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First expert elicitation of knowledge on drivers of emergence of the COVID-19 in pets

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Abstract

Infection with the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) induces the coronavirus infectious disease 19 (COVID-19). Its pandemic form in human population and its probable animal origin, along with recent case reports in pets, make drivers of emergence crucial in domestic carnivore pets, especially cats, dogs and ferrets. Few data are available in these species; we first listed forty-six possible drivers of emergence of COVID-19 in pets, regrouped in eight domains (i.e. pathogen/disease characteristics, spatial-temporal distance of outbreaks, ability to monitor, disease treatment and control, characteristics of pets, changes in climate conditions, wildlife interface, human activity, and economic and trade activities). Secondly, we developed a scoring system per driver, then elicited scientific experts ($N = 33$) to: (a) allocate a score to each driver, (b) weight the drivers scores within each domain and (c) weight the different domains between them. Thirdly, an overall weighted score per driver was calculated; drivers were ranked in decreasing order. Fourthly, a regression tree analysis was used to group drivers with comparable likelihood to play a role in the emergence of COVID-19 in pets. Finally, the robustness of the expert elicitation was verified. Five drivers were ranked with the highest probability to play a key role in the emergence of COVID-19 in pets: availability and quality of diagnostic tools, human density close to pets, ability of preventive/control measures to avoid the disease introduction or spread in a country (except treatment, vaccination and reservoir(s) control), current species specificity of the disease-causing agent and current knowledge on the pathogen. As scientific knowledge on the topic is scarce and still uncertain, expert elicitation of knowledge, in addition with clustering and sensitivity analyses, is of prime importance to prioritize future studies, starting from the top five drivers. The present methodology is applicable to other emerging pet diseases.

KEYWORDS

carnivores, clustering analysis, COVID-19, drivers, expert elicitation, pets, SARS-CoV-2, sensitivity analysis

1 | INTRODUCTION

At the end of December 2019, a cluster of undiagnosed human pneumonia cases, centred on the city of Wuhan (Hubei region), China, was reported (Huang, 2020). Most of these cases were related to a seafood and live animal (including wild animals) market (Xu et al., 2020). They presented clinical and epidemiological characteristics compatible with the severe acute respiratory syndrome (SARS) (ECDC, 2020). The aetiological agent was identified either directly from patient samples, or from virus cultures grown from patients hospitalized with pneumonia in Wuhan, using high-throughput sequencing. This agent was identified as an unknown β -coronavirus genetically close to SARS-CoV and named SARS-CoV-2 (Coronaviridae Study Group of the International Committee on Taxonomy of Viruses, 2020). The associated disease was named 'COVID-19', for coronavirus disease-2019 (WHO, 2020a). Genetic proximity analyses with known sequences of other coronaviruses indicated that this virus originated in the animal world, that is from chiropterans, considered as an animal reservoir (bats), with possible passage through an intermediate host which was initially suspected to be the pangolin (*Manis javanica*) (Liu et al., 2020).

SARS-CoV-2 is the seventh coronavirus known to infect humans, and a zoonotic virus such as SARS-CoV and MERS-CoV (Mackenzie & Smith, 2020) (Appendix S1). Direct contact, rather than airborne spread, seems to be the main transmission route for SARS-CoV-2 according to contact-tracing studies (Bi et al., 2020; Burke et al., 2020). Evidence indicates that SARS-CoV-2 is transmitted from human-to-human by infectious droplets, that is particles $>5\text{--}10\ \mu\text{m}$ in diameter (Federation of European Heating, Ventilation and Air Conditioning Associations, 2020). Potential airborne transmission (by droplet nuclei, which are generally considered to be particles $<5\ \mu\text{m}$) was evidenced by past studies for SARS-CoV (Booth et al., 2005; Xiao, Li, Wong, & Hui, 2017; Yu, Qiu, Tse, & Wong, 2014) and more recently for both SARS-CoV and SARS-CoV-2 in experimental conditions (van Doremalen et al., 2020). Additionally, faeco-oral (Cai et al., 2020; Peng et al., 2020; Wang et al., 2020; Woelfel et al., 2020; World Health Organization, 2020b; Wu et al., 2020) and ocular (Dockery, Rowe, Murphy, & Krzystolik, 2020) transmission should also be considered.

