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Companion Animals in Zoonoses Research – Ethical Considerations

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Abstract

Non-human animals are commonly classified according to their “role”, such as “live-stock”, “wild” or “companion” animals. But what if those classifications overlap? This article presents a report of the retreat week “ZooCan – Zoonoses of companion animals as case study for animal ethics” at the University of Veterinary Medicine Hannover, Germany, in November 2022. The workshop included participants from different European countries with interdisciplinary backgrounds (animal law, bioethics, epidemiology, philosophy, biology and veterinary medicine). We address ethically relevant issues that emerge when companion animals are used as research animals, particularly in zoonoses research. The outcomes of the multi-disciplinary approach are used to i) define criteria to classify “companion” and “research” animals, ii) provide guidance to overcome the challenges with classificational overlaps, iii) give insights into cutting-edge zoonoses research with an example of SARS-CoV-2 in cats, and iv) discuss animal ethics approaches with regard to classifications.

Keywords

animal ethics – companion animals – interdisciplinary research – research animals – zoonoses

1 Introduction

People in Western societies are used to classifying animals according to their relationship to or function for humans, such as “farm animals”, “wild animals”, “research animals”, or “companion animals”. Whilst those classifications overlap on some occasions, Palmer et al. (2022) have emphasized that “relatively little work has focused on the interface between research animals and pets”. The objective of this article is to address ethically relevant issues that emerge when companion animals (who are sometimes referred to as ‘pets’) are used as research animals, with a particular focus on zoonoses research. This article is a joint project of participants in the international and interdisciplinary retreat week “ZooCan – Zoonoses of companion animals as case study for animal ethics”, which took place at the University of Veterinary Medicine, Hannover, Foundation in Hannover, Germany in November 2022, and was funded by the German Federal Ministry of Education and Research. We present the outcome of the discussions held during the retreat week as a foundation for future debates and decision-making processes when it comes to companion animals as research animals. Based on the interdisciplinary nature of the retreat week this article is neither a purely theoretical paper in the humanities nor a typical research report in the natural sciences. Accordingly, some tensions between the participating disciplines (veterinary sciences, animal law, biology, epidemiology, bioethics, philosophy) are not resolved. The fact that such tensions remain underlines the need for interdisciplinary dialogues like ZooCan.

To address our core objectives, we adopt a multi-disciplinary approach to the use of companion animals in (zoonoses) research. We start with a brief overview of what we define as companion and research animals, and clarify cases of companion animals who are used for research. In a further step, public views on those cases will be discussed, in particular, why the use of companion animals as research animals is occasionally questioned or challenged. In addition, we present recent first-hand experiences of using companion animals in zoonotic research, with the example of cats infected by the SARS-CoV-2 virus. Finally, we discuss how approaches in animal ethics developed by Tom Regan (1989), Peter Singer (1990), Mary Midgley (1989), and Ursula Wolf (2018), might

help to guide decision-making processes regarding the use of companion animals for zoonotic research. Although we recognize that human beings are animals, for the sake of simplicity, the concept of ‘animal’ is used here to refer exclusively to non-human animals.

While learning about some examples in zoonosis research outside Europe during the retreat week, the reflections on laboratory work, law, and public perceptions presented here are limited to the European context, given the backgrounds of the workshop participants. When we discuss the views of “the public” we, therefore, acknowledge that there might be further public opinions and attitudes that we do not cover in our discussions as this small group of European scholars cannot access the views of the public across the world.

2 What Are Companion and Research Animals?

Humans use different criteria to classify animals. Besides biological classifications structuring the animal kingdom in, for example, families, orders, and species, legal texts offer different definitions of animals depending on the purposes of the regulations they establish. The legal classifications draw distinctions according to the approach humans have to animals when determining the type of treatment or the level of protection. The legal classification usually reflects the attribution of societal “roles” or “functions”. Referring to an animal as, for example, a “farm animal”, a “watchdog”, a “riding school horse”, or a “companion animal” both influences and is influenced by conventions about the way the animal is taken care of, is attached to humans, or is expected to behave, and how as well as at what stage of life the animal is going to die. The herein presented understandings of “companion animals” and “research animals” are also influenced by these conventions.

Although it has occasionally been suggested that the term “companion animal” should be reserved for explicitly mutually beneficial relationships (Varner, 2002), we decided not to use the formerly common expression “pet” but rather the term “companion animal” for the human-animal relationships that we will discuss below, even for animals who do not have mutually beneficial relationships with human beings. We believe that the term has been established as politically correct also for relationships that are not necessarily mutually beneficial – see, for example, the guidelines of the journal “Society and Animals” (Brill, 2023).

The word ‘companion animal’ refers etymologically to an animal whom one shares one’s bread with. However, this does not fit well with our understanding

of companion animals, since bread is shared with many animal species who do not have close relationships with us, for example, fish in ponds and wild birds. Day's (Day, 2016: 2) definition of "animals, permanently living in a community and kept by people for company, amusement, work ... or psychological support" appears to be reserved for animals with whom we seek to spend a significant amount of time. Accordingly, animals classified as "companion animals" by means of their roles in society are those animals who live with human beings in a manner that is similar to that of family members. This being said, the family relationship with them is not always bidirectional and does not guarantee a social membership that takes into full account their intrinsic value and needs for psycho-physical integrity, but may, in some respects, be based on human dominance and non-human vulnerability (e.g., people often treat their animals anthropomorphically, have an 'instrumental' interpretation of the companionship relationship, and interfere in the lives of animals with drastic and irreversible interventions, such as castration).

