in Hong Kong, was confirmed. The seven-year-old, female, domestic shorthair cat was reported clinically healthy but viral RNA was detected in oral and nasal swab specimens while neutralising antibodies against SARS-CoV-2 were also evidenced. The viral genomes retrieved from the cat and its owner were identical, confirming human-to-cat transmission (19).

Worldwide, over 370 million pet cats share their home with human owners (21). In 2020 the American Veterinary Medical Association (AVMA) ranked the cat as the second most common pet worldwide with 48 % of the people owning one or more than one cat and 25 % of US households owning at least one (22). These high numbers suggests that cats play an important role in society. In May 2020, veterinarians in the USA were asked about their personal assessment and experience regarding pet owners' concerns about their pets potentially having COVID-19. According to the survey, 60 % of the veterinarians interviewed said that they had already dealt with concerned pet owners who feared about their pets either having COVID-19 or being at risk of contracting the virus (23). A study published in 2021 evaluated the susceptibility of domestic and wild animals to SARS-CoV-2 by analysing the sequence homology of the ACE2 proteins. According to the findings, domestic cats ranked 33rd out of the 66 animals investigated. *Puma concolor* (cougar), *Panthera pardus* (leopard), *Lynx canadensis* (Canada lynx), *Lynx pardinus* (Spanish lynx), *Panthera tigris* (tiger) and *Panthera leo* (lion) were also listed as susceptible species (24).

Several studies drew explicitly attention to species at risk of infection with SARS-CoV-2, including cats, so that appropriate measures can be taken to protect them and, mostly, to minimise the potential for human-animal transmission (24,25). For example, during the early stages of the SARS-CoV-2 pandemic, when the initial report of pets testing positive for the virus emerged, a cautionary message was conveyed against panic abandonment of pets (26).

Regarding big cats, in March 2020, there were reports of respiratory signs in several lions and tigers at the Bronx Zoo in New York City, USA. Subsequent testing confirmed the presence of SARS-CoV-2 in these animals. These were the first confirmed cases of natural SARS-CoV-2 infections in non-domestic species, with evidence for human-to-animal transmission (27). As time progressed, an increasing number of big cats across multiple zoos and safari parks worldwide tested positive for SARS-CoV-2 (28–30). This has intensified the need for more comprehensive studies focusing on big cats, and it became imperative to assess the impact of SARS-CoV-2 on the health, welfare, and long-term conservation efforts for big cats.

The objective of this narrative review was to provide a comprehensive overview of the existing literature pertaining to SARS-CoV-2 infection in domestic cats (*Felis catus)* and big cats and describe the current knowledge on this topic.

2 Materials and methods

2.1 Search strategy

In order to find relevant articles for this review, different combinations of the following keywords were used to query search databases: "SARS-CoV-2", "COVID-19", "cat", "cats", big cats", "tiger", "lion", "panther". The logical operators "AND" and "OR" were applied to combine the keywords. The main search was conducted using the PubMed electronic database. We included papers published from January 2020 to the date of search. Since SARS-CoV-2 in animals was described for the first time in February 2020 (31), we were not expecting any paper before this date. Furthermore, Science Direct, Google Scholar, and Web of Science were also screened using the same keywords and operators. Research started on 23/03/2022 and ended on 04/05/2023. Additional papers were subsequently included manually to complete the information.

Citation data and abstracts of the retrieved articles were downloaded and collected in Mendeley Reference Manager. Duplicates were removed manually. Articles were screened to select those that met the review inclusion criteria Table 1. Peer-reviewed papers published in scientific journals and written in English were included. Primary research papers (e. g., reporting experimental studies and studies of natural infections investigated via serosurveys, PCR-based methods or virus isolation studies) as well as case reports were deemed eligible. Papers pertaining to domestic cats (*Felis catus*) and big cats were included. A two-phase approach was performed to screen and select the articles. In the first phase, articles were selected based on titles and abstracts. In the second phase, a full text analysis in Mendeley Reference Manager was performed. Relevant information was highlighted in different colours and annotations were made. Using the tag tool, short descriptions were added to each article to facilitate subsequent keyword searches through tag filtering. Articles that met inclusion criteria were sorted out into chapters (one article was allowed in different chapters) to facilitate the writing of the review. Excluded papers were removed from the citation manager.

Table 1 Inclusion and exclusion criteria used to select papers to be included in the literature review.

Criteria	**Inclusion criteria**	**Exclusion criteria**
Language	English.	Other than English.
Pathogenic agent	SARS-CoV-2.	Other than SARS-CoV-2.
Study design	All	/
Research type	Primary research.	Secondary research.
Study design	Experimental studies; Case reports; Seroprevalence studies including ten or more domestic cats (no sample size limit was set for big cats); PCR-based investigations; Virus isolation studies; Studies presenting data from different animal species and data could be disaggregated by species.	Reviews; Opinion articles; Seroprevalence studies including less than ten domestic cats (no sample size limit was set for big cats); Studies presenting data from different animal species and data could not be disaggregated by species.
Species	Domestic cat, big cat.	Other animals than domestic cat and big cat.
Publication type	Peer-reviewed articles published in scientific journals.	Pre-prints; Research letters; Commentaries; Editorials.

Topics	Epidemiology of SARS-CoV-2 in cats and big cats; Natural spillover and spillback transmission events involving cats or big cats; Experimental infections of cats; Cat-to-cat transmission; Cats living in COVID-19 positive household; Cats as animal model for human SARS-CoV-2 infection; Susceptibility of cats to SARS-CoV-2; Diagnostic PCR or ELISA; Public health implications; Serosurveys; Binding affinity assays involving ACE2 receptors.	Comparison between SARS-CoV-2 and other coronaviruses; Structural virus analysis; Biomechanical topics; Treatment and vaccine assays.

2.2 Data extraction and synthesis

Findings and results were subsequently summarised and discussed in the different chapters of the thesis and presented through tables and figures.

3 Results

3.1 Selected papers

A total of 116 peer-reviewed papers was selected. The papers were published in 49 different scientific journals. We included 103 studies pertaining to domestic cats and 13 studies pertaining to big cats. 15.5 % (18/116) of the papers were published in 2020, 41.4 % (48/116) in 2021, 37.1 % (43/116) in 2022, and 6.9 % (8/116) in 2023.

The main themes identified in the different papers were: infection sources, transmission routes, seroprevalence and prevalence, detection methods, immunity, incubation period, duration of infection, clinical signs, and risk factors of infection in domestic and big cats.

3.2 Common and scientific name of included species

In addition to domestic cats, the review includes all big cats for which data was retrieved via the literature search (Table 2).

Table 2 Mention of all species occurring in the review with common and scientific name.

Common name	**Scientific name**	**Subfamily**
African lion	*Panthera leo leo*	Pantherinae
Amur leopard cat	*Prionailurus bengalensis euptilurus* (3)	Felinae
Asiatic lion	*Panthera leo persica*	Pantherinae
Bengal tiger	*Panthera tigris tigris*	Pantherinae
Domestic cat	*Felis catus*	Felinae
Indian leopard	*Panthera pardus fusca* (32)	Pantherinae
Malayan tiger	*Panthera tigris jacksoni*	Pantherinae
Puma	*Puma concolor*	Felinae
Snow leopard	*Panthera unica*	Pantherinae
Sumatran tiger	*Panthera tigris sumatrae*	Pantherinae
Tiger	*Panthera tigris*	Pantherinae

3.3 Routes of infection in domestic and big cats

3.3.1 Natural routes of infection

The most effective mode of transmission under natural conditions is airborne, via particles and droplets of respiratory fluids (33). Other routes of infection, such as direct contact when contaminated (human) hands come into contact with the nose or mouth of the animal or grooming, could not be proved so far and are only suspected (18,34,35).

Table 3 provides examples of the most likely human-to-cat infection routes reported during spillback events (9) (i. e., transmission of a pathogen from human to animal), along with a qualitative estimation of the strength of the evidence to confirm the source of infection (with strength + < ++ < +++).

Big cats shed the virus via respiratory secretions and faeces, which could lead to infection in cohoused animals (27). For big cats, the infection route was addressed in some case reports as described in Table 3 in more details. Evidence suggest that lions may contract the virus through direct or indirect contact with infected animals or humans via airborne route (28,29,36). However, in the case of tigers, most of the included studies were unable to establish a more specific mode of transmission; other studies mentioned respiratory and faecal secretion as source of infection (30,37,38).

Table 3 Possible routes and most likely sources of infection in naturally occurring SARS-CoV-2 infections in domestic cats and big cats.

Route of infection	Species	Suspected source of transmission	Strength of the evidence[1]	Reference
Airborne route of olfactory disease and upper respiratory excretions	Domestic cat	Human	+++	(33)
Touching their noses or mouth by infected hands defiled with respiratory droplets or saliva	Domestic cat	Human	+	(18)
Airborne route via nasal and oral secretion	Domestic cat	Cat	+	(34)
Direct contact	Lion	Human	+++	(36)
Direct contact	Asiatic lion, Amur leopard cat, Malayan tiger, Sumatran tiger	Asiatic lion, Amur leopard cat, Malayan tiger, Sumatran tiger	+	(39)
Direct contact (petting and feeding)	Captive tiger	Human	+	(37)
Direct contact	Malayan tiger	Malayan tiger	+	(38)
Direct or indirect contact	Lion	Human	+++	(28)
Close contact	Malayan tiger	Human	+	(30)
Unknown	Asiatic lion	Human	+++	(29)
Close (but indirect) contact (fomite, food preparation, shared enrichment items, aerosols, respiratory droplet)	Lion	Human	+	(27)

[1] The strength of the probability regarding a specific source of infection is indicated by the number of pluses assigned to it. An infection source rated with one plus (+) was only suspected (via epidemiological information) but not proven by molecular-based techniques. Two pluses (++) stand for a proven infection through a positive PCR test. Three pluses (+++) mean that the infection of the cat was verified by PCR and that an additionally performed genome sequencing matches the sequences of the suspected source of infection.

4.2.2. Experimentally tested infection routes

Experimental inoculations in domestic cats were performed to evaluate the effectiveness of two main infection routes and simulate natural conditions of infection:

- direct intranasal inoculation, to evaluate the possibility of intra- or interspecies transmission of SARS-CoV-2 through aerosols when coughing or sneezing,
- direct oral inoculation, to simulate infection through licking of contaminated environment or grooming behaviours (40).

Examples of experimental studies aiming to demonstrate the susceptibility of cats to SARS-CoV-2 transmission are presented in Table 4. Both intranasal and oral inoculation led to infection of the animals in all experiments.

Regarding big cats, there are, to date, no experimental studies that have investigated potential infection routes.

Table 4 Experimentally tested infection routes in domestic cats.

Country	**Route of infection**	**Laboratory test to evaluate the effectiveness of the infection route**	**Clinical signs**	**Reference**
United States	Intranasal and oral inoculation	Positive PCR	Asymptomatic	(41)
China	Intranasal inoculation	Positive PCR	Elevated body temperature, arched back posture, diarrhoea	(42)
Spain	Intranasal inoculation (spray simulating a human cough or sneeze)	Positive PCR	No symptoms	(40)
Spain	Oral (distribution over animal hair, simulating infection through grooming behaviour)	Positive PCR	Diarrhoea	
China	Intranasal inoculation	Positive PCR	Respiratory symptoms, subclinical, death	(43)
United States	Not described	Positive PCR	Lesions in the lungs	(44)
United States	Intranasal inoculation	Positive PCR	No clinical signs	(34)

3.4 Transmission sources

3.4.1 Human-to-cat transmission

Spillback transmission events, from humans to cats, are the most common origin of SARS-CoV-2 infection in Felidae (45,46). Human-to-domestic cat transmission was confirmed by viral genome sequencing on several occasions (33). Through comparative analysis of the SARS-CoV-2 genome in domestic cats with the original Wuhan_Hu-1 reference sequence, an average of 14 mutations emerged (45,46). The similarity between SARS-CoV-2 genomes found in cats and people in different cities or regions strongly suggests human-to-cat transmission (19,45–48). This was also confirmed by the fact that the same variants occur in cats and humans in multiple case reports of natural transmission. These cases involved various SARS-CoV-2 Variants of Concern (VOC), including the Alpha variant (B.1.1.7), Gamma variant (P.1), Delta variant (B.1.617, B.1.617.2.3), and Omicron variant (BA.2) (49–57) (Table 5). To date, analysis of SARS-CoV-2 variants retrieved from infected domestic cats has not evidenced any cat-specific mutation (58).

Spillback transmission event has also been reported in big cats including pumas, African lions and Asiatic lions, Amur leopards and Indian leopards, snow leopards as well as Sumatran and Malayan tigers (27–30,36–39,59,60). Genome sequencing revealed two VOC, Delta (Pango lineage B.1.617.2) (29,36,59,61) and Alpha (Pango lineage B.1.1.7), in these species (30,39) as well as one non-variant B.1.2 lineage (60) (Table 6). Additionally, SARS-CoV-2 was detected in a free-ranging leopard in India. The study suggests a spillback from humans (61).

Table 5 SARS-CoV-2 variants retrieved in domestic cats (Felis catus).