Due to the above-mentioned transmission characteristics, the SARS-CoV-2 spread very quickly across China and worldwide since its first appearance (Wu & McGoogan, 2020). As of 30 June 2020, a total of 213 countries or territories have been affected by COVID-19 worldwide, with approximately 10.5 million human cases (including 500,000 deaths) (<https://www.worldometers.info/coronavirus/>). The transmission dynamic of a disease is generally estimated by the calculation of the basic reproductive number, the so-called R_0 . In absence of control measures, the R_0 is the number of individuals that become infected after the arrival of a primary infected individual in a fully susceptible (naive) population. During the COVID-19 pandemic, and based on 21 estimates, the R_0 was between 1.9 and 6.5, including 13 estimates with a R_0 between 2 and 3 (Park, Cook, Lim,

Sun, & Dickens, 2020). This R_0 was generally higher than MERS-CoV (Park, Jung, Kim, & Park, 2018) and pandemic influenza (Biggerstaff, Cauchemez, Reed, Gambhir, & Finelli, 2014) but of similar magnitude to the previous SARS-CoV (Lipsitch et al., 2003; Riley et al., 2003), indicating a risk of global spread (Riou & Althaus, 2020). However, the R_0 is strongly influenced by mitigation measures (mainly effective physical distancing, quarantine and contact tracing) and needs to be less than one to stop the disease spread (Brebant, Riou, & Fontanet, 2013).

Recently, there have been reported cases in felids (cats, tigers), canids (dogs) and with possible high seroconversion (e.g. Zhang et al., 2020; Almendros, 2020; Almendros & Gascoigne, 2020; American Veterinary Medical Association., 2020). Furthermore, recent experimental infections indicate a particular susceptibility of bats, cats and ferrets (Beer, 2020; Shi et al., 2020; Sit et al., 2020; Young-II et al., 2020). Farmed minks (*Neovison vison*) also tested positive to the virus in the Netherlands in April 2020 (Oreshkova et al., 2020) and in Denmark in June 2020 (ProMED-mail, 2020).

Despite the few cases reported (until now reporting of animal COVID-19 is not mandatory in many countries), in comparison with the scale of infection in the human population, these observations in animals have provoked some violent reactions towards dogs and cats such as the panic abandonment of them (Leroy, Ar Gouilh, & Brugère-Picoux, 2020; Qiao, Xiang, & Xian-Tao, 2020).

The pandemic form of COVID-19 in human population and its probable animal origin and the recent serial of reported cases in pets poses the question of what are the drivers of COVID-19 emergence in carnivore domestic pets, specifically cats, dogs and ferrets, as they are close companions to humans and the main pet in the household. Currently, there are no published articles regarding the drivers of disease emergence in animals, with the exception of the recent study in livestock animals (Bianchini et al., 2020).

Indeed, the aim of this study was to list, rank and cluster drivers of COVID-19 emergence in pets, using elicitation of experts' knowledge on each driver and on the relative importance between drivers, in a specific domain of interest, and between these domains.

2 | MATERIALS AND METHODS

2.1 | Species of pets included

The objective was to prioritize the drivers of COVID-19 in domestic carnivore pets. Using the following algorithms ((COVID-19) AND ((2019) OR (2020))), and ((COVID-19) AND (Pets)), search strings were conducted in PubMed (US National Library of Medicine, National Institutes of Health) and ProMED-mail (Program for Monitoring Emerging Diseases of the International Society for Infectious Diseases). The results of the search showed that cats, dogs and ferrets were the domestic carnivore pets with most mentions in the articles, and thus, here the question was drivers for the emergence of COVID-19 in these species of domestic carnivore pets. There was a big difference in the ratio between articles exclusively on 'COVID-19 and pets' and