In any event, laws in various jurisdictions recognize the societal roles of companion animals (despite variations in legal definitions of a "companion animal"). Species whose members are *prima facie* considered as companion animals include, but are not limited to, canines, felines, equines, budgerigars, and guinea pigs. Companion animals play a dynamic and often stabilizing role within the nuclei they are added to, as they are integrated into daily family routines and emotional family systems (Cain, 1983; Walsh, 2009). It is well-known that companion animals and those who care for them can form strong emotional bonds (Kemp et al., 2016). Several studies have described the almost symbiotic relationships that may arise between humans and companion animals, mutual exchanges of physical and psychological benefits, and anthropomorphism in the breeding of such animals, which causes companion animals to exhibit human-like characteristics (Charles, 2014; Dotson & Hyatt, 2008; Wilkins et al., 2015). An extreme case of anthropomorphic thinking of animals is the selection of races with exaggerated pedomorphic appeal. Think, for example, of the human infant-like facial appearance of brachycephalic dogs, also described as 'kindchenschema' (Paul et al., 2023). Modeling animals 'in our image' may represent a lack of understanding and an inability to promote what is best for them. On the other hand, this perspective may strengthen empathic feelings towards animals. This may lead to humans attributing the role of companion animal to a wide range of animal species. The tendencies to frame animals in human-like and familiar images cause even subjects belonging to species usually classified as "farm animals" or "wildlife" sometimes to be regarded as companion animals.

This framing as companion animals of some animal individuals belonging to species usually not considered as such (e.g., mini-pigs or chickens in private gardens) typifies some contemporary societies. These societies give companion animals special consideration and treat them differently compared to other animals, even those belonging to the same species, for example, those who enter the food chains.

The term “research animal” is used in a broad sense here, including animals bred and kept for research in laboratories (usually referred to as “laboratory animals”), but also those animals who are used for clinical research as research animals temporarily while living otherwise as, for example, farm or companion animals. In the process of designing projects involving animal experiments and applying for funding, researchers have to select animal models for their studies. Factors that may influence the decision how likely it is that some animals are chosen as research animals include: i) physiological relevance compared with human or other species (translational aspects); ii) feasibility of (easy) handling, breeding, and housing; iii) common use in research, which makes studies more easily replicable by other research facilities; iv) public opinions that perceive animals as “vermin” or species that deserve certain protection; iv) and particular physiological, metabolic, genetic, or pathogenic features that researchers are interested in (Birke, 2003).

Whilst the Greek doctor Galen used animals for his research in the second century of the common era (CE), the practice of confining some animals to laboratories in order to use them for medical or veterinary research is largely a more recent phenomenon, taking off from the nineteenth century onwards (Sharpe, 1989). The number of research animals who are currently kept in the world has increased greatly since the twentieth century. The total number can only be estimated, and the estimate depends on the definition of “animal experiments” and on the data sources (Taylor & Alvarez, 2019). More resources are spent on basic research into the biology of animals, on the quest for treatment options, and on studying the course of diseases to improve our understanding about disease development and therapeutic interventions in humans. Whilst this last aspect has been the dominant reason why research animals have been used, it has also been the most controversial (Bates, 2017).

When it comes to the question which animal species are chosen as research animals, the range of species is broad. However, most lab animals are rodents, particularly mice, rats, and fish. In Germany, these species account for 72.2%, 7.3%, and 12.2% of all research animals in 2021, respectively (BfR Bundesinstitut für Risikobewertung). We will refer to these as “typical lab animals”. In spite of the fact that many people classify rats and mice as

'vermin', many also consider these and other furry animals to be cute (see e.g., Edelman, 2020).

3 Individuals in the "Wrong Role"

3.1 *Companion Animals Used for Research*

As pointed out above, classifications of animals into companion animals and research animals are not mutually exclusive. Three scenarios can be distinguished where companion animals are used for research.

Firstly, there are research animals who are bred and kept for the purpose of being laboratory animals but who belong to a group or species of animals that are usually considered companion animals, such as hamsters, cats, dogs, ferrets, or horses. There is anecdotal evidence that not only science-related factors come into play when researchers decide on the use of those animals as research models for particular studies, for example, because researchers must be particularly careful to accommodate public perceptions about acceptability when performing experiments with these species of animals.

Secondly, there are also companion animals who are not bred for the purpose of being research animals, but who have close relationships to humans, living inside homes or near to human dwellings. In the case of veterinary clinical studies outside of routine care, animals might be eligible for a study and become research animals if patient owners consent. The procedure is comparable to clinical studies in human medicine, and national laws may also require ethics committee oversight and approval.

A third group of companion animals used for research would be the illegal use of animals such as stray animals or stolen companion animals, which we will discuss below.

The focus of this article will be on the first type of companion animals in the lab. For various reasons, animals belonging to species classified as companion animals may be convenient and appropriate research animals. Companion animals are well-adapted to living with humans. Accordingly, they are easy to tame, to handle, and to work with, and contact with humans is potentially less stressful to them than for other animal groups. Some animals are naturally susceptible for disease and pathogens known in humans and represent translational models for research of disease pathogenesis and reconvalescence in animal and human diseases. Furthermore, compared to companion animals, typical lab animals are genetically more homogeneous. Depending on the research question, a more heterogeneous or a more homogeneous genetic

spectrum can be beneficial, which is why for particular research questions, the genetically more diverse companion animal species might be selected. For comparative medicine, which we define here simply as the comparative study of disease and health in different species, the study of animals with wide genetic diversity is paramount. Whilst knowledge derived from the study of a particular dog breed, for example, may not be relevant for other dog breeds, it may be relevant for animals from different species (Kaeberlein et al., 2016; King, 2021; Kol et al., 2015).

It is clear that research on companion animals has many benefits, not only for human medical research, but also for veterinary medicine. Research on pathomechanisms or drugs ultimately benefits companion animals and their owners, although the owners may be opposed to animal experiments (National Research Council et al., 1991; Quimby, 1998). The German information platform “Tierversuche verstehen” (“Understanding Animal Experiments”) is an association of German scientific organizations, universities, and many other scientific and medical societies and provides information on the topic of animal experiments. The aim is to make it easier for the public to deal with this difficult subject and to counter false statements and prejudices (tierversucheverstehen.de, 2023). Initiatives such as this one aim to bring the topic of “animal experimentation” more strongly into the public and people’s awareness and to ensure appropriate education. However, it remains questionable whether these will increase acceptance of animal experiments on companion animals or whether this awareness will lead to more protests. With the scope of animals potentially being considered as companion animals increasing, opposition might be directed at a broader range of cases in animal experimentation if it includes such animal species.