Sample	**Country**	**Detection method**[1]	**Species**	**Variant**	**Reference**
Oropharyngeal and rectal swabs	Iran	RT-qPCR	Domestic cat	Delta (B.1.617.2) Omicron (BA.2)	(62)
Oral, nasal, faecal swab	Switzerland	RT-qPCR NGS	Domestic cat	Delta (B.1.617.2)	(56)
Spleen, liver, heart, lungs, trachea, intestines, kidneys	Brazil	RT-qPCR	Domestic cat	Gamma (P.1)	(57)
Nasal, oral, rectal swabs	Thailand	RT-PCR	Domestic cat	Delta (B.1.617.2)	(52)
Pharyngeal swabs	Germany	RT-qPCR	Domestic cat	Alpha (B.1.1.7)	(51)
Oropharyngeal and faecal swabs	France	RT-qPCR	Domestic cat	Alpha (B.1.1.7)	(63)
Faecal	United States	RT-PCR	Domestic cat	Delta (AY.3)	(53)
Oropharyngeal, rectal swabs	Italy	RT-qPCR	Domestic cat	Alpha (B.1.1.7)	(55)
Oropharyngeal swabs	Cyprus	RT-PCR	Domestic cat	Alpha (B.1.1.7)	(50)
Rectal swabs	United Kingdom	dRT-PCR	Domestic cat	Alpha (B.1.1.7)	(54)
Oropharyngeal and/or nasal swabs	Thailand	RT-qPCR	Domestic cat[2]	Original European lineage (B.1), Alpha (B.1.1.7), Delta (B.1.617.2), Omicron (BA.2)	(49)
Nasopharyngeal and faecal swabs	Uruguay	qPCR	Domestic cat	Gamma (P.6)	(64)

[1] RT-PCR: Reverse transcription polymerase chain reaction; RT-qPCR: quantitative reverse transcription polymerase chain reaction; dRT-PCR: direct reverse transcription polymerase chain reaction; NGS: Next generation sequencing.

[2] Sheltered and hospitalised animals.

Table 6 SARS-CoV-2 variants in big cats.

Country	**Sample**	**Detection method**[1]	**Species**	**Variant**	**Reference**
India	Nasal and rectal swabs, faecal samples	RT-PCR	Asiatic lion	Delta (B.1.617.2)	(29)
India	Nasal and oral swabs	RT-PCR	Asiatic lion	Delta (B.1.617.2)	(59)
South Africa	Nasal and faecal swabs	RT-PCR	Puma, African lion	Delta (B.1.617.2)	(36)
India	Rectal and nasopharyngeal swabs	RT-PCR	Indian Leopard[2]	Delta (B.1.617.2)	(61)
United States	Faecal samples	RT-PCR	Snow leopard	non-variant B.1.2 lineage	(60)
Czech Republic	Faecal samples	RT-qPCR	Asiatic lion, Sumatran tiger, Malayan tiger, Amur leopard cat	Alpha (B.1.1.7)	(39)
United States	Nasal and faecal swab	RT-PCR	Malayan tiger	Alpha (B.1.1.7)	(30)

[1] RT-PCR: Reverse transcription polymerase chain reaction; RT-qPCR: quantitative reverse transcription polymerase chain reaction.

[2] Free ranging animals.

3.4.2 Cat-to-cat transmission

3.4.2.1 Naturally occurring cat-to-cat transmission

There is suspicion that natural transmission of SARS-CoV-2 may have taken place between domestic cats. In the study of Brandão et al. 2021 (65), after the outdoor cat showed initial symptoms and tested positive for SARS-CoV-2, the indoor cat, which shared the same living environment, subsequently exhibited clinical signs, and tested positive for the virus by RT-qPCR.

Furthermore, transmission of SARS-CoV-2 has been observed among captive tigers in Tennessee, USA, when three Malaysian tigers tested positive consecutively for SARS-CoV-2 (38). Although the SARS-CoV-2 genome sequenced from the tigers and lions at the Bronx Zoo differs only slightly from those of their keepers, tiger-to-tiger transmission cannot be ruled out (27). Similarly, in a zoo in the Czech Republic, although spillback transmission event from keepers to the big cats is the most likely source of infection, big cats can also actively shed the virus and infect other animals (39).

3.4.2.2 Experimental cat-to-cat transmission

Experimental studies have been conducted to investigate the transmission of SARS-CoV-2 between cats. Table 7 provides some selected examples. In all studies, previously negatively tested animals were artificially infected via intranasal or oral inoculation and co-housed with negatively tested cats. SARS-CoV-2 transmission from infected to healthy cat(s), via aerosols or direct contact, was confirmed in all cases (34,41–43,66). However, transmissibility, tested through serial transmissions, decreased in the later stages of infection with no viral RNA found from second passage on (42).

Experimental big cat-to-big cat transmission studies have not been performed yet.

Table 7 Summaries of selected studies reporting experimented cat to cat transmission.

Study design	**Findings**	**Reference**
Cat-to-cat transmission of SARS-CoV-2 after intranasal inoculation and subsequent serial passaging in cohoused cats at 6 dpi[1] via airborne route.	• Quantity viral RNA in throat swabs viral > anal swabs; viral shedding duration from throat swabs > anal swabs. • Decrease of viral shedding and duration after serial passaging. • No viral RNA found from second passage on (P2, P3). • No viral shedding found in P4 cats.	(42)
Cat-to-cat transmission of SARS-CoV-2 after intranasal inoculation (n = 3 cats) and subsequent cohousing with a healthy cat to monitor transmission through respiratory droplets.	• At 3 dpi, one of three exposed cats showed viral RNA in its faeces. • After euthanasia at 11 dpi the cat showed viral RNA in the nasal turbinate, soft palate, tonsils, and trachea.	(43)
Cat-to-cat transmission of SARS-CoV-2 after intranasal inoculation (n = 2) and subsequent cohousing with healthy cats (n = 2) at 2 dpi.	• The two contact cats shed virus orally at 1 dpi with a peak at 7 dpi.	(34)
Cat-to-cat transmission of SARS-CoV-2 after intranasal inoculation (n = 3) and subsequent cohousing with healthy cats (3 pairs of co-housed animals) at day 1.	• At 3 dpi one contact cat tested virus positive in a nasal swab sample. • Five days later, all three contact cats tested positive for SARS-CoV-2. • Viral shedding lasted for 4 to 5 days.	(66)
Cat-to-cat transmission of SARS-CoV-2 after intranasal inoculation (n = 6) and subsequent cohousing with healthy cats (1 healthy animal for 3 challenged cats) at day 1.	• Viral RNA was detected in nasal, oropharyngeal, and rectal swabs as well as bronchoalveolar lavage fluid from 1 to10 dpi.	(41)

[1] dpi: days post infection.

3.4.3 Mink-to-cat transmission

Mink-to-cat transmission was described in the Netherlands. This occurred in the context of heavily impacted farmed mink populations, where the virus underwent transmission from human to mink, circulated in the mink population, and subsequently spilled over back into the human population. This study of van Aart et al. 2022 (67), which presents a rare example of interspecies transmission, tested 101 cats from ten farms in the Netherlands for SARS-CoV-2 by PCR. The results indicated that there was a 12 % likelihood of cats becoming contaminated by minks when present on an infected mink farm. The cats were all feral, which therefore excluded the possibility of transmission from humans (67). Another study examined serum samples from cats living on mink farms in the Netherlands in 2020 and generated a lower seroprevalence of 0.4 % (68). Similarly, in Utah, around one fourth of the 15 free-roaming and feral cats from three different mink farms tested positive by PCR for SARS-CoV-2. Analysis of the movement patterns of the positive animals suggested a mink-to-cat transmission (69).

3.4.4 Domestic cat-to-human transmission

To date, only one cat-to-human transmission event has been described. On August 15, 2021, a female veterinarian in Songkhla Province, Thailand, was tested and confirmed positive for SARS-CoV-2 Delta variant after having examined, five days earlier, a SARS-CoV-2 infected cat. The two positive pet owners were transported together with the cat from Bangkok Province to the hospital in Bangkok, where the cat was separated and sent to the animal hospital alone. The cat was asymptomatic but sneezed in the face of a 32-year-old previously healthy veterinarian while nasal and rectal swab samples were taken. Three days later, the veterinarian showed clinical signs, including fever, clear nasal discharge, and productive cough for two days. The epidemiological link between the infections was confirmed by evidencing identical SARS-CoV-2 genome sequences obtained from the veterinarian, the infected cat, and its owners. This was further supported by the temporal overlap of the infections. Moreover, the genome sequences of the connected patients were distinct from other patients in the Songkhla Province, where the Alpha variant was widely spread at this time (70).

3.5 Seroprevalence of SARS-CoV-2 in domestic cats and big cats.

Out of the 116 selected scientific papers, 34 studies, performed across 21 countries, presented seroprevalence results and included a sample size of at least 10 cats (Table 8). The studies were conducted on domestic pet, stray, and shelter cats. The sample size varies from 19 to 2,160 cats. The detection methods were very diverse, with nine different methods reported across the 34 studies.

The study designs showed high heterogeneity, including random serosurveys, targeted sampling of cats from SARS-CoV-2 positive households, targeted sampling of cats from SARS-CoV-2 negative households and serosurveys conducted on cats that were hospitalised or presented for veterinary consultation. In the following, we limited ourselves to the results of the ELISA, as this was the only detection method cited in all studies. Overall, the prevalence of antibodies against SARS-CoV-2 in domestic cats is relatively low, with several studies demonstrating a seroprevalence < 1 % (68,71–82). Seroprevalences estimated via random serosurveys varied between 0 % and 14.7 % (71,73,74,76,82). Cats living in SARS-CoV-2 positive households had a higher incidence of antibodies than randomly tested animals, with a seroprevalence ranging between 5 % and 43 %, the latter being reported from the US (47,83). Furthermore, investigations on cats from SARS-CoV-2 negative households, found a seroprevalences of 0.7 % (83). One study presented a seroprevalence of 21.7 % in cats living in different SARS-CoV-2-contaminated environments (84). Other studies have found seroprevalences of < 1 % in cats living in areas with high-SARS-CoV-2-prevalence in humans (78,81). Serosurvey of cats admitted to hospital or presented for veterinary examination showed seroprevalences from 0.4 % to 18.9 % (77,85). Two large-scale studies conducted within a short time interval in 2020-2021, demonstrated a two-fold increase of the seroprevalence in cat populations in Germany, from 0.7 % in 2020 to 1.4 % few months later (72,86).

In two serosurveys carried out on big cats living in different environments, including Asiatic lions, Bengal tigers, tigers, and leopards, the estimated seroprevalence was 6.5 % (4/62) and 15 % (48/320) ([1] 20 % cut-off value.

Table 9).

Table 8 Overview of 34 selected seroprevalence studies of SARS-CoV-2 in domestic cats.

Type of cats	**Country**	**Sample size**	**Study design**	**Serological method**	**Seroprevalence of SARS-CoV-2**	**Year of sampling**	**Reference**
Pet	Germany, United Kingdom, Italy, Spain	2160	Random serosurvey	Receptor-binding-domain (RBD)-ELISA	4.3 %	2020	(87)
				Virus neutralisation test (VNT)	4.4 %		
Pet	France	34	Targeted sampling of cats living in SARS-CoV-2 positive households	Multiplex microsphere immunoassay (MIA)	23.5 %	2020	(88)
		16	Random serosurvey	MIA	6.3 %		
Pet, stray	China	87	Random serosurvey	ELISA	0 %	2020	(71)
Pet	Thailand	1112	Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA	0.4 %	2020	(77)
				Surrogate VNT	0 %		
Pet	USA	19	Targeted sampling of cats living in SARS-CoV-2 positive households	VNT	21.1 %	2020	(89)
Pet	Croatia	131	Serosurvey of cats hospitalised or presented for veterinary consultation	Microneutralisation test (MNT)	0.76 %	2020	(75)
Pet	USA	239	Serosurvey of cats hospitalised or presented for veterinary consultation	SARS-CoV-2 nucleocapsid (N) protein-ELISA	8 %	2020	(90)
				RBD-ELISA	3 %		
Shelter, pet	China	39 cats sampled prior the outbreak	Random serosurvey	ELISA	0 %	2019	(73)
		102 cats sampled after the outbreak		ELISA	14.7 %	2020	
				Surrogate VNT	10.8 %		

Pet	Germany	920	Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA + VNT	0.7 %	2020	(72)
Pet	Germany	1173	Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA + VNT	1.4 %	2020-2021	(86)
Pet	Portugal	69	Targeted sampling of cats living in SARS-CoV-2 contaminated environments	ELISA	21.7 %	2020-2021	(84)
Pet	Portugal	40	Targeted sampling of cats living in SARS-CoV-2 positive households	ELISA	5 % (COVID-19-positive household)	2020-2021	(83)
		136	Targeted sampling of cats living in SARS-CoV-2 negative households		0.7 % (COVID-19-negative household)		
Pet	Poland	279	Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA	1.8 %	2020-2021	(91)
Pet	France	143	Targeted sampling of cats living in SARS-CoV-2 positive households	ELISA + VNT	8.4 %	2020-2021	(92)
Stray and shelter	Italy	136 cats tested before the SARS-CoV-2 outbreak	Random serosurvey	ELISA	0 %	2019-2021	(74)
		99 cats tested after the SARS-CoV-2 outbreak		ELISA	1 %		
Pet	Peru	41	Targeted sampling of cats living in SARS-CoV-2 positive households	ELISA + Surrogate VNT	31.7 %[1]	2021	(93)