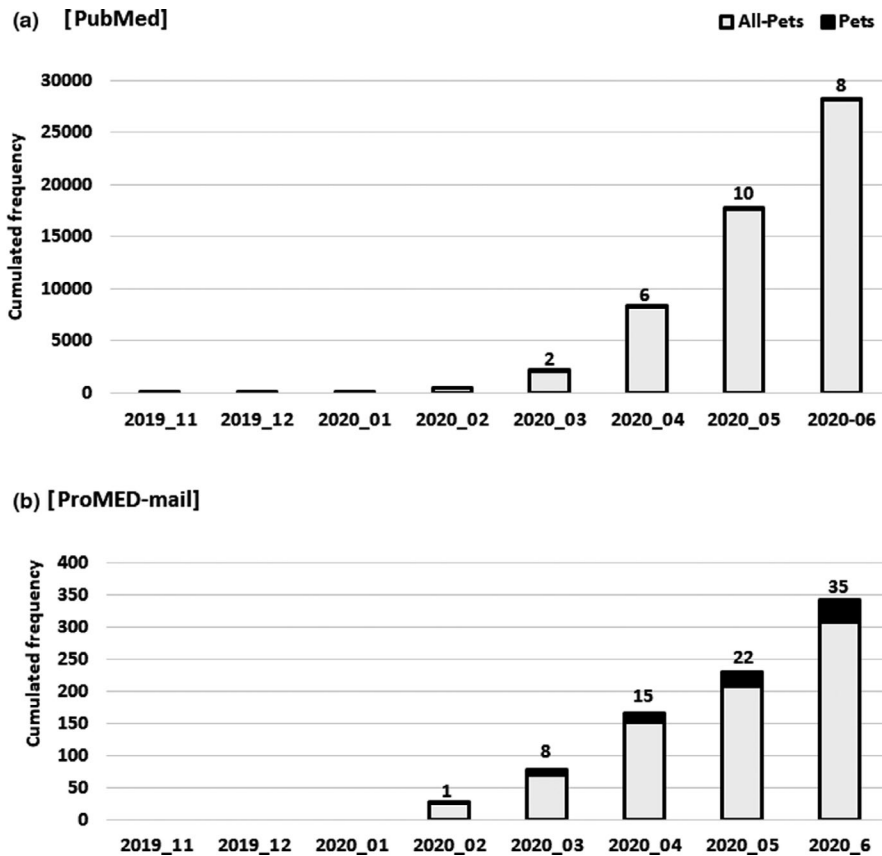


FIGURE 1 Cumulated frequency of pet-related and non-pet-related COVID-19 publications, in PubMed [a] and ProMED-mail [b]. All-pets = all publications on COVID-19 without pet-related publications; Pets = exclusively pet-related publications on COVID-19. Numbers represent the cumulated frequency for pet-related publications

'COVID-19 without pets' (Figure 1). The ratios were 0.00028 and 0.128 for PubMed and ProMED-mail, respectively, at 21 May 2020.

2.2 | Questionnaire design

To determine which are the main drivers of COVID-19 emergence in pets, a questionnaire was used. A driver was defined as a factor that has the potential to directly or indirectly precipitate ('drive') or lead to the emergence of COVID-19 in carnivore domestic pets. A former questionnaire made to rank re-emergence of animal diseases based on drivers (Bianchini et al., 2020) was modified and adjusted for COVID-19 in pets. For this, specific drivers of COVID-19 were identified by searching through the available scientific literature and discussion with experts from academia, government agencies and international bodies. These were then added into the questionnaire, or some other drivers were deleted from it as they were not considered pertinent. Finally, a total of forty-six drivers were established and classified in eight different domains (Table 1). The domains (D) were as follows: (D1) pathogen/disease characteristics ($N = 9$ drivers); (D2) distance of outbreaks (spatial-temporal scales) ($N = 3$ drivers); (D3) ability to monitor, treat and control the disease ($N = 7$ drivers); (D4) characteristics of pets ($N = 7$ drivers); (D5) changes in climate conditions ($N = 3$ drivers); (D6) wildlife interface ($N = 6$ drivers); (D7) human activity ($N = 6$ drivers); and (D8) economic and trade activities ($N = 5$ drivers).

These were formatted in an Excel® (Microsoft, Redmond, WA, USA, 2013) file with one spreadsheet per domain, each domain with the respective drivers. Each driver had a score with its definition, which could

range from 0 to 4 or 1 to 4 and a cell to be given the intra driver weight point. A last spreadsheet was added, in which the 8 domains were listed, with a cell to be given the inter-domain weight (Appendix S2).

2.3 | Expert elicitation on drivers used to assess the emergence of COVID-19 in pets

An expert elicitation of knowledge was conducted, which consisted in gathering the opinion of people with recognized scientific expertise and/or experience in the field of COVID-19 in pets (Appendix S3). For guidance purposes, an explanatory letter accompanied the questionnaire that each expert had to fill out (Appendix S4). The questionnaire was prepared as an Excel file based on Appendix S2.

Each expert was contacted personally and responded individually to the questionnaire. Data generated by the elicitation were based on the individual values provided by experts in order to capture the degree of variability of expert knowledge. The elicitation was performed from 24 April 2020 to 15 May 2020.

2.4 | Scoring and weighting system

The elicited experts were asked to provide three types of information. First, they were asked to score the driver (as established in Appendix S2). For each driver, higher is the score more the driver has a chance to contribute to the emergence of the COVID-19 in pets.

TABLE 1 Forty-six drivers of emergence of COVID-19 in pets including in eight different domains of interest