3.2 *Public Criticism of the Use of Companion Animals in Research – Why Does the Role Matter Here?*

In spite of these arguments for using species that are usually considered as companion animals in experiments, research on companion animals has met significant opposition. In this section, both the “outsiders” view and researchers’ perspectives on challenges regarding companion animals in laboratory research will be elaborated on.

The Brown Dog Affair in the United Kingdom, for example, relates to a 1903 case where William Bayliss of the Department of Physiology at University College London vivisected on a brown terrier dog. It ignited the societal movement that opposed animal research. Similarly, the case of Pepper, a Dalmatian dog who was kidnapped and sold for medical experimentation in 1965 in the

USA, sparked significant public protest and led to the passing of the 1966 Animal Welfare Act (Shew & Johnson, 2018). The use of companion animals in research is now clearly regulated, rendering such an event highly unlikely today. Paragraph 19 of the German Animal Welfare Ordinance, for example, stipulates that only animals who have been bred for this purpose may be used. The ruling that only animals bred for experimental purposes may be used is intended to prevent stray or supposedly stray animals from being used for experimental purposes. Even stricter regulations apply to dogs, cats, and primates, where dogs and cats must be marked directly by the breeder so that the identity of each animal is identifiable (Animal Welfare Act §11a). Similar regulations concerning dogs and cats are established by the European Directive 2010/63/EU, which, in Annex 1, also stipulates a list of animals who can be bred for use in animal experiments.

We hypothesize that – from a perspective of the global North, as the workshop was mainly based on animal research and its perception in Europe – the use of companion animals as research animals has been questioned more deeply by the public for two major reasons (Douglas, 2019; Rose, 2022). Firstly, animals typically associated with lab study, mice and rats, are widely regarded as ‘vermin’ or animals whom one would rather not have close contact with. In contrast, typical companion animals such as dogs and cats are animals whom many people like to have close and ongoing contacts with (see also section 1). The desire to have continuing contact with these animals conflicts with the fact that laboratory animals are killed at pre-determined endpoints. This is, for example, recognized by Shew and Johnson (2018: 406), who write that “pets’ special status is visible in the emotional response to euthanasia and animal control measures being used on populations of dogs and cats without owners; these are often considered tragic in a way that the intentional elimination of rats and skunks is not”.

Secondly, some people may keep mice or rats as companion animals and object to either pain or death being inflicted on these animals when it is not in their interests, but are much less concerned about pain or death being inflicted on laboratory animals, for example, mice or rats, when these are not perceived to be companion animals. Accordingly, their moral judgement is not based on the animals’ species, in that case, but on their role as either a companion animal or a research animal. This is recognized as follows by Bates (2017: 178), who claims that opposition to the use of animals in research has decreased since World War II in spite of a significant increase in the number of animals being used: “A solitary physiologist choosing to vivisect a stolen dog in a private laboratory was more likely to provoke an emotive response than any number of

routine tests carried out by white-coated technicians on anonymous animals that would never see life outside a laboratory.”

Legal judgments also differ depending on the role that an animal is allowed to fulfill. Many jurisdictions have different laws related to the treatment of animals depending on the use of the animals in question or what species the animal belongs to. In England, for example, the Animal Welfare Act 2006, which is the primary law related to the human use of nonhuman vertebrates, states that “a person commits an offence if ... he administers any poisonous or injurious drug or substance to a protected animal, knowing it to be poisonous or injurious” (Animal Welfare Act 2006, section 7). A protected animal is defined as a vertebrate who is “of a kind which is commonly domesticated”, or under human “control” or “not living in a wild state” (Animal Welfare Act 2006, section 2). This would suggest that the intentional poisoning of lab animals who are vertebrates is legally suspect. This, however, is not the case, as the Animal Welfare Act 2006 does not apply “to anything lawfully done under the Animals (Scientific Procedures) Act 1986”, which is the key law related to the use of animals for research (Animal Welfare Act 2006, section 58). Whilst this law demands that one should try to “reduce to the minimum any possible pain” (Animals (Scientific Procedures) Act 1986, section 2A), it does not demand that researchers should refrain from poisoning any animals whom it is concerned with (mainly vertebrates and cephalopods from particular developmental stages onwards).

Another example of how legal protection differs depending on the role that an animal is allowed to fulfill is the law in the European Union. Recital 12 of Council Directive 2010/63/EU states that “the use of animals for scientific or educational purposes should ... only be considered where a non-animal alternative is unavailable” (Council Directive 2010/63/EU). This suggests, in line with the internationally acknowledged principles of 3R (“Reduce”, “Refine”, “Replace”), that animal research can only be justified where we do not have a non-animal alternative. This contrasts greatly with the lack of legal concern in the European Union for the human use of non-human animals for food, even where non-animal alternatives are available (Deckers, 2016). The same EU Directive demands that “primates, dogs and cats ... have a personal history file from birth covering their lifetimes in order to be able to receive the care, accommodation and treatment that meet their individual needs and characteristics” (Council Directive 2010/63/EU, art. 33), raising the question why these animals in particular have been selected.

In Germany, again, many animals are used for food without the protection of complex laws, which contrasts to the complexity that surrounds the law on

animal experimentation. Before an animal experiment can be carried out in Germany, a specific application and approval procedure must be adhered to. This is shown schematically as an exemplary overview of a complex process in Fig. 1. It shows the parts that the application must contain as well as the criteria that the applicant and the authority must observe in order for the application to be accepted. Advisory bodies assist both the applicant and the authority in this process. Good cooperation of all parties involved is important.