Stray, pet	Italy	99	Random serosurvey + Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA + VNT	0 %	2021	(76)
Shelter	Netherlands	240	Targeted sampling of cats living in shelters in high-risk areas	ELISA + VNT	0.8 %	2021	(78)
Stray	Spain	114	Random serosurvey + Serosurvey of cats hospitalised or presented for veterinary consultation	RBD-ELISA	3.5 %	2021	(94)
Pet	Poland	243	Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA + iIFA (indirect immunofluorescence assay)	18.9 %	2021-2022	(85)
Pet	Korea	488	Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA, sVNT, Plaque reduction neutralisation test (PRNT)	4.5 % 1.6 % 0.4 %	2020	(95)
Pet	Hong Kong	251	Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA, sVNT, PRNT	2.5 % 0.2 % 0 %	2020-2021	
Pets	Lebanon	145	Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA	13.8 %	2020-2021	(96)
Pet	Japan	1969	Serosurvey of cats hospitalised or presented for veterinary consultation	Protein-A/G- ELISA RBD-ELISA	0.5 % 0.2 %	2020	(79)
Pet	USA	32	Targeted sampling of cats living in SARS-CoV-2 positive households	ELISA	43 %	2020-2021	(47)

Stray, shelter, pet	Italy	215	Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA sVNT	3.7 % 1.9 %	2021-2022	(97)
Pet	Italy	54	Targeted sampling of cats living in SARS-CoV-2 positive households	ELISA	20.4 %	2020	(82)
		14	Random serosurvey		0 %		
Stray	Israel	131	Random serosurvey + Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA	2.3 %	2021	(98)
Pet	Serbia	36	Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA	5.6 %	2020-2021	(99)
Pet	Thailand	93	Targeted sampling of cats living in a high-risk area	ELISA sVNT	0 %	2021	(81)
Pet	USA	956	Serosurvey of cats hospitalised or presented for veterinary consultation	ELISA	1.2 %	2020	(100)
Pet	22 European countries	1005	Random serosurvey	ELISA, iIFT, sVNT	1.9 %	2020	(101)

[1] 20 % cut-off value.

Table 9 Seroprevalence studies in big cats.

Species	**Country**	**Sample size**	**Study design**	**Method of detection**	**(sero)prevalence of SARS-CoV-2**	**Year of sampling**	**Reference**
Asiatic lion, Bengal tiger, leopard	India	320	Serosurvey of big cats living in wildlife sanctuaries, zoos, and national parks	Microneutralisation assay Plaque reduction neutralisation test (PRNT)	15 %	2020-2021	(102)
Tiger	Thailand	62	Serosurvey of captive tigers living in a private zoo	PRNT	6.5 %	2020-2021	(37)

3.6 SARS-CoV-2 detection in domestic cats and big cats

3.6.1 Virus prevalence in domestic cats and big cats

Table 10 presents the results of 19 selected surveys conducted in eleven different countries that investigated the prevalence (i. e., they evidenced the presence of the virus or viral RNA) of SARS-CoV-2 in cats (only studies including ten or more individuals were included in this review). Cats from different backgrounds were sampled, e. g., domestic cats selected randomly, domestic cats living in SARS-CoV-2 positive households, patients screening in veterinary clinics, and stray cats. The studies included prospective and retrospective surveys that were performed before, during, or after the pandemic. For the detection of the virus in cats, RT-PCR (reversed transcriptase-polymerase chain reaction) and RT-qPCR (quantitative RT-PCR) were generally carried out. The principle of a RT-PCR is to evidence viral RNA by performing cycles of genome amplification before a signal becomes detectable. The number of cycles required for the signal to appear is described by the cycle threshold (CT) value, which is used to reflect the quantity of virus in the sample (RT-qPCR) (103).

In domestic cats sampled from SARS-CoV-2 positive households, the prevalence of the virus ranged from 0 % to 17.6 % (45,89), with one “outlier” study from Switzerland reporting a prevalence of 63.6 % (56). Randomly sampled cats generated a prevalence ranging from 0 % to 3 % (49,52,74,97,98). In retrospective studies that tested samples sent to laboratories for several reasons, SARS-CoV-2 prevalence ranged from 0 % to 0.5 % (104–106) whereas in a prospective study, 3.1 % of 130 randomly sampled cats tested positive for SARS-CoV-2 (63).Two studies investigated stray, shelter, and colony cats before and during the pandemic. The results showed that no cats were SARS-CoV-2 positive (74,107). The largest study was conducted across several animal research facilities in Asia, Europe and North America, screening 2,466 feline samples for respiratory pathogens including SARS-CoV-2 in early 2020. No cat was found SARS-CoV-2 positive, although some presented respiratory symptoms (105).

In a study investigating SARS-CoV-2 prevalence in big cats in Thailand, none of the 64 captive tigers tested were found to be positive for SARS-CoV-2 (37).

Table 10 Prevalence of SARS-CoV-2 RNA in domestic cats.

Type of cats	Country	Sample size	Study design	Method of detection	Prevalence	Year of sampling	Reference
Pet	USA	17	Targeted sampling of cats living with positive owner	RT-PCR	17.6 %	2020	(45)
Pet	Iran	124	Targeted sampling of cats living with positive owner	RT-PCR	0.8 %	2020	(108)
Pet	UK	387	Retrospective screening of patients at veterinary clinics	RT-qPCR	0.5 %	2020	(104)
Pet	USA	19	Targeted sampling of cats living with positive owner	RT-PCR	0 %	2020	(89)
Pet	China	50	Targeted sampling of cats living with positive owner	RT-PCR	12 %	2020	(19)
Pet	Spain	184	Targeted sampling of cats living with positive owner	RT-qPCR	1.6 %	2020-2021	(109)
		569	Random survey of SARS-CoV-2 in cats		0.2 %		
Pet	France	130	Prospective survey	RT-qPCR	3.1 %	2020-2021	(63)
Stray	Switzerland	523	Survey of SARS-CoV-2 in stray cats; Pre- pandemic	RT-qPCR	0 %	2019-2020	(107)
		882	Survey of SARS-CoV-2 in stray cats; During pandemic		0 %	2020-2021	
Pet	Iran	20	Targeted sampling of cats living with positive owner	RT- PCR	10 %	2021-2022	(62)
Pet	Uruguay	15	Targeted sampling of cats living with positive owner	RT-qPCR	6.7 %	2020	(64)

Pet	USA	32	Targeted sampling of cats living with positive owner	RT-PCR	8 %	2020-2021	(47)
Pet	Asia, Europe, North America	2466	Retrospective survey whilst pathogen testing	RT-PCR	0 %	2020	(105)
Shelter, stray colony	Italy	148	Patient screening at veterinary clinics	RT-PCR	0 %	2021-2022	(97)
Stray	Israel	131	Random survey of SARS-CoV-2 in cats	RT-PCR	0 %	2021	(98)
Pet, catteries, stray	Italy	52	Retrospective survey whilst pathogen testing	RT-PCR	0 %	2019-2021	(106)
Pet	Switzerland	14	Targeted sampling of cats living with positive owner	RT-qPCR	78.6 %	2020-2022	(56)
Pet	Thailand	120	Random survey of SARS-CoV-2 in cats	RT-PCR	0.8 %	2021	(52)
Shelter, hospitalised, pet	Thailand	639	Random survey of SARS-CoV-2 in cats	RT-PCR	3 %	2019-2022	(49)
Stray colony, shelter	Italy	136	Survey of SARS-CoV-2 in stray cats; Pre- pandemic	RT-qPCR	0 %	2019-2021	(74)
		105	Survey of SARS-CoV-2 in stray cats; During- pandemic		0 %		

3.7 Protective immunity after infection in domestic cats

Infection with SARS-CoV-2 in cats induces immunity to re-infection under experimental conditions when the antibody titre reaches a certain threshold (34,44). Few studies have reported experimental re-infection with SARS-CoV-2 in cats (34,44,110). In all trials listed in Table 11, the animals were artificially infected with the virus and re-infected after 21 to 28 days.

In two studies, infection in domestic cats triggered some immunity that protected from re-infection, i. e., no virus replication in the respiratory tract nor lung damage were observed after re-infection and high levels of neutralising antibody were produced (34,44). In one experiment, cats were divided into two cohorts and re-infection was successful in 3/8 animals, although the virus was shed intermittently and at minimal concentration. Very likely, re-infections were possible due to low antibody titres (110). In one study, the antibody titres doubled to quadrupled 14 days after re-infection (34).

Finally, a previous infection with other enzootic coronaviruses, such as canine coronavirus or feline coronavirus, does not induce a protective immunity against SARS-CoV-2 in domestic cats (80).

Table 11 Experimental re-infection performed to investigate the elicited immune response after SARS-CoV-2 infection, its role in providing protection against subsequent re-infection, and the duration of immunity following initial infection.

No. positive cats[1] (total No. cats) *	**Efficiency of re-infection**	**Test**	**Tissue sampled**	**Time between initial infection and re-infection**	**Infection route**	**Titre (virus neutralising antibodies) *****	**Reference**
0 (3)	Not efficient in 7 DP2C**	PCR	Oral and nasal	28 days	Intranasal inoculation	1:1,280-1:2,560	(34)
2 (3)	Efficient in 2 cats	RT-qPCR	Nasal and rectal cavities positive; oropharyngeal swabs negative	21 days	Intranasal and per os inoculation	1:40-1:320	(110)
1 (5)	Efficient in one cat	RT-qPCR	Nasal and oropharyngeal swabs positive, rectal swab negative	21 days	Intranasal and per os inoculation	1:40-1:320	
0 (3)	Not efficient in 9 DP2C	PCR	Nasal and rectal, organs	28 days	Inoculation (route not specified)	1:5120-1:20,480****	(44)

* No. = Number; ** DP2C = days post second challenge; *** on the day of re-infection; **** IgG antibody titre in day 24 after first inoculation.

1 Detection of viral shedding after re-infection challenge, usually by viral isolation or RT-PCR.

3.8 Clinical manifestations

3.8.1 Incubation period in domestic cats

Table 12 lists some studies that have estimated the incubation period of SARS-CoV-2 in cats. The incubation period varied between 1 and 25 days. However, the methods to evaluate it and the conditions of the studies differed significantly and results cannot be compared. For example, significant variations were observed in the approaches used to define the time from which an animal is considered SARS-CoV-2 positive. Some studies considered as day 1 of the infection the day when the test was carried (19), others used the day when the positive test result was obtained (49), some studies used the day when symptoms first appeared in the suspected source of infection (generally human) (111), and some others used the day when SARS-CoV-2 infection was laboratory confirmed in the suspected source of infection (49,50,56,66,87). One study defined the incubation period as the time between the onset of symptoms in the suspected source of infection and the first positive test in the cat (19).

Table 12 Incubation period in domestic cats after infection.

Number of cats	**Incubation period[1]**	**Definition of incubation period**	**Setting**	**Reference**
7	1 day	First contact to artificially inoculated cat - positive test of the cat	Experimental	(34)
4	3 days	First contact to artificially inoculated cat - positive test of the cat	Experimental	(42)
1	2 days	First contact to artificially inoculated cat - positive test of the cat	Experimental	(66)
1	5 days			
1	4 days			
1	1 day	Onset of owner’s symptoms - positive test of the cat	Natural	(19)
23	10 days	Onset of owner´s symptoms – onset of cats´ symptoms	Natural	(111)
7	7 days	First positive tests from owner – first positive test from the cat	Natural	(56)
1	7 days	First positive tests from owner – first positive test from the cat	Natural	(50)
5	19 days	First positive test from caretaker – first positive test of the cat	Natural	(49)
1	< 25 days	First positive tests from direct contact person – first positive test of the cat	Natural	(112)
3	4 days	Day of artificial inoculation of contact cat - positive test of the cat	Experimental	(43)

[1] Average duration (time interval), calculated over the study sample, between infection and recognition of infection, as defined specifically for each study.

3.8.2 Duration of SARS-CoV-2 infection in domestic cats

The duration of SARS-CoV-2 infection in domestic cats was evaluated in natural and experimental settings as shown in Table 13. Since the duration of infection was determined, depending on the study, for a sample size ranging from one to 16 cats, a mean value is given in the table.

Overall, the mean duration of the incubation period ranged between four and 21 days. Routes and sources of infection differed among studies. Furthermore, cat follow-ups and tests were conducted over different time periods, making comparison of the results between studies impossible.

Table 13 Duration of SARS-CoV-2 infection in domestic cats.

Number of cats included in the study	Duration of infection in days (mean)	Setting	Source of infection	Reference
3	4	Natural (co-housing)	Experimental	(43)
3	5.7	Experimental	Experimental	(66)
3	4.7	Natural	Cat	(66)
1	21	Natural	Human	(112)
1	4	Natural	Human	(50)
16	15	Natural	Human	(111)

3.8.3 Clinical signs

Domestic cats show different clinical manifestations following SARS-CoV-2 infection, from asymptomatic disease to fatal outcome. A list of the symptoms mentioned in the studies included in this review is displayed in Table 14 and summarised, for each organ, in Figure 1.