D1. Disease/pathogen characteristics
D1-1. Current knowledge of the pathogen
D1-2. The current species specificity of the disease-causing agent
D1-3. Genetic variability of the infectious agent
D1-4. Transmission of the agent in relation with the possible spread of the epidemic or pandemic (i.e. ease/speed of spread)
D1-5. Risk of showing no clinical signs and silent spread during infection and post-infection
D1-6. Wildlife reservoir and potential spread from it
D1-7. Existence of vectors (vertebrate and invertebrate, e.g. mosquitoes, bats, rodents, ticks, midges, culicoides) and potential spread.
D1-8. Transmission of the pathogen.
D1-9. Environmental persistence
D2. Distance from your country
D2-1. Current incidence (cases)/prevalence of the disease in the world
D2-2. European geographic proximity of the pathogen/disease to Belgium
D2-3. To your knowledge when was the disease last reported in Europe
D3. Ability to monitor, treat and control the disease
D3-1. Ability of preventive/control measures to stop the disease from entering the country or spreading (containment of the epidemic/pandemic), EXCEPT FOR treatment, vaccination and vector(s)/reservoir(s) control
D3-2. Vaccine AVAILABILITY
D3-3. Control of reservoir(s) and/or vector(s)
D3-4. Availability and quality of diagnostic tools
D3-5. Disease is currently under surveillance overseas (OIE, EU)
D3-6. Eradication experience in other countries
D3-7. Detection of emergence—for example difficulties for the pet owner/veterinarian to declare the disease or clinical signs not so evident
D4. Pets characteristics
D4-1. Monospecies – One single pet (e.g. only cats) or multi species (house with more than one species e.g. cats and dogs in the same house)
D4-2. Pet demography/management, such as type of pets
D4-3. Animal density of pets in a same place (e.g. house), for example owners with single pet versus owners with many pets (group housing)
D4-4. Feeding practices of pets (e.g. raw meat feeding)
D4-5. Human density close to pets (consider the possibility that human can be the source of infection for zoonotic diseases)
D4-6. Proximity of pets to wildlife and wildlife reservoirs of disease, for example contact with wild or feral birds and animals which have been scavenging on landfill sites that contain contaminated animal products
D4-7. Changes of land use, for example field fragmentation, creation of barriers, landfill sites

(Continues)

TABLE 1 (Continued)

D5. Changes in climate conditions
D5-1. Influence of annual rainfall in the survival and transmission of the pathogen/disease
D5-2. Influence of annual humidity in the survival and transmission of the pathogen/disease
D5-3. Influence of annual temperature in the survival and transmission of the pathogen/disease
D6. Wildlife interface
D6-1. Potential roles of zoo's in the (re)emergence of the pathogen
D6-2. Pet-wildlife interface
D6-3. Increase of autochthon (indigenous animal) wild mammals in Belgium and neighbouring countries
D6-4. Increase in endemic/migrating populations of wild birds
D6-5. Hunting activities; hunted animals can be brought back to where pets are present
D6-6. Transboundary movements of terrestrial wildlife from other countries
D7. Human activities
D7-1. In- and out-people movements linked to tourism
D7-2. Human Immigration
D7-3. Transport movements, more specifically commercial flights, commercial transport by ships, cars or military (excluding transport vehicles of live animals)
D7-4. Transport vehicles of pets
D7-5. Bioterrorism potential
D7-6. Inadvertent release of an exotic infectious agent from a containment facility, for example Laboratory
D8. Economy and Trade Activities
D8-1. Decrease of resources allocated to the disease surveillance
D8-2. Modification of the disease status (i.e. reportable disease becoming not reportable) or change in screening frequency due to a reduced national budget
D8-3. Decrease of resources allocated to the implementation of biosecurity measures at border controls (e.g. harbours or airports)
D8-4. Most likely influence of (il)legal movements of live pets from neighbouring/European Union member states (MS) for the disease to (re)emerge
D8-5. Most likely influence of (il)legal movements of pets from Third countries for the disease to (re)emerge

Note that uncertainty score was not asked due to lack of evidence-based data at this stage regarding the COVID-19 in pets. Secondly, experts were requested to weight each driver within a specific domain (intra-domain weight). This relative weight was determined using the Las Vegas technique (Gore, 1987). Briefly, experts were given a number of points to be distributed between the drivers according to their importance in the specific domain. If all the drivers of a specific domain would have been considered as equivalent by experts, each of them would have received the same number of points. Lastly, the relative importance of each domain was subsequently weighted by experts (inter-domain weight).

2.5 | Calculation of an overall weighted score for each driver and ranking process

To obtain the overall score per driver, an aggregation method that combined the two types of weighting (i.e. the intra and inter-domain) was used. First, the driver score (coefficients attributed by experts) was standardized by dividing it by the number of possibilities. Indeed, some drivers were allocated coefficients from 0 to 4 (5 possibilities) and others from 1 to 4 (4 possibilities). Afterwards, this standardized score was multiplied by the intra-domain weight and the inter-domain weight, as given by the expert. These results allowed obtaining an overall weighted score for each driver and per expert:

$$OWS_{Dri} = SDr_i \times WDr_i \times WDo_j \quad (1)$$

In this formula, OWS_{Dri} = overall weighted score for a specific driver_{*i*}; SDr_i = standardized score for a specific driver_{*i*}; WDr_i = intra-domain weight for a specific driver_{*i*}; WDo_j = inter-domain weight for a specific driver_{*i*} included in a specific domain_{*j*}.

Furthermore, all drivers were ranked based on the median overall weighted score obtained for each driver and taking into account the answers of all the experts, which answered the questionnaire.

The statistical difference of the median, depending of the specific driver or the group of drivers considered, was assessed through a non-parametric Kruskal-Wallis equality-of-populations rank test (State SE 14.2; StataCorp).