A final example of how legal protection differs between species and contexts is the Italian law that transposes EU Directive (Legislative Decree No. 26/2014). It only prohibits the breeding of dogs, cats, and non-human primates for scientific research. Meanwhile, the Italian law on the protection of companion animals and the prevention of straying (Law No. 281/91) prohibits the use of stray dogs and cats and those from kennels or shelters for scientific purposes, raising the question why these animals have been selected. Italy has also decided that animals with a recent history of abandonment and/or mistreatment, including those housed in kennels and shelters, will not be admitted to animal assisted interventions (AAI) unless they participate in a re-education and socialization program conducted by a veterinarian with animal behaviour experience

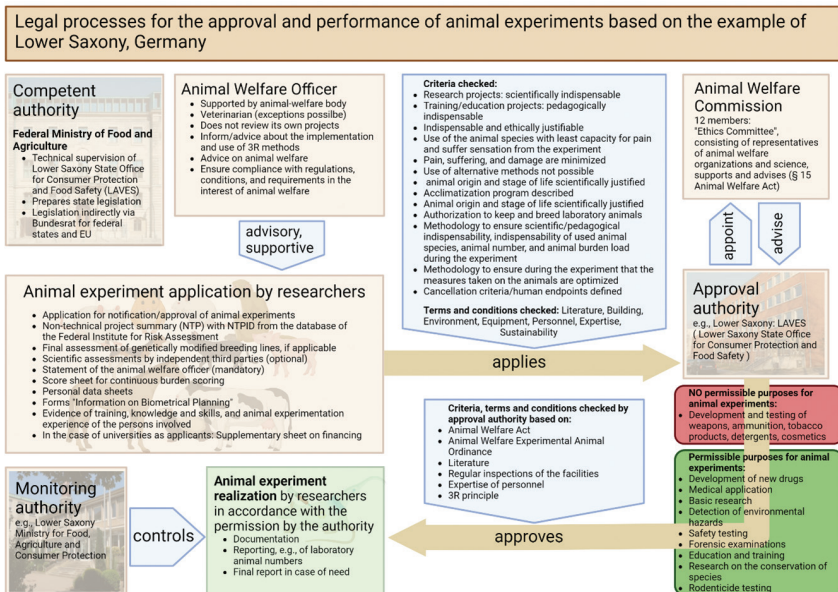


FIGURE 1 Legal processes for the approval and performance of animal experiments based on the example of Lower Saxony, Germany
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(Italian National Guidelines for Animal Assisted Interventions, 2015). The rationale behind this decision is to avoid using animals whose history, genetics, and temperament are unknown. Using such animals would impair the quality of the intervention as well as the quality of the resulting research data.

Ever since experiments with animals have been conducted, researchers have faced ethical questions and personal emotional issues (Franco, 2013). These issues increase when we consider the use of companion animals in research, as humans have different emotional relationships with, for example, cats, dogs, or ferrets than with animals such as mice and rats (whom we do not tend to keep as companion animals, as discussed above). These strong emotional relationships form partly because of the ways the animals interact with laboratory staff. For example, ferrets seek contact with humans and want to play or cuddle. Thus, whether a researcher or animal technician keeps ferrets privately or not, a close relationship can develop with these animals, especially if the animals live in laboratory animal facilities for extended periods of time. Compared to mice, they are often easier to handle and show a more playful behavioral repertoire, which also leads to more intense bonding. Due to this closer relationship to laboratory animals, killing, which is pre-determined in the research plan in most cases at the end or in the middle of the experiment, is mentally more straining and ethically challenging. When companion animals are kept for a long time and researchers get to know the individual animals' characters and pay more attention to details, it can become more emotionally stressful to perform experiments with them and to kill them (Bayne, 2002).

Whilst it is good to take heed of public (including legal) perceptions, it would be wrong to base our moral evaluations on whether and, if so, when companion animals should be used for research simply based on public perceptions. Firstly, such an approach fails to justify why particular animals should be given a particular standing. Secondly, without moral justification, public (including legal) distinctions that are based on scientific classifications (e.g., whether or not an animal is a vertebrate), or on domains of human interests (e.g., research or companion) are arbitrary. Two animals of the same species can be legally entitled to different forms of treatment, depending on who owns the animals and on the contexts in which they live or are being used, which can be considered counter-intuitive (Grimm & Hartnack, 2013; Michel & Stucki, 2014). Classifying different human-animal relationships, Federico Zuolo (2020) differentiates between exploitation, use, cooperation, and individualised relationships. This ambivalence in our relationships with non-human animals came to the fore during the SARS-CoV-2 pandemic. We will describe this ambivalence in the following section.

4 Companion Animals in Zoonosis Research: a Case Report of SARS-CoV-2-Infected Cats

4.1 *How Do Zoonoses Affect Our Relationships with Companion Animals?*

During the pandemic, the public approach towards companion animals was ambivalent and the public view not only of cats, but also of bats (Zhao, 2020), who originally symbolized luck and happiness in China (Sung, 2002), has changed. Especially during the early stages, when new information about the virus was publicly reported on a daily basis, there were reports of significant concern about the potential for companion animals to contract the virus and potentially transmit it to humans (BBC News, 2020). In April 2020, a Malayan tiger at Bronx Zoo, Bronx, NY, USA was infected by his caretaker and tested positive for SARS-CoV-2 (BBC News, 2020). This was one of the first cases of virus spillover from a human to an exotic animal. Soon after, seven more big cats, including three lions, also tested positive, which raised concerns among the public. Naturally, people started to question whether, if big cats can be infected, their own companion cats can too, and whether they might be a threat to their owners.

Although many concerns were unfounded (CDC, 2023), companion animals in general became victims of the pandemic. For example, the animal welfare organization PETA reported that in Romania, among other countries, the economic consequences of the pandemic (Tageschau, 2022) also impacted negatively upon the companion animals of people living there. In the wake of worsening poverty, many owners could no longer adequately care for their companion animals, resulting in increased abandonment (PETA Deutschland e.V., 2020). In China, many people reportedly developed fear of companion animals, resulting in increased abandonment and killing. At the end of January 2020, a dog and five cats were thrown from high-rise buildings in the cities of Tianjin and Shanghai (Yin et al., 2020). There was also an incident in Jiangsu Province in which community management staff gained access to the home of an infected resident while he was in hospital and killed the resident's cat (AP News, 2021). After the outbreak of a SARS-CoV-2 delta variant, originating from a pet store, at least 2,000 small mammals (mainly hamsters) in China's companion animal stores were killed as a preventive measure. Additionally, people were called upon to hand over to the authorities any hamsters they had acquired after December 22, 2021. As a result, the import of these rodents was banned for one year, with the ban being lifted in mid-January 2023 (Der Spiegel, 2022). In Denmark, 17 million minks were culled from mink farms in

November 2020 after a mutant of the virus was transmitted from minks back to humans (Der Spiegel, 2020).