Big cats also show several clinical signs of SARS-CoV-2 infection (

Table 15, Figure 2). Death related to SARS-CoV-2 infection was reported in an Asiatic lion (29). In contrast to domestic cats, neurological, dermatological, cardiac and gastrointestinal symptoms as well as asymptomatic animals are not mentioned in big cats.

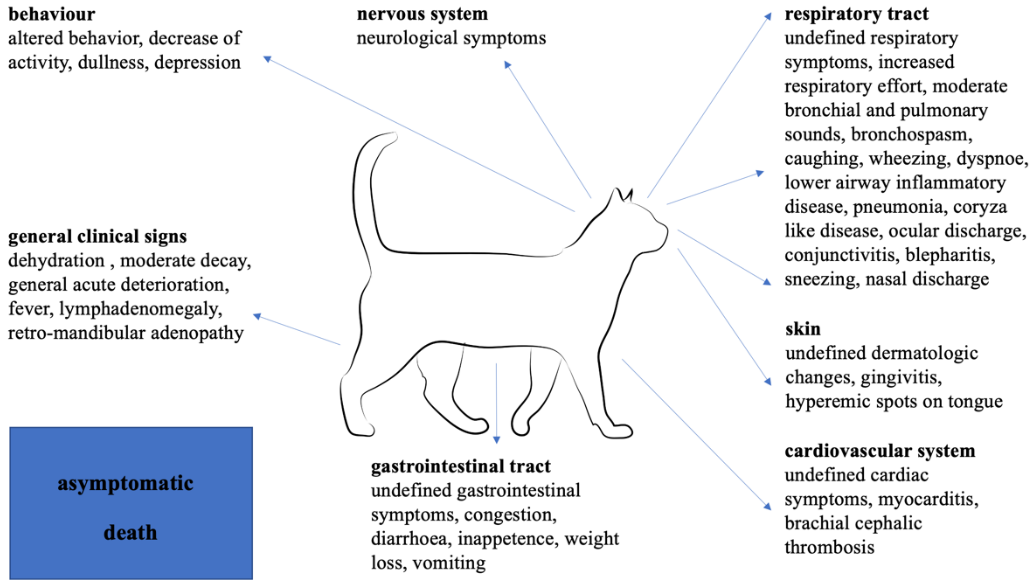

Figure 1 Clinical signs in domestic cats assigned to organ systems or body regions.

Table 14 Clinical signs in domestic cats.

Clinical sign	Reference
Respiratory tract	
Undefined respiratory symptoms	(48,49,84,107,108,113–115)
Increased respiratory effort	(114,116,117)
Moderate bronchial and pulmonary sounds	(116)
Bronchospasm	(118)
Coughing	(49,64,89,114,116–121)
Wheezing	(117,120)
Dyspnoea	(55,111,115,120)
Lower airway inflammatory disease	(63)
Pneumonia	(49,82)
Coryza like disease	(63)
Ocular discharge	(111,122,123)
Conjunctivitis	(104,107)
Blepharitis	(108)
Sneezing	(45,49,63,64,70,89,111,118,121,122,124–126)
Nasal discharge	(82,89,111,124)
Gastrointestinal tract	
Undefined gastrointestinal symptoms	(84,116,127)
Congestion	(115)
Diarrhoea	(107,111,117)
Inappetence	(84,113,121)
Weight loss	(108,114)
Vomiting	(111,117,127,128)
Skin	
Undefined dermatologic changes	(108)
Gingivitis	(126)
Hyperaemic spots on the tongue	(126)
Cardiovascular system	
Undefined cardiac symptoms	(50,54)
Myocarditis	(54)
Brachial cephalic thrombosis	(82)
Behaviour	
Altered behaviour	(114,117)

Decrease of activity	(45,84,108,111,114,117,119,121)
Dullness	(119,120)
Depression	(120)
General clinical signs	
Dehydration	(116)
Moderate decay	(118)
General acute deterioration	(124)
Fever	(84,111,114,117–120,129)
Lymphadenomegaly	(116,126)
Retro-mandibular adenopathy	(124)
Nervous system	
Neurological symptoms	(84,118)
Death	(57,108,129,130)
Asymptomatic	(34,41,44,48,49,52,58,63,82,116,119,126,131,132)

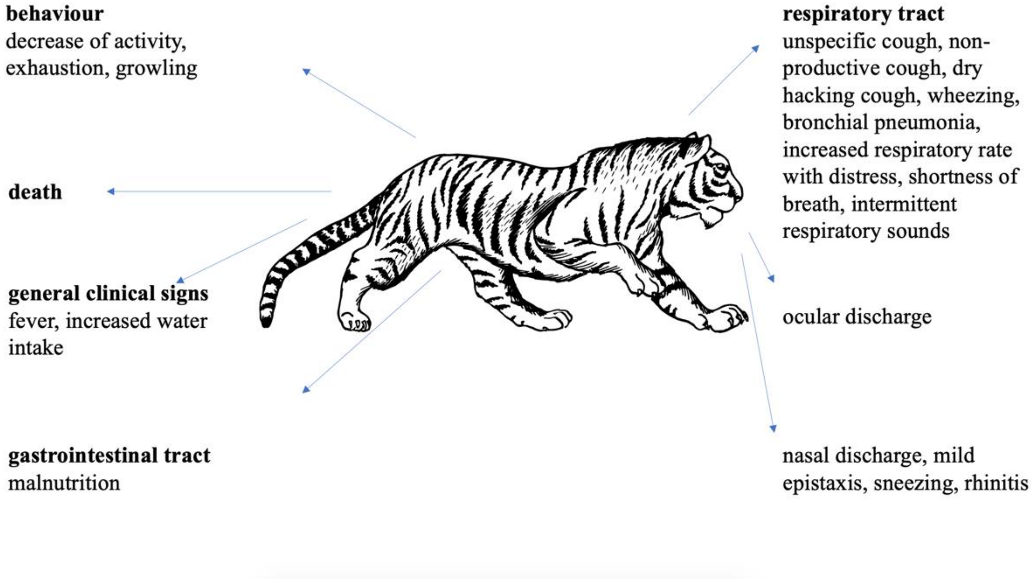

Figure 2 Clinical signs in big cats.

Table 15 Clinical signs in big cats.

Clinical sign	**Species**	**Reference**
Respiratory tract		
Unspecific cough	Lion, Asiatic lion, Malayan tiger, tiger, Snow leopard	(27,28,30,36,39,133)
Non-productive cough	Tiger	(38)
Dry hacking cough	Snow leopard	(60)
Wheezing	Snow leopard, Malayan tiger	(27,39,60)
Bronchial pneumonia	Lion	(36)
Increased respiratory rate with distress	Asiatic lion	(59)
Shortness of breath	Malayan tiger	(30)
Intermitted respiratory sounds	Malayan tiger	(30)
Ocular discharge	Lion, Asiatic lion	(29,36)
Nasal discharge	Lion, Asiatic lion, Amur leopard cat, Malayan tiger	(28–30,36,39)
Mild epistaxis	Asiatic lion	(59)
Sneezing	Amur leopard cat, Lion	(28,39)
Rhinitis	Amur leopard cat	(39)
Behaviour		
Decrease of activity	Tiger, Malayan tiger, Lion	(28,30,38,39)
Exhaustion	Asiatic lion	(39)
Growling	Malayan tiger	(39)
General clinical signs		
Fever	Asiatic lion	(59)
Increased water intake	Asiatic lion	(29,59)
Gastrointestinal tract		
Malnutrition	Malayan tiger, Asiatic lion, Puma	(29,30,36,38,39,59)
Death	Asiatic lion	(29)

3.9 Risk factors for SARS-CoV-2 infection in domestic cats

Table 16**Fehler! Verweisquelle konnte nicht gefunden werden.** shows the results of several studies evaluating the association between certain risk factors and the occurrence of SARS-CoV-2 infection assessed by the presence of antibodies and/or the presence of the virus. The relationship between SARS-CoV-2 infection and each risk factor is categorised as “positive”, “negative”, or “not significant” (i. e., p-value was bigger than 0.05). Overall, few studies presented significant outcomes.

For example, the age of the animal has a positive association with SARS-CoV-2, although this only applies in young adults (1-7 years) (97). Living with SARS-CoV-2 affected owners was positively associated with SARS-CoV-2 infection in domestic cats (40,134). Additionally, the risk of infection increased with the number of positive people living in the same household (134). Furthermore, cats originating from shelter, rescue or foster facilities and domestic cats sleeping on the owner's bed presented an increased risk of SARS-CoV-2 infection (135). Being positive for FeLV or presenting the blood phenotype AB was also positively associated with SARS-CoV-2 infection (97).

In experimental settings, air ventilation was negatively associated with SARS-CoV-2 infection (40).

Table 16 Risk factors of infection with SARS-CoV-2 in domestic cats.

Risk factor	**Association with SARS-CoV-2**	**Reference**
Origin	Not significant	(97)
Breed	Not significant	(97)
Age	Positive association	(97)
	Not significant	(84,91,135)
Sex	Not significant	(84,91,94,135,136)
Reproductive status	Not significant	(97)
Close contact to owner	Not significant	(92)
Positive household/owner	Positive association	(82,84,134)
	Not significant	(92,135,136)
Cats originating from shelter, rescue, or foster facility cats	Positive association	(135)
Number of positive people in the household	Positive association	(134)
Outdoor access	Not significant	(82,84)
Air ventilation	Negative association	(40)
Health status	Not significant	(91)
Kissed by owner	Not significant	(135)
Sleeping in/on owners' bed	Positive association	(135)
Licked hands/face of owner	Not significant	(135)
New respiratory signs	Not significant	(135)
New clinical signs	Not significant	(135)
Presence of multiple animals in the household	Not significant	(135)
Positive FeLV serostatus	Positive association	(97)
Blood phenotype AB	Positive association	(97)

3.10 Risk factors of SARS-CoV-2 infection in big cats

In big cats, no large-scale epidemiological studies have evaluated risk factors for SARS-CoV-2 infection. However, it is generally accepted that big cats kept in zoos or animal parks that have very close contact with humans, especially animal keepers, are particularly at risk of contracting SARS-CoV-2 (27,38,137). In captive settings, direct (28,30,36,39,60) or indirect contact with humans can lead to SARS-CoV-2 infection in big cats.(25)

4 Discussion

SARS-CoV-2 infection in cats: implications for animal health

The clinical signs reported in domestic and big cats are very similar. It remains unclear why fewer clinical symptoms have been described in big cats than in domestic cats, but very likely, clinical examination and monitoring of captive wild animals in large enclosures, where several animals may also live, is very challenging and limits data collection.

The infection and clinical patterns observed in Felidae especially the most typical symptoms, such as fever, chills, dyspnoea and, less frequently, gastrointestinal symptoms, resemble that of humans (138). The airborne route was the most commonly observed route of infection in domestic and big cats. Under experimental conditions, both intranasal and oral inoculation resulted in infection in domestic cats, supporting that the airborne route is the most likely mode of transmission for SARS-CoV-2 in Felidae.

The overall seroprevalence in domestic cats is relatively low. In addition, serosurveys of cats living in SARS-CoV-2-positive households have a higher risk of testing SARS-CoV-2 positive compared to randomly tested animals. These findings align with a household transmission as observed among human patients in a study conducted in Geneva, Switzerland in 2021. The study revealed a risk of infection that was more than three times higher for individuals residing in the same household as a person who tested positive for SARS-CoV-2 (139).

Several factors were found to be positively associated with SARS-CoV-2 infection in domestic cats, e. g. living in a positive household, presenting an immunocompromised immune system (i. e., positive FeLV serostatus), and being of a certain blood phenotype (AB). Similarly, several studies in humans tend to indicate that people living in a positive household (140) or those with blood group A have a higher risk of contracting SARS-CoV-2 (141). Also, as in cats, immunocompromised persons, such as people living with HIV, might present more severe symptoms of SARS-CoV-2 than those who are HIV-negative (142).

Although cats are susceptible to SARS-CoV-2 and positive owners in close contact with the animal pose an immediate risk of infection, cats generally remain asymptomatic or show only mild symptoms. The likelihood of a cat experiencing direct fatalities solely due to SARS-CoV-2 is rare (29). Consequently, SARS-CoV-2 poses a limited risk to the health and welfare of domestic cats.

Similarly, big cats, while susceptible to SARS-CoV-2 and able to transmit it to other big cats, still show a narrow range of clinical signs (27,39). Nevertheless, big cats in zoos are mostly infected through contact with humans (most commonly animal keepers) and are thus exposed to an increased risk related to captivity (37,133).