2.6 | Cluster analysis

A cluster analysis was done using a regression tree analysis (Salford Predictive Modeler[®], Version 8.2, Salford Systems). The median overall weighted score (median OWS_{Dri}) being a continuous variable, the aim was to obtain groups of drivers with minimal within-group variance, with comparable likelihood to play a role in the emergence of COVID-19 in pets (e.g. very high importance, high importance, moderate importance and low importance). In addition, the statistical difference between medians after grouping drivers in clusters was assessed using a non-parametric Kruskal-Wallis equality-of-populations rank test. Indeed, each driver is characterized by a median (based on all experts' answers), and then, drivers are grouped. The test allows highlighting potential significant differences between groups, in terms of driver medians, after clustering.

2.7 | Sensitivity analysis to test the robustness of the expert elicitation

In order to identify whether the ranking of COVID-19 drivers of emergence in pets was influenced or not by the choice of experts, a sensitivity analysis was performed.

First, we started by ranking the drivers using the obtained median OWS_{Dri} . Second, an expert was not considered in the analysis and the ranking of the drivers was done using the same methodology previously described. This was done expert by expert. Third, we counted how many changes in the ranking were observed, for each driver, only considering changes of more than five ranks (i.e. around 10% of all drivers). A graph was created to visualize any modification of rank induced by the withdrawal of a given expert.

3 | RESULTS

3.1 | Response rate and field of expertise mobilized by the experts

From the 46 professionals regarded as having scientific knowledge and/or proven field knowledge or experience on COVID-19 in pets that were contacted, 33 of them agreed to participate (77% response rate) with a balance between male ($N = 18$) and female ($N = 14$). The field of expertise was summarized in Appendix S3.

3.2 | Estimating the overall weighted score and ranking of drivers of COVID-19 emergence in pets

According to the non-parametric Kruskal-Wallis test, the medians of the weight between domains of drivers are not equal (chi-squared test = 114 with 7 *df* and $\alpha = 0.05$; p -value = .0001) (Figure 2).

Moreover, according to the non-parametric Kruskal-Wallis test, the medians of the overall weighted scores for the different drivers are not equal (chi-squared test = 772 with 45 *df* and $\alpha = 0.05$; p -value = .0001). Five of them were ranked as having the highest probability to play a key role in the emergence of COVID-19 in pets. These were in decreasing order: 'availability and quality of diagnostic tools', 'human density close to pets', 'ability of preventive/control measures to stop the disease from entering the country or spreading (except for treatment, vaccination and reservoir(s) control)', 'current species specificity of the disease-causing agent' and 'current knowledge on the pathogen' (Figure 3).

3.3 | Cluster analysis

The regression tree analysis determined four clusters (Figure 4) that were significantly different (non-parametric Kruskal-Wallis equality-of-populations rank test; chi-squared test = 38.7 with 3 *df* and $\alpha = 0.05$; p -value = .0001). These four clusters were classified as, respectively 'low importance' with 22 drivers, 'moderate importance' with 14 drivers, high importance and very high importance each with 5 drivers each. The drivers in the 'very high importance' node are the five highest ranked, mentioned in the previous paragraph.

3.4 | Sensitivity analysis of the impact of experts on the final ranking of COVID-19 drivers of emergence in pets

The result of the sensitivity analysis indicated that ignoring any expert had only a limited effect on the ranking of drivers (Figure 5). However, a change of maximum six ranks was observed for the driver D1-8 (i.e. mode of transmission of the SARS-CoV-2) when four experts were ignored (represented by the number of crosses in Figure 5). In the overall ranking, this driver ranks in the middle. In addition, they are no or very few changes of ranks in the extremes (first and last drivers) of the initial ranking.