In March 2020, a survey was conducted in the United Kingdom (Williams, 2020) to gather public opinions on the use of animals in scientific research, especially in the light of the persistent pandemic. The majority (85%) of respondents said that their views about animal testing and animal research had not changed in light of the COVID-19 outbreak, while 11% stated their opinions had changed (Williams, 2020). The research also showed that the majority of people (79%) believed that animal research and testing should be allowed for the development of new medical treatments. However, many respondents also felt that more animal research takes place in the UK than necessary. Three-quarters of them (75%) stated that they accepted the use of animals in research if the animals do not suffer unnecessarily and there is no alternative, while 29% of people said, for animal welfare reasons, that they could not accept the use of animals in any scientific research. Regarding COVID-19, almost three-quarters of the respondents (73%) thought that it is acceptable for scientists to develop tests, treatments, or vaccines for COVID-19 using animals such as mice, dogs, or monkeys if there is no other alternative. Trust in science and scientists to provide a solution to COVID-19 was high (77%). Nevertheless, many people were conflicted about welfare concerns and the potential harm to the animals. Finally, 95% of people felt a solution to COVID-19 would come through international collaboration.

4.2 *Lessons Learned about the Ethical and Bio-risk Assessments Required for Quarantine of Cats in Biosafety Level 3 Conditions – a Case Report*

The susceptibility of companion animals, particularly cats and dogs, raised public concerns about what to do with the companion animals if a human or companion animal tests positive for SARS-CoV-2 in a private household (CDC, 2023; Friedrich-Loeffler-Institut [FLI], 2020) and what the possible consequences for SARS-CoV-2-positive animals might be (FLI, 2022; Schulz et al., 2021a; Schulz et al., 2021b). Finally, similar diagnostic and hygienic measures were recommended for animals as those known for humans (CDC, 2021, 2023; Schulz et al., 2021b).

Furthermore, the frequency of SARS-CoV-2 infections in animals in the field was unknown. To allow improved risk assessment and monitoring of the distribution and frequency of natural SARS-CoV-2 infections in animals in the field, the SARS-CoV-2 infection in animals was announced as notifiable in Germany in June 2020 (Die Bundesregierung, 2020). In a European field study with more than 2,000 cats, a seroprevalence of 4.4% was found during the first COVID-19 wave, April to August 2020 (Schulz et al., 2021a).

In our following case description, we would like to give insights into decision criteria the animal researchers involved in the writing of this article faced when deciding on the future of cats with COVID-19 at a time when knowledge about their role in SARS-CoV-2 epidemiology was scarce. Therefore, we would like to briefly introduce the history of the case as described previously (Schulz et al., 2021b).

In March 2020, one of three cats housed in close contact with the inhabitants in a retirement home were tested SARS-CoV-2-RNA positive after multiple infection events had occurred in some residents despite strict separation of infected from non-infected persons. Of 21 SARS-CoV-2 infected people, three succumbed to the disease. At the time, the role of cats in SARS-CoV-2 epidemiology remained unknown. Due to concerns about the possibility of spillback from the cat to humans or forward transmission to the other two cats, all three cats were isolated for a short period at a responsible authority. Since the time of SARS-CoV-2 shedding by cats was still unknown, a long-term possibility to isolate the cats was found in a biosafety level 3 (BSL-3) facility. In the BSL-3 facility, the cats were regularly monitored for virus shedding with PCR to determine whether the one infected cat had transmitted the virus to the other two cats and when SARS-CoV-2 shedding ceased, to determine the end of the isolation. Finally, the one cat showed long-term shedding of SARS-CoV-2-RNA for 21 days after the first positive PCR-result, but neither of the other two cats was infected. Co-infection of the PCR-positive cat with feline immunodeficiency virus (FIV) indicated an impaired immunity of the cat. To avoid re-activation or infection occurring unnoticed, the cats were monitored for a longer time period. After 10 weeks of isolation, seven weeks after the last PCR-positive result, all three cats found new homes with private owners (Schulz et al., 2021b).

In the presented case report, we mainly faced ethical questions before and during the housing of the cats. Therefore, we had to answer three main questions (Fig. 2):

1. Should we keep the animals in their private home or isolate them in a competent BSL-3 research facility?
2. How should we communicate any decision to the public?
3. Should we give the cats to private owners after the observational study or euthanize the cats for scientific reasons (e.g., to collect organs)?

Therefore, we identified seven key criteria that were important for our decisions: animal welfare (including their health in case they developed symptoms), experience of the staff, personal emotions (emotional aspect), scientific value, biosafety risk, resources, and public opinion (Fig. 2).