Potential threat posed by SARS-CoV-2 to conservation initiatives targeting big cats

Although the establishment of virus reservoirs in wild big cat populations could pose a potential threat to the welfare and conservation status of these species, the risk remains low since the majority of SARS-CoV-2 natural infections in big cats originated from humans (143). In captivity, guidelines have been developed to reduce the risk of human-to-big cat infection and therefore protect the animals (144,145). In particular, specific measures are recommended for ensuring the safe handling of wild animals in zoos and parks. These measures include implementing hygiene protocols such as wearing freshly laundered quarantine clothing, practicing frequent hand washing and disinfection, decontamination procedures, wearing face masks and gloves, and maintaining physical distancing. In addition, animals that have had contact with a suspected or positive SARS-CoV-2 case (staff or animal) should be segregated from other animals and quarantined for 14 days. If an animal tests positive, it should remain in quarantine until it has tested negative twice within a five-day interval. (25,146).

In natural settings, activities such as wildlife research, conservation activities, forestry, pest control, management of feral populations, ecological consulting, management of protected areas and natural environments, wildlife tourism and wildlife rehabilitation increase the risk of human-to-wildlife transmission of SARS-CoV-2 (25). Therefore, specific guidelines have been developed to address the handling and management of free-ranging wild mammals in the context of the SARS-CoV-2 pandemic. In summary, the guidelines emphasize several preventive principles when working with wild animals that include minimizing direct contacts and interactions with wild animals whenever possible, evaluating the risk of infection associated with working with wild animals and considering postponing such activities if necessary. If work with wild animals must proceed, it is essential to protect the animals from potential asymptomatic transmission by implementing appropriate protective clothing for humans and rigorous biosecurity measures. (143).

Uncertainty regarding some transmission events in captive big cats emphasizes the importance of epidemiological investigations of SARS-CoV-2 infections in zoo animals and highlights the need for continuous monitoring in zoos and animal parks to gather more evidence and better understand the potential risk factors for human-to-feline and inter-feline transmission (37,147,148).

Need for a One Health surveillance and monitoring

Humans were identified as the primary source of transmission in cats and big cats. Additionally, SARS-CoV-2 variants circulating in domestic cats exhibit a similar diversity as retrieved in humans, with the VOC Alpha, Gamma, Delta, and Omicron, which strongly supports the hypothesis of human-to-cat transmission (19,45,46). Regarding big cats, the literature describes reverse zoonotic transmission in *Puma concolor, Panthera leo, Panthera pardus, Panthera unica,* and *Panthera tigris*. Only two VOC were described in big cats, namely Alpha and Delta. This can be attributed to the presence of specific virus variants circulating among humans at the time of animal infection (36,39).

Because infection in cats mostly results from anthropogenic transmission, monitoring and reporting SARS-CoV-2 infection in Felidae, especially sharing genomic data on circulating variants, can complement surveillance efforts in human populations. This approach can help in the early detection of emerging variants or changes in the transmissibility of circulating variants, providing valuable insights for public health and mitigation strategies (149).

Analysis of genomic sequences of SARS-CoV-2 retrieved from domestic cats proved that no cat-specific mutation occurred while the viral sequences identified in cats differ only slightly from the original Wuhan_Hu-1 reference sequence. However, this result may be due to the small number of available SARS-CoV-2 sequences from cats (150). Although cat-to-human transmission has been reported in one case only (70), it highlights the potential risk of cats transmitting the virus to humans. The limited number of published cases of cat-to-human transmission raises several unanswered questions that require further investigation. It is worth considering whether there is a lack of regular genome sequencing for SARS-CoV-2 positive cats and their owners, or humans who have had contact with these cats, potentially hindering our ability to trace transmission routes accurately. Additionally, it is unclear whether the conditions for cat-to-human transmission are rare, as household members may infect each other before the cat shows symptoms or sheds the virus, making it challenging to identify the cat as the source of infection. Furthermore, even in cases where sequencing has been performed in multi-person households with a cat, it is possible that the cat's role as the source of infection in a human may be overlooked, particularly if there are very similar mutations among the humans involved. These further stresses the need for studying mutations specific to SARS-CoV-2 in cats and better understand their potential implications for both human and animal health (150). By examining these mutations, we can gain insights into the dynamics of the virus (151) and develop strategies to mitigate the risks associated with cat-to-human transmission.

Interspecies transmission has been documented from farmed minks to cats, as reported by Amman et al. 2022 and van Aart et al. 2022 (67,69). This raises concerns about the potential risks from mink and other Mustelinae species, which may coexist with domestic cats, to act as intermediate SARS-CoV-2 hosts between cats and humans (152). Additional investigations are required to assess the potential risk of minks playing a role in the further spread of SARS-CoV-2 to cats and, potentially, to humans (67,153).

SARS-CoV-2 being a multi-host pathogen, a One Health approach is crucial to comprehensively understand and mitigate risks at the interfaces between humans, cats, and the environment. This approach acknowledges the interconnectedness and interdependence of human, animal, and environmental health (154). Monitoring spillover events is a key element to controlling and limiting the spread of SARS-CoV-2 and other emerging pathogens with zoonotic potential (155,156). Monitoring and surveillance of SARS-CoV-2 infections in cats (157) is essential to gain a comprehensive understanding of transmission dynamics and to assess the significance of cats in the transmission chain. However, assessing the risk of SARS-CoV-2 transmission at human-cat interfaces requires considering the complexity of human behaviour and the sociological aspects associated with the human-cat relationship (158).

Identified data and research gaps

The incubation periods observed in domestic cats range from 1 to 25 days according to the included studies. However, there are significant variations in how the studies defined incubation period. Similarly, the mean duration of SARS-CoV-2 infection in domestic cats varies between 4 and 21 days, based on the included studies. However, different CT cut-off values were considered to determine the positivity threshold and these findings should therefore be interpreted with caution.

Multiple studies on re-infection in cats have indicated that cats can develop a form of protective immunity that prevents them from being re-infected with SARS-CoV-2 for a minimum of 21 to 28 days. However, these studies have only examined re-infection within this specific timeframe, the outcome of a re-infection beyond this period remains uncertain. Further investigations are necessary to understand the long-term dynamics of re-infection in cats and the potential duration of their protective immunity against SARS-CoV-2.

Overall, it is necessary to establish standardised protocols for conducting experimental trials, enabling the collection of data such as incubation times and duration of immunity in a consistent manner, as they are also carried out in human medicine for different types of research (159–161). Additionally, it is crucial to develop uniform reference values in diagnostics to facilitate objective interpretation of results and enhance comparability between studies. These measures would contribute to a more reliable and comprehensive understanding of SARS-CoV-2 infections in domestic cats.

While cat-to-cat transmission has been observed in laboratory settings, further research is needed to evaluate the potential for transmission of the virus between cats and big cats in natural settings.

Long COVID (also referred to as “post-acute sequelae of COVID-19”) affects at least 10-25 % of the infected human population (162,163). To date, there are no studies on long-term clinical manifestations following SARS-CoV-2 infections in cats. Given the long-life expectancy of cats, it is important to study the potential occurrence and effects of long COVID in Felidae. Additionally, comparative medicine research can provide valuable insights into understanding long COVID in humans by studying its manifestations and potential treatments in both humans and cats (164).

Finally, there is evidence suggesting that certain VOCs, such as Omicron in humans, present an increased transmissibility (165). There have been no comparative studies about variant transmissibility in cats although areas with increasing SARS-CoV-2 prevalence in humans generally present higher seroprevalence and virus prevalence in cats (74,88).

Limitations of this work

This thesis provides an overview of the topic of SARS-CoV-2 in cats. As the search and paper selection were not conducted in a strictly systematic manner (e. g. as described in the PRISMA guidelines (166)), not all existing studies on SARS-CoV-2 in cats have been included.

Furthermore, this review provides a snapshot of the current knowledge and understanding of SARS-CoV-2 in cats at the time of submission. However, considering the dynamic nature of the virus and its potential for evolution, as well as the continuous accumulation of new knowledge, it is important to recognise that our understanding of SARS-CoV-2 in cats is subjected to change.

This thesis describes SARS-CoV-2 infection in eleven Felidae species/subspecies. However, infection with SARS-CoV2 has been reported in more species than those listed above. Namely, the World Organisation for Animal Health (WOAH) (167) and the last Food and Agriculture Organization situation update (32) mention together three additional species as susceptible to SARS-CoV-2. As the list of keywords did not include "Felidae", no publications on the species fishing cat (*Prionailurus viverrinus*), Eurasian Lynx (*Lynx lynx*) and Canada Lynx (*Lynx canadensis*) were retrieved. Yet, the Amur leopard cat (*Prionailurus bengalensis*) has been mentioned in one study included in this review, but the above-mentioned organisations have not yet counted it as a susceptible species (39).

The studies included in this review may vary in terms of their quality, despite adherence to predefined inclusion criteria. While efforts were made to ensure rigorous selection, the absence of a comprehensive quality assessment (168,169) introduces some level of uncertainty regarding the reliability and validity of the included studies. Consequently, the focus was on presenting and describing the findings, rather than critically analysing them.

Conclusion

Overall, the findings of this review suggest that, at present, domestic cats and big cats do not appear to pose a substantial public health threat regarding SARS-CoV-2. Moreover, studies usually report a limited direct impact of SARS-CoV-2 infection on the health of the infected cats. By actively monitoring SARS-CoV-2 infections in cats, we can gather valuable data that will contribute to informed decision-making and the development of effective One Health strategies for preventing and mitigating the spread of the virus at cat-human interfaces.

Bibliography

1. Ye ZW, Yuan S, Yuen KS, Fung SY, Chan CP, Jin DY. Zoonotic origins of human coronaviruses. Int J Biol Sci. 2020;16(10):1686–97.
2. Centers for Disease Control and Prevention. CDC SARS Response Timeline [Internet]. [cited 2023 Jun 19]. Available from: https://www.cdc.gov/about/history/sars/timeline.htm
3. Schoch CL, Ciufo S, Domrachev M, Hotton CL, Kannan S, Khovanskaya R, et al. NCBI Taxonomy: A comprehensive update on curation, resources and tools. Database. 2020;2020:1–21.
4. Martina BEE, Haagmans BL, Kuiken T, Fouchier RAM, Rimmelzwaan GF, van Amerongen G, et al. SARS virus infection of cats and ferrets. Nature. 2003;425(6961):915.
5. Memish ZA, Al-Rabeeah AA. Public health management of mass gatherings: The Saudi Arabian experience with MERS-CoV. Bull World Health Organ. 2013;91(12):899.
6. World Health Organization. Disease Outbreak News; Middle East respiratory syndrome coronavirus (MERS-CoV) – Saudi Arabia. [Internet]. [cited 2023 Jan 3]. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON422
7. World Health Organization. Regional Office for the Eastern Mediterranean. MERS situation update, January 2023 [Internet]. [cited 2023 Jun 21]. Available from: https://apps.who.int/iris/handle/10665/366285
8. Weidinger P, Kolodziejek J, Camp J V., Loney T, Kannan DO, Ramaswamy S, et al. MERS-CoV in sheep, goats, and cattle, United Arab Emirates, 2019: Virological and serological investigations reveal an accidental spillover from dromedaries. Transbound Emerg Dis. 2022;69(5):3066–72.
9. Fagre AC, Cohen LE, Eskew EA, Farrell M, Glennon E, Joseph MB, et al. Assessing the risk of human-to-wildlife pathogen transmission for conservation and public health. Ecol Lett. 2022;25(6):1534–49.
10. World Health Organization. Pneumonia of unknown cause – China [Internet]. [cited 2023 Jun 21]. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON229

11. Zhou P, Yang X Lou, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579(7798):270–3.
12. Alwine JC, Casadevall A, Enquist LW, Goodrum FD, Imperiale MJ. A critical analysis of the evidence for the SARS-CoV-2 origin hypotheses. J Virol. 2023;97(4):1–7.
13. Pekar JE, Magee A, Parker E, Moshiri N, Izhikevich K, Havens JL, et al. The molecular epidemiology of multiple zoonotic origins of SARS-CoV-2. Science (1979). 2022;377(6609):960–6.
14. Worobey M, Levy JI, Serrano LM, Crits-Christoph A, Pekar JE, Goldstein SA, et al. The Huanan seafood wholesale market in Wuhan was the early epicenter of the COVID-19 pandemic. Science (1979). 2022;377(6609):951–9.
15. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020 [Internet]. [cited 2023 Jan 3]. Available from: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
16. World Health Organization. WHO Coronavirus (COVID-19) Dashboard [Internet]. [cited 2023 Jun 21]. Available from: https://covid19.who.int
17. Mastutik G, Rohman A, I'tishom R, Ruiz-Arrondo I, de Blas I. Experimental and natural infections of severe acute respiratory syndrome-related coronavirus 2 in pets and wild and farm animals. Vet World. 2022;15(3):565–89.
18. Chen J. Pathogenicity and transmissibility of 2019-nCoV-A quick overview and comparison with other emerging viruses. Microbes Infect. 2020;22(2):69–71.
19. Barrs VR, Peiris M, Tam KWS, Law PYT, Brackman CJ, To EMW, et al. SARS-CoV-2 in quarantined domestic cats from COVID-19 households or close contacts, Hong Kong, China. Emerg Infect Dis. 2020;26(12):3071–4.
20. University of Cambridge. Opinion: Can cats really get or pass on COVID-19, as a report from Belgium suggests? [Internet]. [cited 2023 Jun 6]. Available from: https://www.cam.ac.uk/research/news/opinion-can-cats-really-get-or-pass-on-covid-19-as-a-report-from-belgium-suggests#:~:text=Thankfully%2C%20there%20is%20still%20zero,2%20with%20no%20positive%20cases.