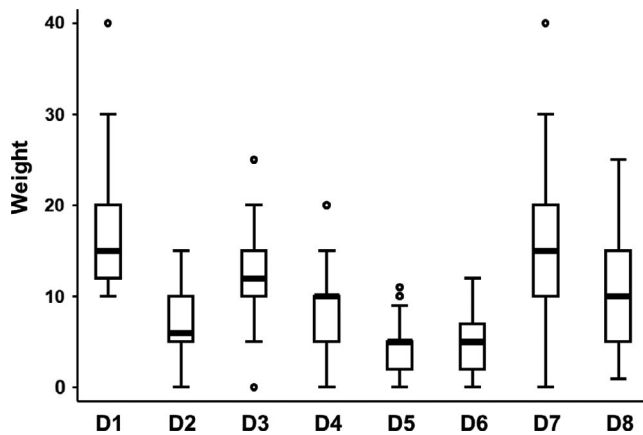


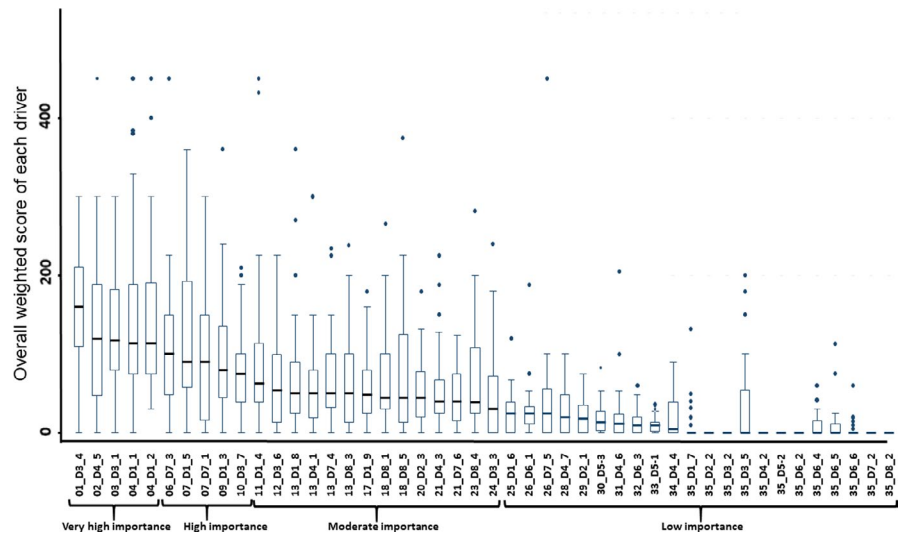
FIGURE 2 Boxplot of the relative importance of the eight domains of COVID-19 drivers of emergence in pets (N = 33 experts). The dashed line represents the median of the score distribution between the different experts; the solid lines below and above each rectangle represent, respectively, the first and the third quartiles; adjacent lines to the whiskers represent the limits of the 95% confidence interval; small circles represent outside values. The eight domains of drivers are as follows: D1, pathogen/disease characteristics; D2, distance of outbreaks (spatial-temporal scales); D3, ability to monitor, treat and control the disease; D4, pets characteristics; D5, changes in climate conditions; D6, wildlife interface; D7, human activity; and D8, economic and trade activities

4 | DISCUSSION

According to this expert elicitation of knowledge, forty-six drivers of COVID-19 emergence in carnivore domestic pets (cats, dogs and ferrets) were ranked and aggregated into four homogenous groups. The first group of drivers categorized in the ‘very high importance’ node will be further discussed and it includes in decreasing order: availability and quality of diagnostic tools, human density close to pets, ability of preventive/control measures to stop the disease from entering the country or spreading (except for treatment, vaccination and reservoir(s) control), current species specificity of the disease-causing agent and current knowledge on the pathogen. The sensitivity analysis indicated a limited effect of the experts involved in the elicitation, which shows that there is an acceptable robustness of the elicitation.

Considering as the highest driver of emergence of COVID-19 in pets, the availability and quality of diagnostic tools of COVID-19 infection in pets seemed to be critical (driver: D3-4). Currently, diagnostic tests are only available in specialized laboratories, for example polymerase chain reaction assay (PCR), virus neutralization assay (VNT), microsphere immunoassay (MIT), enzyme-linked immunosorbent assay (ELISA) (e.g. Sailleau et al., 2020; Zhang et al., 2020). Indeed, the capacity to confirm a suspected case is very limited. Some of these laboratories are also often prioritize to diagnose human cases of COVID-19 and not animal cases. The PCR assay allows the specific detection of SARS-CoV-2 RNA and helps finding the source of infection (e.g. subsequent phylogenetic tree). Addition of serological assays would allow differentiating between environmental contamination (PCR positive and serological test negative) and (transient) infection (PCR positive or negative depending of the stage of infection but serological test positive) in pets. Another aspect is the usefulness to collect and share the different information on pets at national and international levels to be able to assess properly the true status of pets in the transmission of the COVID-19, based on evidence, and to guide both risk management and risk communication under the One Health approach. This is particularly important to avoid any inadequate behaviour of owners like

FIGURE 3 Ranking of the overall weighted score for each potential COVID-19 driver of emergence in pets (Boxplot based on 33 experts). X-axis represents the drivers with the following codification: D1 to D8 refer to the eight domains of drivers and D1_1 to D8_5 refer to a specific driver (for the codification, see Table 1). Relation to Figure 4 was provided by the group named as, respectively, ‘very high’, ‘high’, ‘moderate’ and ‘low’ importance of the COVID-19 drivers of emergence in pets