For animal welfare reasons, we aimed to provide optimal conditions for the housing of the animals, including species-specific natural enrichment and experienced staff. In a private home or research facility, the animals had to

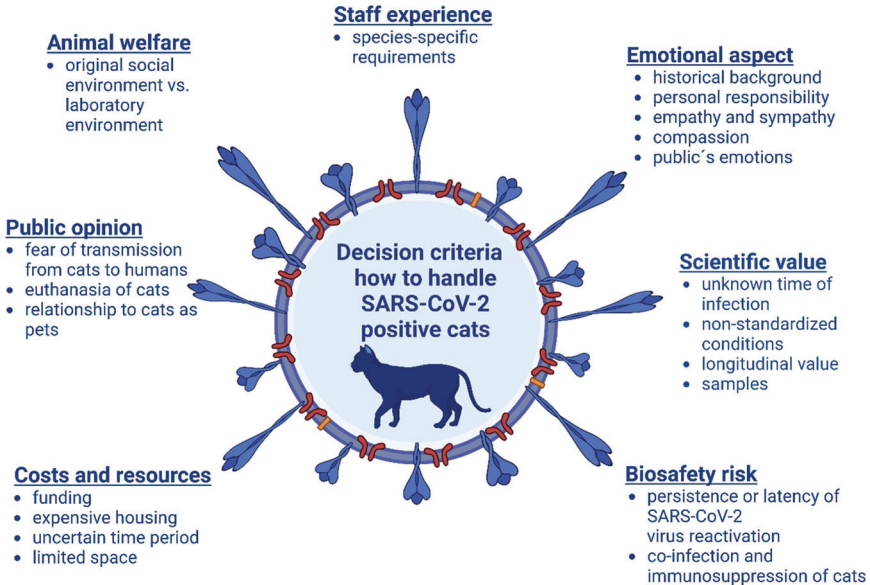


FIGURE 2 Decision criteria on how to handle naturally infected SARS-CoV-2 positive cats from private owners in the beginning of the COVID-19 pandemic in 2020

be kept isolated from humans, unlike their previous environment. The costs, resources, and experience in a BSL-3 facility when handling infectious animals are considerably higher and allow maximal protection from transmission of SARS-CoV-2 to humans or other animals. Therefore, the cats were kept in the BSL-3 facility. However, it had to be clarified if it was possible to finance the costs and provide enough personnel for long-term isolation of the cats in case of long-term shedding or re-activation of the virus due to the immune suppression and co-infection with FIV. A possible compromise was to keep the animals until no SARS-CoV-2-RNA was detected for over one month. Euthanasia of the cats would have provided information from one naturally infected cat with an unknown stage/time after SARS-CoV-2 infection and an immune compression due to co-infection with FIV. Nevertheless, the scientific value of controlled, standardized experiments with an appropriate number of animals is considerably higher to evaluate the pathogenesis and the role of cats in the epidemiology of SARS-CoV-2.

Staff experienced with cats as a species ensure an appropriate handling and care of animals according to species-specific requirements. However, animal care of cats as companion animals may increase our emotional response, igniting feelings of empathy, sympathy, and compassion with the animals. Also, the emotions of the public had to be considered and a reasonable public

communication was of major importance to avoid wrong assumptions and conclusions about the cats in the research facility. In contrast, the case of the cats was important to raise and contribute to the awareness about how to handle SARS-CoV-2-infected animals in private homes.

All three cats remained clinically healthy during their stay at the BSL-3 facility and were housed in private homes after an isolation period of 10 weeks (Schulz et al., 2021b). The case of the three cats was published in the scientific community (Schulz et al., 2021b) and to the general public (Neue Presse, 2020). Accordingly, temporal isolation and hygiene measures established for humans can be assigned to animals (FLI, 2020) in case of SARS-CoV-2 infection. The lessons learned from the presented case report about the ethical and bio-risk assessments during the SARS-CoV-2 pandemic, together with guidelines published, e.g., by reference centers for disease prevention and control, about how to handle pets during the COVID-19 pandemic (CDC, 2021, 2023; FLI, 2020, 2022; Schulz et al., 2021a; Schulz et al., 2021b) can be adapted, and provide guidance for future outbreaks of known and unknown pathogens.

Experimental animal models provide an efficient, safe, rapid, and therefore indispensable basis for the development and testing of preventive and therapeutic measures against SARS-CoV-2 infections in humans. However, cats are not the first choice of companion animal used for such kind of scientific research. Also, at the beginning of the COVID-19 pandemic, it was of utmost importance to establish animal models that mimic the normal and the therapeutically improved disease progression of COVID-19 in humans for optimal risk reduction.

The advent of the SARS-CoV-2 pandemic immediately prompted *in silico*, *in vitro*, and *in vivo* experiments to identify susceptible host species that may act as amplifying hosts by transmission or spillback of SARS-CoV-2 to humans or other animals. Furthermore, suitable animal models were required for translational studies of SARS-CoV-2 pathogenesis in humans (Ciurkiewicz et al., 2022; Conceicao et al., 2020; Schlottau et al., 2020; Shi et al., 2020; Zhai et al., 2020). *In silico* analysis of the angiotensin-converting enzyme 2 (ACE2) amino acid sequences, including residues interfacing with SARS-CoV and SARS-CoV-2 receptor binding domain (RBD) as well as *in vitro* assays such as surrogate and live virus entry assays revealed that the spike glycoprotein of SARS-CoV-2 has a broad host tropism for mammalian ACE2 receptors without adaptation to the respective intermediate host (Conceicao et al., 2020; Zhai et al., 2020) (Fig. 3 and Supplemental Fig. S1).

In accordance with the *in silico* and *in vitro* data, *in vivo* experiments demonstrated the susceptibility of various companion and laboratory animal species (e.g., cats, dogs, ferrets, hamsters, rabbits) as well as ruminants (e.g., cattle,

white tailed deer) (Pickering et al., 2022; Ulrich et al., 2020), while pigs, chickens, and guinea pigs were not susceptible (FLI, 2022; Schlottau et al., 2020).

5 Companion Animals as Research Animals from the Animal Ethicists' Point of View

Given that many people question the use of (particular) companion animals for research, some might be inclined to answer the general question whether we should use companion animals for research with a simple 'no'. They might be in good company here as one scholar who is renowned for his work on animal ethics, Tom Regan, provided a negative answer for all animals whom he considered to be 'subjects of a life'. Thus, he wrote that "there is abundant reason to believe that the members of mammalian species of animals do have a psychophysical identity over time, do have an experiential life, do have an individual welfare" (Regan, 1989: 39), which he considered to be necessary criteria for being a subject of a life. Regan's account, however, is subject to two criticisms. Firstly, whilst he considered the possibility that many animals apart from mammals might be subjects of a life, his account fails to establish clearly how we could separate animals who are subjects of a life from those who are not (see, for example, Deckers, 2016), and is overly restrictive by questioning animal research nearly exclusively when it concerns mammals. Secondly, Regan argued that those who are subjects of a life "have inherent value, and have it equally relative to all who meet it" (Regan, 1989: 39). He combined this notion of equality with a non-utilitarian stance where all those who have inherent value should be treated with respect, which he argued would imply that their value should never be subordinated to the value of another. This is problematic as there may be situations where the inherent value of one animal can only be respected at the cost of the inherent value of another.