21. Murphy HL, Ly H. Understanding the prevalence of SARS-CoV-2 (COVID-19) exposure in companion, captive, wild, and farmed animals. Virulence. 2021;12(1):2777–86.
22. American Veterinary Medical Association. U.S. pet ownership statistics [Internet]. [cited 2023 Jan 3]. Available from: https://www.avma.org/resources-tools/reports-statistics/us-pet-ownership-statistics
23. Watson KM, Zhang Y, Towns K, Kahe K. Owner concerns that pets have COVID-19. Veterinary Record. 2020;186(18):608–9.
24. Kumar A, Pandey SN, Pareek V, Narayan RK, Faiq MA, Kumari C. Predicting susceptibility for SARS-CoV-2 infection in domestic and wildlife animals using ACE2 protein sequence homology. Zoo Biol. 2021;40(1):79–85.
25. Gryseels S, De Bruyn L, Gyselings R, Calvignac-Spencer S, Leendertz FH, Leirs H. Risk of human-to-wildlife transmission of SARS-CoV-2. Mamm Rev. 2021;51(2):272–92.
26. Huang Q, Zhan X, Zeng XT. COVID-19 pandemic: Stop panic abandonment of household pets. J Travel Med. 2021;27(3):1–2.
27. McAloose D, Laverack M, Wang L, Killian ML, Caserta LC, Yuan F, et al. From people to Panthera: Natural SARS-CoV-2 infection in tigers and lions at the Bronx Zoo. mBio. 2020;11(5):1–13.
28. Fernández-Bellon H, Rodon J, Fernández-Bastit L, Almagro V, Padilla-Solé P, Lorca-Oró C, et al. Monitoring natural SARS-CoV-2 infection in lions (Panthera leo) at the Barcelona Zoo: Viral dynamics and host responses. Viruses. 2021;13(9):1683.
29. Mishra A, Kumar N, Bhatia S, Aasdev A, Kanniappan S, Sekhar AT, et al. SARS-CoV-2 Delta variant among Asiatic lions, India. Emerg Infect Dis. 2021;27(10):2732–2725.
30. Mitchell PK, Martins M, Reilly T, Caserta LC, Anderson RR, Cronk BD, et al. SARS-CoV-2 B.1.1.7 variant infection in Malayan tigers, Virginia, USA. Emerg Infect Dis. 2021;27(12):3771–3.
31. Sit THC, Brackman CJ, Ip SM, Tam KWS, Law PYT, To EMW, et al. Infection of dogs with SARS-CoV-2. Nature. 2020;586(7831):776–8.
32. Food and Agriculture Organization of the United Nations. SARS-CoV-2 in animals situation update [Internet]. [cited 2023 Jun 19]. Available from: https://www.fao.org/animal-health/situation-updates/sars-cov-2-in-animals/en

33. Pagani G, Lai A, Bergna A, Rizzo A, Stranieri A, Giordano A, et al. Human-to-cat SARS-CoV-2 transmission: Case report and full-genome sequencing from an infected pet and its owner in Northern Italy. Pathogens. 2021;10(2):1–6.
34. Bosco-Lauth AM, Hartwig AE, Porter SM, Gordy PW, Nehring M, Byas AD, et al. Experimental infection of domestic dogs and cats with SARS-CoV-2: Pathogenesis, transmission, and response to reexposure in cats. Proc Natl Acad Sci U S A. 2020;117(42):26382–8.
35. Lauzi S, Stranieri A, Giordano A, Lelli D, Elia G, Desario C, et al. Do dogs and cats passively carry SARS-CoV-2 on hair and pads? Viruses. 2021;13(7):1357.
36. Koeppel KN, Mendes A, Strydom A, Rotherham L, Mulumba M, Venter M. SARS-CoV-2 reverse zoonoses to pumas and lions, South Africa. Viruses. 2022;14(1):120.
37. Sangkachai N, Chaiwattanarungruengpaisan S, Thongdee M, Suksai P, Tangsudjai S, Wongluechai P, et al. Serological and molecular surveillance for SARS-CoV-2 infection in captive tigers (Panthera tigris), Thailand. Animals. 2022;12(23):3350.
38. Grome HN, Meyer B, Read E, Buchanan M, Cushing A, Sawatzki K, et al. SARS-CoV-2 outbreak among Malayan tigers and humans, Tennessee, USA, 2020. Emerg Infect Dis. 2022;28(4):833–6.
39. Nagy A, Stará M, Vodička R, Černíková L, Jiřincová H, Křivda V, et al. Reverse-zoonotic transmission of SARS-CoV-2 lineage alpha (B.1.1.7) to great apes and exotic felids in a zoo in the Czech Republic. Arch Virol. 2022;167(8):1681–5.
40. Barroso-Arévalo S, Sánchez-Morales L, Barasona JA, Rivera B, Sánchez R, Risalde MA, et al. Evaluation of the clinical evolution and transmission of SARS-CoV-2 infection in cats by simulating natural routes of infection. Vet Res Commun. 2022;46(3):837–52.
41. Gaudreault NN, Trujillo JD, Carossino M, Meekins DA, Morozov I, Madden DW, et al. SARS-CoV-2 infection, disease and transmission in domestic cats. Emerg Microbes Infect. 2020;9(1):2322–32.
42. Bao L, Song Z, Xue J, Gao H, Liu J, Wang J, et al. Susceptibility and attenuated transmissibility of SARS-CoV-2 in domestic cats. J Infect Dis. 2021;223(8):1313–21.

43. Shi J, Wen Z, Zhong G, Yang H, Wang C, Huang B, et al. Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS-Coronavirus 2. Science (1979). 2020;368(6494):1016–20.
44. Chiba S, Halfmann PJ, Hatta M, Maemura T, Fan S, Armbrust T, et al. Protective immunity and persistent lung sequelae in domestic cats after SARS-CoV-2 infection. Emerg Infect Dis. 2021;27(2):660–3.
45. Hamer SA, Pauvolid-Corrêa A, Zecca IB, Davila E, Auckland LD, Roundy CM, et al. SARS-CoV-2 infections and viral isolations among serially tested cats and dogs in households with infected owners in Texas, USA. Viruses. 2021;13(5):938.
46. Bessière P, Fusade-Boyer M, Walch M, Lèbre L, Brun J, Croville G, et al. Household cases suggest that cats belonging to owners with COVID-19 have a limited role in virus transmission. Viruses. 2021;13(4):673.
47. Meisner J, Baszler T V., Kuehl KE, Ramirez V, Baines A, Frisbie LA, et al. Household transmission of SARS-CoV-2 from humans to pets, Washington and Idaho, USA. Emerg Infect Dis. 2022;28(12):2425–34.
48. Hamdy ME, El-Deeb AH, Hagag NM, Shahein MA, Liyanage NPM, Shalaan M, et al. SARS-CoV-2 infection of companion animals in Egypt and its risk of spillover. Vet Med Sci. 2023;9(1):13–24.
49. Piewbang C, Poonsin P, Lohavicharn P, Wardhani SW, Dankaona W, Puenpa J, et al. SARS-CoV-2 transmission from human to pet and suspected transmission from pet to human, Thailand. J Clin Microbiol. 2022;60(11):e0105822.
50. Curukoglu A, Ergoren MC, Ozgencil FE, Sayiner S, Ince ME, Sanlidag T. First direct human-to-cat transmission of the SARS-CoV-2 B.1.1.7 variant. Aust Vet J. 2021;99(11):482–8.
51. Keller M, Hagag IT, Balzer J, Beyer K, Kersebohm JC, Sadeghi B, et al. Detection of SARS-CoV-2 variant B.1.1.7 in a cat in Germany. Res Vet Sci. 2021;140:229–32.
52. Jairak W, Chamsai E, Udom K, Charoenkul K, Chaiyawong S, Techakriengkrai N, et al. SARS-CoV-2 Delta variant infection in domestic dogs and cats, Thailand. Sci Rep. 2022;12(1):8403.
53. Lenz OC, Marques AD, Kelly BJ, Rodino KG, Cole SD, Perera RAPM, et al. SARS-CoV-2 Delta variant (AY.3) in the feces of a domestic cat. Viruses. 2022;14(2):421.

54. Ferasin L, Fritz M, Ferasin H, Becquart P, Corbet S, Ar Gouilh M, et al. Infection with SARS-CoV-2 variant B.1.1.7 detected in a group of dogs and cats with suspected myocarditis. Veterinary Record. 2021;189(9):e944.

55. Zoccola R, Beltramo C, Magris G, Peletto S, Acutis P, Bozzetta E, et al. First detection of an Italian human-to-cat outbreak of SARS-CoV-2 Alpha variant – lineage B.1.1.7. One Health. 2021;13:100295.

56. Kuhlmeier E, Chan T, Agüí CV, Willi B, Wolfensberger A, Beisel C, et al. Detection and molecular characterization of the SARS-CoV-2 Delta variant and the specific immune response in companion animals in Switzerland. Viruses. 2023;15(1):245.

57. Carneiro RL, Farias JP, Pinheiro JR, Farias J, Vielmo AC, Birbrair A, et al. First description of a multisystemic and lethal SARS-CoV-2 variant of concern P.1 (Gamma) infection in a FeLV-positive cat. Virol J. 2022;19(1):93.

58. Chaintoutis SC, Siarkou VI, Mylonakis ME, Kazakos GM, Skeva PN, Bampali M, et al. Limited cross-species transmission and absence of mutations associated with SARS-CoV-2 adaptation in cats: A case study of infection in a small household setting. Transbound Emerg Dis. 2022;69(3):1606–16.

59. Karikalan M, Chander V, Mahajan S, Deol P, Agrawal RK, Nandi S, et al. Natural infection of Delta mutant of SARS-CoV-2 in Asiatic lions of India. Transbound Emerg Dis. 2021;69(5):3047–55.

60. Wang L, Gyimesi ZS, Killian ML, Torchetti M, Olmstead C, Fredrickson R, et al. Detection of SARS-CoV-2 clade B.1.2 in three Snow leopards. Transbound Emerg Dis. 2022;69(5):e3346–51.

61. Mahajan S, Karikalan M, Chander V, Pawde AM, Saikumar G, Semmaran M, et al. Detection of SARS-CoV-2 in a free ranging leopard (Panthera pardus fusca) in India. Eur J Wildl Res. 2022;68(5):59.

62. Akhtardanesh B, Jajarmi M, Shojaee M, Salajegheh Tazerji S, Khalili Mahani M, Hajipour P, et al. Molecular screening of SARS-CoV-2 in dogs and cats from households with infected owners diagnosed with COVID-19 during Delta and Omicron variant waves in Iran. Vet Med Sci. 2023;9(1):82–90.

63. Krafft E, Denolly S, Boson B, Angelloz-Pessey S, Levaltier S, Nesi N, et al. Report of one-year prospective surveillance of SARS-CoV-2 in dogs and cats in France with

various exposure risks: Confirmation of a low prevalence of shedding, detection and complete sequencing of an Alpha variant in a cat. Viruses. 2021;13(9):1759.

64. Panzera Y, Mirazo S, Baz M, Techera C, Grecco S, Cancela F, et al. Detection and genome characterisation of SARS-CoV-2 P.6 lineage in dogs and cats living with Uruguayan COVID-19 patients. Mem Inst Oswaldo Cruz. 2023;117:e220177.

65. Brandão LNS, Homochiski DP, Oliveira LB de, Oliveira RMS de, Maciel SA. Detection of SARS-CoV-2 by the RT-qPCR in domestic cats. Res Soc Dev. 2021;10(9):e40110918184.

66. Halfmann PJ, Hatta M, Chiba S, Maemura T, Fan S. Transmission of SARS-CoV-2 in domestic cats. N Engl J Med. 2020;383(6):590–2.

67. van Aart AE, Velkers FC, Fischer EAJ, Broens EM, Egberink H, Zhao S, et al. SARS-CoV-2 infection in cats and dogs in infected mink farms. Transbound Emerg Dis. 2022;69(5):3001–7.

68. Zhao S, Schuurman N, Li W, Wang C, Smit LAM, Broens EM, et al. Serologic screening of severe acute respiratory syndrome coronavirus 2 infection in cats and dogs during first coronavirus disease wave, the Netherlands. Emerg Infect Dis. 2021;27(5):1362–70.

69. Amman BR, Cossaboom CM, Wendling NM, Harvey RR, Rettler H, Taylor D, et al. GPS tracking of free-roaming cats (Felis catus) on SARS-CoV-2-infected mink farms in Utah. Viruses. 2022;14(10):2131.

70. Sila T, Sunghan J, Laochareonsuk W, Surasombatpattana S, Kongkamol C, Ingviya T, et al. Suspected cat-to-human transmission of SARS-CoV-2, Thailand, July–September 2021. Emerg Infect Dis. 2022;28(7):1485–8.