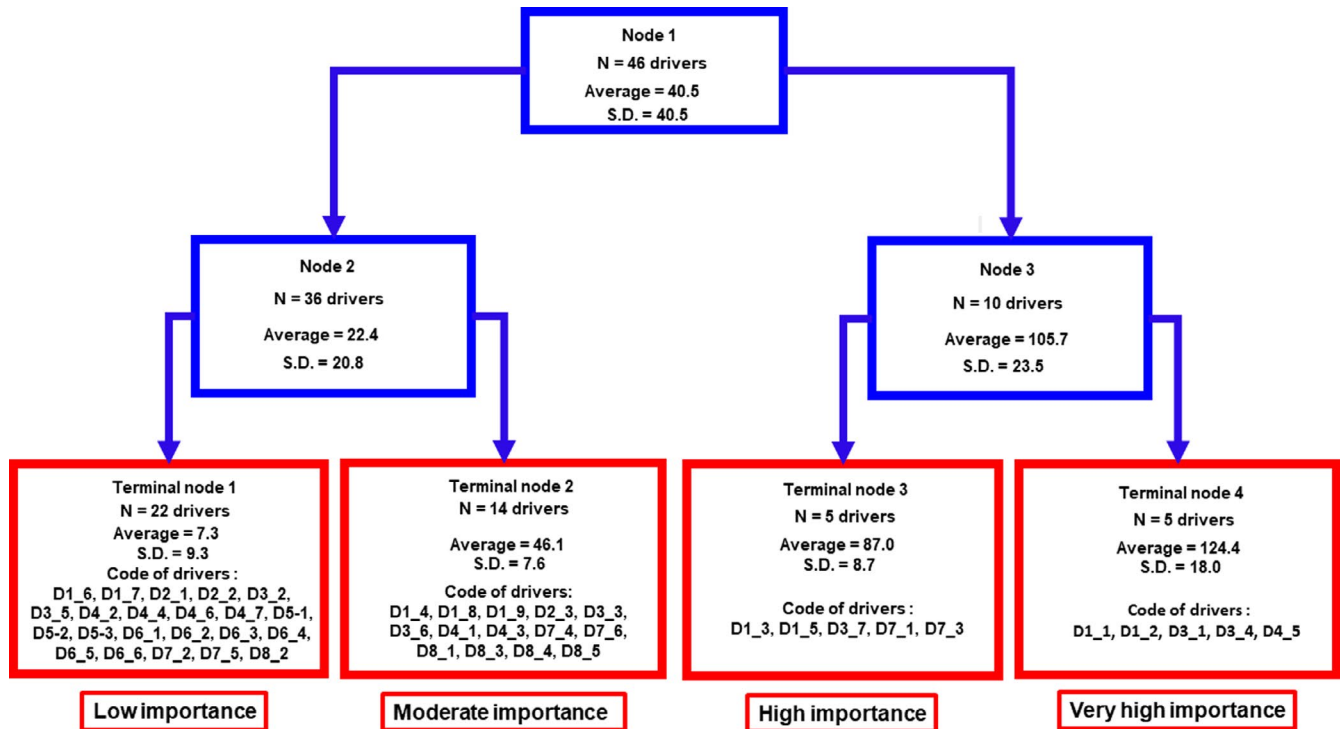


FIGURE 4 Aggregation of COVID-19 drivers of emergence in pets into four homogenous groups using a regression tree analysis. N, number; SD, standard deviation

panic abandonment of household pets. Recently, the OIE published guidelines for pet sampling (based on epidemiological contexts, for example close contact with a suspected or confirmed SARS-CoV-2-infected patient, or animal exposed to a known high-risk environment, and clinical presentation, for example clinical signs suggestive of SARS-CoV-2 infection), testing (based on validated tests, suitable for its intended use, which is essential when testing different species due to possible variation in sensitivity and specificity), and reporting of SARS-CoV-2 in animals (OIE, 2020). In addition, according to the Terrestrial Animal Health Code, the notification of COVID-19 cases in animals should be reported to the OIE as an emerging disease through the World Animal Health Information System (WAHIS).

The second most important driver was the human density close to pets (driver: D4-5). Indeed, humans have a strong effect on the introduction and spread of COVID-19 in pets. In Europe, at least 80 million households own at least one pet and the number of cats and dogs accounts for 103,828,000 and 85,184,000 heads, respectively. Around 25% of owners have at least one cat and 25%, one pet (FEDIAF, 2019). This percentage is not homogeneous and large disparities exist depending of the region for a same country. As an example, this percentage is higher in the Southern part (around 33%—more rural part) than in the Northern part (around 25%) of Belgium. No data on households with ferret are available at national level despite its important experimental susceptibility regarding the SARA-CoV-2. However, more studies are needed to assess properly the human density close to pets in Europe, in particular species by species (Aegerter, Fouracre, & Smith, 2017; Studer et al., 2019).

The third most important driver was the ability of preventive/control measures to stop the disease from entering the country or spreading (containment of the pandemic), except for treatment, vaccination and reservoir(s) control (driver: D3-1). Most experts mentioned the current lack of sanitary certification, incomplete traceability of animals, ineffective disinfection measures, incomplete restriction of contacts between pets and wild animals and ineffective biosecurity measures. The main present interest of this driver is that the more human infection will be limited, and the more risks of pet infections by humans will be reduced. Moreover, reporting of all confirmed COVID-19 infections of pets should be mandatory. Additionally, several initiatives need to be emphasized to improve the situation like the OIE guidelines for sampling, testing and reporting of SARS-CoV-2 in animals (OIE, 2020) and several pet management recommendations given by national (e.g. Académie Nationale de Médecine, 2020) or international (e.g. American Veterinary Medical Association., 2020) expert committees. More evidence-based information and protocols should be stimulated and shared.