This is what is emphasized by a utilitarian perspective such as that of Peter Singer. Singer writes that the long-term goal is "the elimination of all exploitation of sentient animals" (Singer, 1990: 94). However, it is clear that some of his writings support the view that not all use of sentient animals as "tools for research" should be considered to be exploitative. His general concern is with the principle of equal consideration of morally significant interests. Subordinating (a being with) lesser interests (for example, an interest in not being used as a tool for research) to (a being with) greater interests (for example, an interest in using another organism as a tool for research), is justified for Singer if it increases "the total surplus of pleasure over pain" (Singer, 1979: 147). Singer's account raises questions about which interests are morally significant

and about which interests should be allowed to trump others. When it comes to animal research, for example, the human interest in scientific or medical progression is up against the animals' interests not to be harmed. To what extent the human interest in gaining knowledge is morally relevant, or as relevant as the animals' interest in not being harmed, remains unclear.

What unites the perspectives of Regan and Singer is the desire to come up with a list of non-human animals who, respectively, make the mark of being a subject of a life or of having morally relevant interests, particularly an interest in pleasure or the absence of pain. Both approaches are thus based on the intrinsic properties of animals as moral objects. Once moral agents would know which animals have inherent value or particular interests, moral agents would then know what to do if they are willing to be guided by the principles of respect or equal consideration of interests, i.e., the animals would have moral status.

This approach has been criticized by other scholars who think that these scholars have got it the wrong way round. Mary Midgley, for example, thought that it is crucial to explore the emotions that animals trigger in moral agents and to use these as the basis for moral decision-making. In contrast to Regan and Singer, she does not focus on the animals' intrinsic properties, but rather, on relational aspects between moral agent and moral patient. Thus, she wrote: "This decision is in no way scientific; it is purely social and emotional, and a lot of it is pure chance" (Midgley, 1989: 15). This led her to conclude that animal experimentation is "not an easy topic", and she found it "interesting to note that laboratory technicians sometimes pick out a particular mouse or mice to keep as pets, viewing them quite differently from their mass of relations in the metal cages" (Midgley, 1989: 15–17). In summarizing Midgley's position, Cooper (Cooper, 2020: 249) argued that Midgley thought that "our attitudes to animals are warped by approaches that are ... excessively abstract, over-theoretical", adding that, in keeping with her position, "what is required is not yet another theory of how and why animals matter, but attention to actual engagements with animals and to the moral failings or vices that distort people's relationships with them".

The importance of relationships is also emphasized by recent empirical findings on attempts to rehome animals after they have been used in research. Turning the focus of this article upside-down, the laboratory animals become companion animals here. Skidmore and Roe (2020) found that in most cases of rehoming in the UK, it was the laboratory staff members who either took laboratory animals home after they were no longer used for research or asked their friends and family if they could find a new home for them. Apparently, the bond between humans working and animals living in a laboratory occasionally

goes beyond that of a professional relationship (in a similar fashion to how colleagues might become friends). Additionally, there was a strong preference for rehoming dogs and cats, rather than mice or rats (despite the greater total number of the latter used in research; see section 1) (Skidmore & Roe, 2020: 7). However, the same study revealed that two of the most important factors for a company to implement a rehoming process were to show “a good ethical stance” or to build “staff morale”, which might not be related closely to theories about the animals’ intrinsic values (Skidmore & Roe, 2020: 12). Companies who emphasise these factors seem to perceive a public expectation of how research animals should be treated on the basis of our emotional attachments, especially those who are commonly viewed as companion animals and, accordingly, live in a home. This idea that some of our emotional attachments matter a great deal in our moral engagements is also highlighted in the work of Deckers (2016), as well as a by a reviewer of this article who pointed out that people are frequently troubled by the pain and suffering of animals not (so much) because they want to make the animals better but because they wish to relieve their own discomfort.

The idea that a certain kind of relationship comes with a set of obligations is also emphasized strongly in Ursula Wolf’s and Clare Palmer’s animal ethics approaches. According to relational animal ethics, obligations come from the relationship that we build with an animal and the animal’s corresponding expectations (Wolf, 2018). The expectations might not always be consciously perceived but they characterise the kind of relationship that is built. For example, a companion animal may not know that they expect food at a particular time of the day, but they still expect (i.e., show behavioural signs of expectation) to be fed when it is that time of the day. According to relation-based animal ethics, the obligations we have towards, for example, free-living animals are mainly negative, e.g., not to inflict harm and not to interfere with them (Wolf, 2018: 100). We should not arbitrarily interfere with their habitats or resources, but we are not obliged to feed or vaccinate them. As the welfare of (all) animals should not be undermined by humans unless there is a strong moral justification, Wolf has a critical attitude towards all animal experimentation that involves “notable suffering” (Wolf, 2018: 146). She rather approves of those studies that motivate animal participants to volunteer for getting a treat in return (p. 147) and, most likely, would exclude most zoonosis research if it includes pain, harm, or suffering. When it comes to those laboratory animals whom we purposively took into captivity, we are obliged to feed them, clean their cages, and provide medical care, in line with, e.g., the five freedoms that are demanded by animal welfarists for animals in captivity. However, we are not obliged to take laboratory animals for walks, play with them, or provide