71. Deng J, Jin Y, Liu Y, Sun J, Hao L, Bai J, et al. Serological survey of SARS-CoV-2 for experimental, domestic, companion and wild animals excludes intermediate hosts of 35 different species of animals. Transbound Emerg Dis. 2020;67(4):1745–9.

72. Michelitsch A, Hoffmann D, Wernike K, Beer M. Occurrence of antibodies against SARS-CoV-2 in the domestic cat population of Germany. Vaccines (Basel). 2020;8(4):1–10.

73. Zhang Q, Zhang H, Gao J, Huang K, Yang Y, Hui X, et al. A serological survey of SARS-CoV-2 in cat in Wuhan. Emerg Microbes Infect. 2020;9(1):2013–9.

74. Spada E, Vitale F, Bruno F, Castelli G, Reale S, Perego R, et al. A pre-and during pandemic survey of SARS-CoV-2 infection in stray colony and shelter cats from a high endemic area of Northern Italy. Viruses. 2021;13(4):618.
75. Stevanovic V, Vilibic-Cavlek T, Tabain I, Benvin I, Kovac S, Hruskar Z, et al. Seroprevalence of SARS-CoV-2 infection among pet animals in Croatia and potential public health impact. Transbound Emerg Dis. 2021;68(4):1767–73.
76. Stranieri A, Lauzi S, Giordano A, Galimberti L, Ratti G, Decaro N, et al. Absence of SARS-CoV-2 RNA and anti-SARS-CoV-2 antibodies in stray cats. Transbound Emerg Dis. 2021;69(4):2089–95.
77. Udom K, Jairak W, Chamsai E, Charoenkul K, Boonyapisitsopa S, Bunpapong N, et al. Serological survey of antibodies against SARS-CoV-2 in dogs and cats, Thailand. Transbound Emerg Dis. 2021;69(4):2140–7.
78. van der Leij WJR, Broens EM, Hesselink JW, Schuurman N, Vernooij JCM, Egberink HF. Serological screening for antibodies against SARS-CoV-2 in Dutch shelter cats. Viruses. 2021;13(8):1634.
79. Imanishi I, Asahina R, Hayashi S, Uchiyama J, Hisasue M, Yamasaki M, et al. Guest edited collection serological study of SARS-CoV-2 antibodies in Japanese cats using protein-A/G-based ELISA. BMC Vet Res. 2022;18(1):443.
80. Oliveira-Filho EF de, de Carvalho O V., Carneiro IO, Fernandes FD, Vaz SN, Pedroso C, et al. Frequent infection of cats with SARS-CoV-2 irrespective of pre-existing enzootic coronavirus immunity, Brazil 2020. Front Immunol. 2022;13:857322.
81. Jairak W, Charoenkul K, Chamsai E, Udom K, Chaiyawong S, Hangsawek A, et al. Survey of SARS-CoV-2 in dogs and cats in high-risk areas during the second wave of COVID-19 outbreak, Thailand. Zoonoses Public Health. 2022;69(6):737–45.
82. Colitti B, Bertolotti L, Mannelli A, Ferrara G, Vercelli A, Grassi A, et al. Cross-sectional serosurvey of companion animals housed with SARS-CoV-2-infected owners, Italy. Emerg Infect Dis. 2021;27(7):1919–22.
83. Oliveira A, Pereira MA, Mateus TL, Mesquita JR, Vala H. Seroprevalence of SARS-CoV-2 in client-owned cats from Portugal. Vet Sci. 2022;9(7):363.

84. Barroso R, Vieira-Pires A, Antunes A, Fidalgo-Carvalho I. Susceptibility of pets to SARS-CoV-2 infection: Lessons from a seroepidemiologic survey of cats and dogs in Portugal. Microorganisms. 2022;10(2):345.

85. Kaczorek-Łukowska E, Wernike K, Beer M, Wróbel M, Małaczewska J, Mikulska-Skupień E, et al. High seroprevalence against SARS-CoV-2 among dogs and cats, Poland, 2021/2022. Animals. 2022;12(16):2016.

86. Michelitsch A, Schön J, Hoffmann D, Beer M, Wernike K. The second wave of SARS-CoV-2 circulation-antibody detection in the domestic cat population in Germany. Viruses. 2021;13(6):1009.

87. Schulz C, Martina B, Mirolo M, Müller E, Klein R, Volk H, et al. SARS-CoV-2-specific antibodies in domestic cats during first COVID-19 Wave, Europe. Emerg Infect Dis. 2021;27(12):3115–8.

88. Fritz M, Rosolen B, Krafft E, Becquart P, Elguero E, Vratskikh O, et al. High prevalence of SARS-CoV-2 antibodies in pets from COVID-19+ households. One Health. 2021;11:100192.

89. Goryoka GW, Cossaboom CM, Gharpure R, Dawson P, Tansey C, Rossow J, et al. One Health investigation of SARS-CoV-2 infection and seropositivity among pets in households with confirmed human COVID-19 cases-Utah and Wisconsin, 2020. Viruses. 2021;13(9):1813.

90. Dileepan M, Di D, Huang Q, Ahmed S, Heinrich D, Ly H, et al. Seroprevalence of SARS-CoV-2 (COVID-19) exposure in pet cats and dogs in Minnesota, USA. Virulence. 2021;12(1):1597–609.

91. Pomorska-Mól M, Turlewicz-Podbielska H, Gogulski M, Ruszkowski JJ, Kubiak M, Kuriga A, et al. A cross-sectional retrospective study of SARS-CoV-2 seroprevalence in domestic cats, dogs and rabbits in Poland. BMC Vet Res. 2021;17(1):322.

92. Bessière P, Vergne T, Battini M, Brun J, Averso J, Joly E, et al. SARS-CoV-2 infection in companion animals: Prospective serological survey and risk factor analysis in France. Viruses. 2022;14(6):1178.

93. Jara LM, Ferradas C, Schiaffino F, Sánchez-Carrión C, Martínez-Vela A, Ulloa A, et al. Evidence of neutralizing antibodies against SARS-CoV-2 in domestic cats living with owners with a history of COVID-19 in Lima – Peru. One Health. 2021;13:100318.

94. Villanueva-Saz S, Giner J, Tobajas AP, Pérez MD, González-Ramírez AM, Macías-León J, et al. Serological evidence of SARS-CoV-2 and co-infections in stray cats in Spain. Transbound Emerg Dis. 2022;69(3):1056–64.
95. Go YY, Carrai M, Choi YR, Brackman CJ, Tam KWS, Law PYT, et al. Low prevalence of SARS-CoV-2 antibodies in canine and feline serum samples collected during the COVID-19 pandemic in Hong Kong and Korea. Viruses. 2023;15(2):582.
96. Khalife S, Abdallah M. High seroprevalence of SARS-CoV-2 antibodies in household cats and dogs of Lebanon. Res Vet Sci. 2023;157:13–6.
97. Spada E, Bruno F, Castelli G, Vitale F, Reale S, Biondi V, et al. Do blood phenotypes of feline AB blood group system affect the SARS-CoV-2 antibody serostatus in cats? Viruses. 2022;14(12):2691.
98. Kleinerman G, Gross S, Topol S, Ariel E, Volokh G, Melloul S, et al. Low serological rate of SARS-CoV-2 in cats from military bases in Israel. Comp Immunol Microbiol Infect Dis. 2022;90–91:101905.
99. Stanojevic S, Radojicic S, Misic D, Srejić D, Vasiljevic D V., Prokic K, et al. Frequency of SARS-CoV-2 infection in dogs and cats: Results of a retrospective serological survey in Šumadija District, Serbia. Prev Vet Med. 2022;208:105755.
100. Barua S, Hoque M, Adekanmbi F, Kelly P, Jenkins-Moore M, Torchetti MK, et al. Antibodies to SARS-CoV-2 in dogs and cats, USA. Emerg Microbes Infect. 2021;10(1):1669–74.
101. Adler JM, Weber C, Wernike K, Michelitsch A, Friedrich K, Trimpert J, et al. Prevalence of anti-severe acute respiratory syndrome coronavirus 2 antibodies in cats in Germany and other European countries in the early phase of the coronavirus disease-19 pandemic. Zoonoses Public Health. 2022;00:1–12.
102. Borkakoti R, Karikalan M, Nehul SK, Jogi HR, Sharma K, Nautiyal S, et al. A retrospective study showing a high rate of seropositivity against SARS-CoV-2 in wild felines in India. Arch Virol. 2023;168(4):109.
103. Robert F. Service. One number could help reveal how infectious a COVID-19 patient is. Should test results include it? [Internet]. Science. Portland; 2020 [cited 2023 Jun 19]. Available from: https://www.science.org/content/article/one-number-could-help-reveal-how-infectious-covid-19-patient-should-test-results

104. Hosie MJ, Epifano I, Herder V, Orton RJ, Stevenson A, Johnson N, et al. Detection of SARS-CoV-2 in respiratory samples from cats in the UK associated with human-to-cat transmission. Veterinary Record. 2021;188(8):e247.

105. Michael HT, Waterhouse T, Estrada M, Seguin MA. Frequency of respiratory pathogens and SARS-CoV-2 in canine and feline samples submitted for respiratory testing in early 2020. J Small Anim Pract. 2021;62(5):336–42.

106. Amoroso MG, Serra F, Miletti G, Cardillo L, de Martinis C, Marati L, et al. A retrospective study of viral molecular prevalences in cats in Southern Italy (Campania region). Viruses. 2022;14(11):2583.

107. Kuhlmeier E, Chan T, Klaus J, Pineroli B, Geisser E, Hofmann-Lehmann R, et al. A pre- and within-pandemic survey of SARS-CoV-2 RNA in saliva swabs from stray cats in Switzerland. Viruses. 2022;14(4):681.

108. Mohebali M, Hassanpour G, Zainali M, Gouya MM, Khayatzadeh S, Parsaei M, et al. SARS-CoV-2 in domestic cats (Felis catus) in the northwest of Iran: Evidence for SARS-CoV-2 circulating between human and cats. Virus Res. 2022;310:198673.

109. Barroso-Arévalo S, Barneto A, Ramos ÁM, Rivera B, Sánchez R, Sánchez-Morales L, et al. Large-scale study on virological and serological prevalence of SARS-CoV-2 in cats and dogs in Spain. Transbound Emerg Dis. 2021;69(4):e759–74.

110. Gaudreault NN, Carossino M, Morozov I, Trujillo JD, Meekins DA, Madden DW, et al. Experimental re-infected cats do not transmit SARS-CoV-2. Emerg Microbes Infect. 2021;10(1):638–50.

111. Liew AY, Carpenter A, Moore TA, Wallace RM, Hamer SA, Hamer GL, et al. Clinical and epidemiologic features of SARS-CoV-2 in dogs and cats compiled through national surveillance in the United States. J Am Vet Med Assoc. 2023;261(4):480–9.

112. Schulz C, Wylezich C, Wernike K, Gründl M, Dangel A, Baechlein C, et al. Prolonged SARS-CoV-2 RNA shedding from therapy cat after cluster outbreak in retirement home. Emerg Infect Dis. 2021;27(7):1974–6.

113. Carvallo FR, Martins M, Joshi LR, Caserta LC, Mitchell PK, Cecere T, et al. Severe SARS-CoV-2 infection in a cat with hypertrophic cardiomyopathy. Viruses. 2021;13(8):1510.

114. Rudd JM, Tamil Selvan M, Cowan S, Kao YF, Midkiff CC, Narayanan S, et al. Clinical and histopathologic features of a feline SARS-CoV-2 infection model are analogous to acute COVID-19 in humans. Viruses. 2021;13(8):1550.

115. Tewari D, Boger L, Brady S, Livengood J, Killian ML, Nair MS, et al. Transmission of SARS-CoV-2 from humans to a 16-year-old domestic cat with comorbidities in Pennsylvania, USA. Vet Med Sci. 2022;8(2):899–906.

116. Natale A, Mazzotta E, Mason N, Ceglie L, Mion M, Stefani A, et al. SARS-CoV-2 natural infection in a symptomatic cat: Diagnostic, clinical and medical management in a One Health vision. Animals. 2021;11(6):1640.

117. Tamil Selvan M, Gunasekara S, Xiao P, Griffin K, Cowan SR, Narayanan S, et al. SARS CoV-2 (Delta variant) infection kinetics and immunopathogenesis in domestic cats. Viruses. 2022;14(6):1207.

118. Panei CJ, Bravi ME, Moré G, De Felice L, Unzaga JM, Salina M, et al. Serological evidence of SARS-CoV-2 infection in pets naturally exposed during the COVID-19 outbreak in Argentina. Vet Immunol Immunopathol. 2022;254:110519.

119. Neira V, Brito B, Agüero B, Berrios F, Valdés V, Gutierrez A, et al. A household case evidences shorter shedding of SARS-CoV-2 in naturally infected cats compared to their human owners. Emerg Microbes Infect. 2021;10(1):376–83.

120. Ozer K, Yilmaz A, Carossino M, Yuzbasioglu Ozturk G, Erdogan Bamac O, Tali HE, et al. Clinical, virological, imaging and pathological findings in a SARS CoV-2 antibody positive cat. J Vet Sci. 2022;23(4):e52.