The fourth most important driver was the current species specificity of the disease-causing agent (driver: D1-2). The number of pet species susceptible to SARS-CoV-2 is not yet completely elucidated (OIE, 2020) but according to field studies, animals such as cats, dogs, ferrets, tigers, minks and small rodents have been identified as susceptible (e.g. Zhang et al., 2020; Almendros, 2020; Almendros & Gascoigne, 2020; American Veterinary Medical Association., 2020; van der Poel, 2020).

In addition, experimental infections indicate a particular susceptibility of bats, cats and ferrets (Beer, 2020; Sit et al., 2020;



FIGURE 5 Sensitivity analysis according to the experts. The diagram visualizes any modification in the rank of COVID-19 drivers of emergence in pets induced by the withdrawal of a given expert's input. X, crosses represent the cut-off of more than five ranks between different steps. Withdrawal of experts have little effect on the ranking. X-axis represents the expert considered: All, all experts; All-Exp1 to All-Exp33 all, experts minus the first (Exp1), the second (Exp2), until the last (Exp33). Y-axis represents the ranking of the COVID-19 drivers of emergence in pets, which are presented in Table 1 (i.e. the domain code followed by driver code). Several drivers occupy the same rank because their overall weighted scores are similar

Young-II et al., 2020). The species specificity is related to the aptitude of the coronavirus to interact with the host receptor (Li, 2012). The receptor recognition mechanism of the SARS-CoV-2 regulates, in great part, its infectivity, pathogenesis and host range (Shang et al., 2020). SARS-CoV-2, SARS-CoV and RaTG13 (a bat coronavirus that is closely related to SARS-CoV-2) recognize the same receptor angiotensin-converting enzyme 2 (ACE2) in humans (Li, Li, Farzan, & Harrison, 2005; Li et al., 2003; Shang et al., 2020). However, some specific structural characteristics of the receptor-binding domain (RBD) of SARS-CoV-2 spike protein increase its ACE2-binding affinity (Shang et al., 2020). Differences among the three cited viruses in ACE2 recognition could contribute to explain their differential potentials for animal-to-human transmission, which appears more limited for SARS-CoV-2 and SARS-CoV than for MERS-CoV, but also for human-to-human transmission (conversely more reduced for MERS-CoV than for SARS-CoV-2 & SARS-CoV), and eventually for human-to-animal transmission, which is supposed to occur for SARS-CoV-2 only. With the exception of few works (Bao et al., 2020; Xu et al., 2009), more studies are needed to investigate the ACE2 receptor in various animal species. In addition, other unknown important factors conditioning animal-to-human and/or human-to-animal could deserve to be characterized (McNamara, Richt, & Glickman, 2020).

The fifth most important driver was the current knowledge on the pathogen (driver: D1-1). Scientific knowledge on the SARS-CoV-2 is limited so far because it is still under characterization, even if it belongs to a well-known and studied family of pathogens. The pathogen

includes multiple variants that are not characterized yet. A recent study on SARS-CoV-2 sequences ($N = 95$), from the first 3 months of the pandemic, reveals a beginning of diversification and phylogenetic clustering due to base substitutions and deletions in the genomes. This preliminary result should permit tracing of source infection but such variability could induce differences in virulence or antigenicity, with possible consequence in virulence (implication on population immunity) or antigenicity (implication on the diagnostic) (Kaden, 2020). This variability could also contribute to a change in species barriers, which could contribute to variants more adapted to pets and potentially to retransmission to humans (or to reduced zoonotic potential for these variants). More global studies are needed with good sharing of information to ensure progress in tracing of source infection and the development of accurate vaccines and diagnostic assays.

The methodology that was developed in this paper should be extended to a wide number of other diseases of pets, starting from cats and dogs, the two main species in households (FEDIAF, 2019). In addition, this expert elicitation of knowledge should be refined in the future (some months) when more evidence data will be available. In this case, addition of an uncertainty rate should be recommended during elicitation.

5 | CONCLUSION

The nature of SARS-CoV-2, its wide distribution and the susceptibility of some animal species to infection mean that close contact

between humans and animals can probably induce infections in animals. Since scientific knowledge on COVID-19 drivers of emergence is scarce and associated uncertainty high, expert elicitation of knowledge, in addition with clustering and sensitivity analyses, is of prime importance to prioritize future studies, starting from the top five ranked drivers. The present methodology can also be applied to other pet diseases in pets in order to anticipate decision-making and awareness.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICAL APPROVAL

Due to the nature of the study and the low risk posed to participants, formal approval from an Ethics Committee was not a requirement at the time of the study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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