palliative care when they grow old. Those obligations are restricted to companion animals if they have reasons to expect such behaviors from us due to the relationship between companion animal and “owner” (Wolf, 2018: 95–97). Importantly, though, for laboratory animals – depending on the experimental set-up – physiological and psychological needs ought to be fulfilled within the experimental requirements and harmful restrictions to their needs should be ethically considered prior to experiment. A potential ethical conflict may arise when the relationship of a laboratory animal towards a member of the laboratory staff becomes “companion-like”. From Wolf’s perspective, an animal who is considered as a companion animal and is used to a particular interaction (for example playing games, being cuddled, receiving treats, or being talked to) develops expectations based on that relationship that are the basis for positive obligations (obligations “to do”). The idea might be comparable to human relationships, when someone who is treated like a friend by another person might develop the expectation to have a friendship with that person, including the usual interactions between friends (for example, listening to each other’s problems, sharing intimate thoughts, spending quality time together). Similarly, an animal who is treated like a companion animal might be considered entitled to expect the usual interaction between companion animal and “owner”. Accordingly, animals who are considered and treated like companion animals by staff members should have the same moral rights as other companion animals, including, for example, the right to play games or go for walks until their life comes to an end. No pain, harm, or premature killing should be inflicted on them. Wolf’s approach thereby underlines the difficulties pointed out in our retreat week. While we are used to and morally obliged to treat distinct groups of animals in different ways, we struggle if these groups overlap.

If we apply the ideas of Midgley and Wolf to the use of companion animals in research, we should give moral significance both to the possibility that we have established a particular relationship with an animal and to the possibility that an animal may have particular expectations from us. As companion animals who are used as research animals may have relationships and expectations that are not possessed by other research animals, we should be particularly cautious about using such animals for research where it jeopardizes these relationships and expectations. While some research will jeopardize these, we think that there are at least four general situations where the use of companion animals for research can be justified.

First, if we did not use companion animals for research, some animals would not stand to benefit in situations where the only hope that we have of making the animals in question better is to use an experimental procedure. Their use can be justified in a similar way to how we justify research on, for example,

a human patient with dementia or a very young child. Whilst neither people with dementia nor young children are able to consent, the research may be appropriate if it is a last resort to try to make the person healthier or to improve their quality of life, which we consider to be two aspects of health, holistically conceived (Deckers, 2016).

Second, research that is likely to promote the interests of the animal in question more compared to not doing the research also survives moral scrutiny. Think for example of a simple procedure where one would need a blood sample from a dog in order to subject the sample to a new piece of equipment that was being tested to determine whether it might diagnose whether the dog might be suffering from a particular disease. If there were a good chance that the dog might suffer from this disease, the inconsequential harm of taking the blood sample would seem to be outweighed by the potential benefits, even if a conventional procedure that did not involve the taking of a blood sample could also have been used to diagnose the dog, but perhaps less reliably so.

Third, research that has a small probability of undermining the interests of the companion animal in question more compared to not doing the research may survive moral scrutiny. If we apply this reasoning to human beings, it would be hard to argue this point unless the human being consented to this. In the case of companion animals, they are unable to consent. One condition to justify approval is the animal having a small chance of achieving a better health outcome compared to a non-experimental procedure, even if the chance of achieving a worse health outcome might be greater. Yeates and McKeegan (2019) envisage such a scenario when they write about a dog (Fido) with mouth cancer. An experimental procedure might be curative for Fido, unlike a non-experimental procedure. We would approve of this if the experiment had a reasonable chance of being curative and if the degree of discomfort that the dog were likely to experience was unlikely to be much greater than the discomfort associated with the conventional treatment. Yeates and McKeegan (2019: 133) write that the procedure would not be justified if it concerned “experimental surgery to help develop future surgery”, presumably because the dog would have no chance to benefit from it.

Fourth, research that has a great probability of undermining the interests of the companion animal in question may be justified where it promotes human health more compared to not doing the research (Deckers, 2016). An example of a situation where such research may be justified is when doing the research on other animals would not promote human health to the same extent. In this regard, the characteristics of companion animals are an important consideration. For example, the fact that typical companion animals like dogs can easily be trained and even enjoy interaction with humans can make handling

less stressful (for both the animal and the researcher) and sedation or fixation unnecessary for some procedures. Furthermore, zoonosis research is targeted at diseases that are transferable between animals and humans. In many situations, companion animals are better models for such research due to the fact that they live more closely together with humans and suffer from diseases that can be passed on to them. Results from such research produce more meaningful results.

6 Conclusion

This article provides an example of how multidisciplinary dialogue on a complex issue, initiated during a research retreat at the University of Veterinary Medicine in Hannover in November 2022, can shed new light on a vexing moral issue. Certainly, more research is needed on the attitudes of i) those working in laboratories towards different kinds of research animals, and ii) companies or institutions whose policies decide on the fate of their research animals. Nevertheless, we provide some ethical considerations about the use of animals belonging to species classified as companion animals with a focus on zoonoses research that may be useful. We started from the observation that species identified and usually kept as companion animals may be better research models under certain conditions compared to typical lab animals, but that their usage for research has been publicly criticized, and went on to discuss some public reservations about the use of companion animals for research. We provided a case report about natural SARS-CoV-2 infection in a cat to highlight key criteria (animal health and welfare, experience of the staff, personal emotions, scientific value, biosafety risk, resources, and public opinion) required to decide for or against the use of companion animals in zoonoses research. We argued that companion animals should be used as research animals, subject to a number of conditions. Whilst research proposals that are highly likely to undermine the interests of such companion animals must particularly be subjected to serious scrutiny, we argued that such proposals must not necessarily be discarded. We summarized the approaches to animal ethics of Regan, Singer, Midgley, and Wolf to provide perspectives on the use of particular groups of animals for scientific purposes. Finally, we argued that research on companion animals may be justified in at least four situations: 1) as a last resort to make the individual healthier or improve their welfare; 2) if the harm to the individual is outweighed by the benefits; 3) if an experimental procedure might be curative or have a better outcome when a non-experimental procedure might not, even if chances are

small; and 4) if conducting the research promotes human health more than not conducting the research.

Supplementary Material

Supplementary material is available online at:
<https://doi.org/10.6084/m9.figshare.24504106>

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