121. Klaus J, Meli ML, Willi B, Nadeau S, Beisel C, Stadler T, et al. Detection and genome sequencing of SARS-CoV-2 in a domestic cat with respiratory signs in Switzerland. Viruses. 2021;13(3):496.

122. Newman DVM A, Smith D, Ghai RR, Wallace RM, Kim Torchetti M, Loiacono C, et al. First reported cases of SARS-CoV-2 infection in companion animals — New York, March–April 2020 [Internet]. Vol. 69, Centers for Disease Control and Prevention. New York; 2020 [cited 2023 Jun 22]. Available from: https://www.cdc.gov/mmwr/volumes/69/wr/mm6923e3.htm?s_cid=mm6923e3_w

123. Klaus J, Palizzotto C, Zini E, Meli ML, Leo C, Egberink H, et al. SARS-CoV-2 infection and antibody response in a symptomatic cat from Italy with intestinal B-cell lymphoma. Viruses. 2021;13(3):527.

124. Fritz M, Nesi N, Denolly S, Boson B, Legros V, Rosolen SG, et al. Detection of SARS-CoV-2 in two cats during the second wave of the COVID-19 pandemic in France. Vet Med Sci. 2022;8(1):14–20.

125. Fuentealba NA, Moré G, Bravi ME, Unzaga JM, De Felice L, Salina M, et al. First detection and molecular analysis of SARS-CoV-2 from a naturally infected cat from Argentina. Vet Microbiol. 2021;260:109179.

126. Calvet GA, Pereira SA, Ogrzewalska M, Pauvolid-Corrêa A, Resende PC, Tassinari W de S, et al. Investigation of SARS-CoV-2 infection in dogs and cats of humans diagnosed with COVID-19 in Rio de Janeiro, Brazil. PLoS One. 2021;16(4):e0250853.

127. Garigliany M, Van Laere AS, Clercx C, Giet D, Escriou N, Huon C, et al. SARS-CoV-2 natural transmission from human to cat, Belgium, March 2020. Emerg Infect Dis. 2020;26(12):3069–71.

128. Sailleau C, Dumarest M, Vanhomwegen J, Delaplace M, Caro V, Kwasiborski A, et al. First detection and genome sequencing of SARS-CoV-2 in an infected cat in France. Transbound Emerg Dis. 2020;67(6):2324–8.

129. Botero Y, Ramírez JD, Serrano-Coll H, Aleman A, Ballesteros N, Martinez C, et al. First report and genome sequencing of SARS-CoV-2 in a cat (Felis catus) in Colombia. Mem Inst Oswaldo Cruz. 2022;117:e210375.

130. Carpenter A, Ghai RR, Gary J, Ritter JM, Carvallo FR, Diel DG, et al. Determining the role of natural SARS-CoV-2 infection in the death of domestic pets: 10 cases (2020-2021). J Am Vet Med Assoc. 2021;259(9):1032–9.

131. Dutra V, Jarrah SA, Kmetiuk LB, de Carvalho OV, Ito de Sousa ATH, Franco Souza VR, et al. Persistent SARS-CoV-2 antigen presence in multiple organs of a naturally infected cat from Brazil. J Venom Anim Toxins Incl Trop Dis. 2022;28(e20210074).

132. Patania OM, Chiba S, Halfmann PJ, Hatta M, Maemura T, Bernard KA, et al. Pulmonary lesions induced by SARS-CoV-2 infection in domestic cats. Vet Pathol. 2022;59(4):696–706.

133. Wang L, Mitchell PK, Calle PP, Bartlett SL, Mcaloose D, Killian ML, et al. Complete genome sequence of SARS-CoV-2 in a tiger from a U.S. zoological collection. Microbiol Resour Announc. 2020;9(22):e00468-20.
134. Kannekens-Jager MM, de Rooij MMT, de Groot Y, Biesbroeck E, de Jong MK, Pijnacker T, et al. SARS-CoV-2 infection in dogs and cats is associated with contact to COVID-19-positive household members. Transbound Emerg Dis. 2022;69(6):4034–40.
135. Bienzle D, Rousseau J, Marom D, MacNicol J, Jacobson L, Sparling S, et al. Risk factors for SARS-CoV-2 infection and illness in cats and dogs. Emerg Infect Dis. 2022;28(6):1154–62.
136. Patterson EI, Elia G, Grassi A, Giordano A, Desario C, Medardo M, et al. Evidence of exposure to SARS-CoV-2 in cats and dogs from households in Italy. Nat Commun. 2020;11(1):6231.
137. Rendon-Marin S, Martinez-Gutierrez M, Whittaker GR, Jaimes JA, Ruiz-Saenz J. SARS CoV-2 spike protein in silico interaction with ACE2 receptors from wild and domestic species. Front Genet. 2021;12:571707.
138. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. Nat Rev Microbiol. 2021;19(3):141–54.
139. Bi Q, Lessler J, Eckerle I, Lauer SA, Kaiser L, Vuilleumier N, et al. Insights into household transmission of SARS-CoV-2 from a population-based serological survey. Nat Commun. 2021;12(1).
140. Ramírez Varela A, Contreras-Arrieta S, Tamayo-Cabeza G, Salas Zapata L, Caballero-Díaz Y, Hernández Florez LJ, et al. Risk factors for SARS-CoV-2 transmission in close contacts of adults at high risk of infection due to occupation: results from the contact tracing strategy of the CoVIDA epidemiological surveillance study in Bogotá, Colombia, in 2020-2021. BMJ Open. 2022;12(12):e062487.
141. Bullerdiek J, Reisinger E, Rommel B, Dotzauer A. ABO blood groups and the risk of SARS-CoV-2 infection. Protoplasma. 2022;259(6):1381–95.
142. Ambrosioni J, Blanco JL, Reyes-Urueña JM, Davies MA, Sued O, Marcos MA, et al. Overview of SARS-CoV-2 infection in adults living with HIV. Lancet HIV. 2021;8(5):e294–305.

143. World Organisation for Animal Health. Guidelines for Working with Free-Ranging Wild Mammals in the Era of the COVID-19 Pandemic [Internet]. [cited 2023 Jun 21]. Available from: https://www.woah.org/app/uploads/2021/12/a-whsg-and-oie-covid-19-guidelines.pdf

144. Delahay RJ, de la Fuente J, Smith GC, Sharun K, Snary EL, Flores Girón L, et al. Assessing the risks of SARS-CoV-2 in wildlife. One Health Outlook. 2021;3:7.

145. WCSNewsroom. WCS fact sheet: big cats, SARS-CoV-2 and COVID-19. [Internet]. [cited 2023 Jun 20]. Available from: https://newsroom.wcs.org/News-Releases/articleType/ArticleView/articleId/14048/WCS-Fact-Sheet-BIG-CATS-SARS-COV-2-AND-COVID-19.aspx

146. Zoo and Aquarium All Hazards Partnership. Updated guidance for working around non-domestic felid species during the COVID-19 pandemic [Internet]. [cited 2023 Jun 20]. Available from: https://zahp.org/updated-guidance-for-working-around-non-domestic-felid-species-during-the-covid-19-pandemic/

147. World Organisation for Animal Health. Preparedness and Resilience Department. Considerations on monitoring SARS-CoV-2 in animals [Internet]. [cited 2023 Jun 21]. Available from: https://www.woah.org/app/uploads/2022/08/en-sars-cov-2-surveillance.pdf

148. Joffrin L, Cooreman T, Verheyen E, Vercammen F, Mariën J, Leirs H, et al. SARS-CoV-2 surveillance between 2020 and 2021 of all mammalian species in two Flemish zoos (Antwerp Zoo and Planckendael Zoo). Vet Sci. 2023;10(6):382.

149. Tyson GB, Jones S, Logan N, McDonald M, Marshall L, Murcia PR, et al. SARS-CoV-2 seroprevalence and cross-variant antibody neutralization in cats, United Kingdom. Emerg Infect Dis. 2023;29(6):1223–7.

150. Naderi S, Chen PE, Murall CL, Poujol R, Kraemer S, Pickering BS, et al. Zooanthroponotic transmission of SARS-CoV-2 and host-specific viral mutations revealed by genome-wide phylogenetic analysis. Elife. 2023;12:e83685.

151. Maurya R, Mishra P, Swaminathan A, Ravi V, Saifi S, Kanakan A, et al. SARS-CoV-2 mutations and COVID-19 clinical outcome: mutation global frequency dynamics and structural modulation hold the key. Front Cell Infect Microbiol. 2022;12:868414.

152. Oude Munnink BB, Sikkema RS, Nieuwenhuijse DF, Molenaar RJ, Munger E, Molenkamp R, et al. Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans. Science (1979). 2021;371(6525):172–7.
153. Hammer AS, Lauge Quaade M, Bruun Rasmussen T, Fonager J, Rasmussen M, Mundbjerd K, et al. SARS-CoV-2 transmission between mink (Neovison vison) and humans, Denmark. Emerg Infect Dis. 2021;27(2):547–51.
154. Adisasmito WB, Almuhairi S, Behravesh CB, Bilivogui P, Bukachi SA, Casas N, et al. One Health: A new definition for a sustainable and healthy future. PLoS Pathog. 2022;18(6):e1010537.
155. Ellwanger JH, Chies JAB. Zoonotic spillover and emerging viral diseases – time to intensify zoonoses surveillance in Brazil. Braz J Infect Dis. 2018;22(1):76–8.
156. Kuchipudi S V., Tan C, van Dorp L, Lichtveld M, Pickering B, Bowman J, et al. Coordinated surveillance is essential to monitor and mitigate the evolutionary impacts of SARS-CoV-2 spillover and circulation in animal hosts. Nat Ecol Evol. 2023;
157. Nielsen SS, Alvarez J, Bicout DJ, Calistri P, Canali E, Drewe JA, et al. SARS-CoV-2 in animals: susceptibility of animal species, risk for animal and public health, monitoring, prevention and control. EFSA Journal. 2023;21(2):7822.
158. Gass JD, Waite KB, Hill NJ, Dalton KR, Sawatzki K, Runstadler JA, et al. A standardized instrument quantifying risk factors associated with bi-directional transmission of SARS-CoV-2 and other zoonotic pathogens: The COVID-19 human-animal interactions survey (CHAIS). One Health. 2022;15:100422.
159. Duvignaud A, Lhomme E, Pistone T, Onaisi R, Sitta R, Journot V, et al. Home treatment of older people with symptomatic SARS-CoV-2 infection (COVID-19): A structured summary of a study protocol for a multi-arm multi-stage (MAMS) randomized trial to evaluate the efficacy and tolerability of several experimental treatments to reduce the risk of hospitalisation or death in outpatients aged 65 years or older (coverage trial). Trials. 2020;21(1):846.
160. Urwyler P, Charitos P, Moser S, Heijnen IAFM, Trendelenburg M, Thoma R, et al. Recombinant human C1 esterase inhibitor (conestat alfa) in the prevention of severe SARS-CoV-2 infection in hospitalized patients with COVID-19: A structured summary

of a study protocol for a randomized, parallel-group, open-label, multi-center pilot trial (protect-COVID-19). Trials. 2021;22(1):1.

161. Brakenhoff TB, Franks B, Goodale BM, van de Wijgert J, Montes S, Veen D, et al. A prospective, randomized, single-blinded, crossover trial to investigate the effect of a wearable device in addition to a daily symptom diary for the remote early detection of SARS-CoV-2 infections (COVID-RED): a structured summary of a study protocol for a randomized controlled trial. Trials. 2021;22(1):412.
162. Ballering A V., van Zon SKR, olde Hartman TC, Rosmalen JGM. Persistence of somatic symptoms after COVID-19 in the Netherlands: an observational cohort study. The Lancet. 2022 Aug 6;400(10350):452–61.
163. Centers for Disease Control and Prevention. Post–COVID conditions among adult COVID-19 aurvivors aged 18–64 and ≥65 years — United States, March 2020–November 2021 [Internet]. [cited 2023 Jun 25]. Available from: https://www.cdc.gov/mmwr/volumes/71/wr/mm7121e1.htm?s_cid=mm7121e1_w
164. Yong SJ. Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. Infect Dis. 2021;53(10):737–54.
165. Torjesen I. COVID-19: Omicron may be more transmissible than other variants and partly resistant to existing vaccines, scientists fear. BMJ. 2021;375:n2943.
166. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev. 2021;10(1):89.
167. World Organisation for Animal Health. WAHIS: World Animal Health Information System [Internet]. [cited 2023 Jun 25]. Available from: https://wahis.woah.org/#/home
168. Institute of Medicine. Finding what works in health care: Standards for systematic reviews [Internet]. Eden J, Levit L, Berg A, Morton S, editors. Washington, DC: The National Academies Press; 2011. Available from: https://nap.nationalacademies.org/catalog/13059/finding-what-works-in-health-care-standards-for-systematic-reviews
169. Cochrane Training. Cochrane handbook for systematic reviews of interventions [Internet]. [cited 2023 Jun 20]. Available from: https://handbook-5-1.cochrane.org/chapter_8/8_2_2_risk_of_bias_and_quality.htm

5 List of tables and figures