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Pets, People, and Pandemic Preparedness: First insights from the BEready longitudinal cohort study

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Submitted by

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List of abbreviations

ALAT	alanine aminotransferase
BCS	Body Condition Score
COVID-19	Coronavirus Disease 2019
DBS	Dried Blood Spot
EDTA	Ethylenediaminetetraacetic acid
ESCCAP	European Scientific Counsel Companion Animal Parasites
GNC	German National Cohort
MERS	Middle East Respiratory Syndrome
PCR	Polymerase Chain Reaction
SAA	Serum Amyloid A
SAF	Sodium Acetate–Acetic Acid–Formalin
SARS-CoV-2	Severe Acute Respiratory Syndrome Corona Virus 2
SVK-ASMPA	Swiss Veterinary Association for Small Animals (Schweizer Vereinigung für Kleintiermedizin)
UK	United Kingdom
US	United States
WHO	World Health Organization

Abstract

Vetsuisse-faculty University of Bern 2025

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Pets, People, and Pandemic Preparedness: First insights from the BEready longitudinal cohort study

Background: Pandemics and zoonotic diseases pose a significant threat to human health. Household pets are often overlooked in surveillance, despite their close contact with humans.

Objective: To present first findings from the BEready cohort, a longitudinal study integrating humans and pets to assess zoonotic risks and pandemic preparedness in Swiss households.

Materials and methods: We analysed data from the pilot study and the first nine months of the main cohort enrolment, focusing on pet demographics, preventive care, and behaviours relevant to the acquisition and transmission of zoonotic pathogens.

Results: Endoparasites were found in 11% of cats and 33% of dogs. Many pets had contact with birds, wildlife, livestock, or other animals. Owners lived in close contact with their pets. Preventive measures such as vaccinations and deworming were more consistently implemented in dogs than in cats.

Conclusion: These initial results highlight zoonotic risks in the household setting. Including pets in pandemic preparedness cohorts is challenging but essential to a more comprehensive One Health approach and to strengthen future public health responses.

Keywords: One Health, pandemic preparedness, longitudinal study

Bern, 23.07.2025

Place, Date

Signature, Prof. Dr. Simone Schuller

Santa Maria Coghinas, 28.07.2025

Place, Date

Signature, Dr. Eva Maria Hodel

Zusammenfassung

Vetsuisse-Fakultät Universität Bern 2025

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Pets, People, and Pandemic Preparedness: First insights from the BEready longitudinal cohort study

Hintergrund: Pandemien und zoonotische Erkrankungen stellen eine erhebliche Bedrohung für die menschliche Gesundheit dar. Haustiere werden in der Überwachung häufig übersehen, obwohl sie in engem Kontakt mit Menschen leben.

Ziele: Vorstellung erster Ergebnisse der BEready-Kohorte, einer longitudinalen Studie, die Menschen und Haustiere einbezieht, um zoonotische Risiken und Pandemievorbereitung in Schweizer Haushalten zu untersuchen.

Material und Methoden: Wir haben Daten aus der Pilotstudie und den ersten neun Monaten der Hauptstudie analysiert, mit Fokus auf die Demografie der Haustiere, prophylaktische Gesundheitsmassnahmen, und Verhaltensweisen, die für den Erwerb und die Übertragung von zoonotischen Pathogenen relevant sein können.

Ergebnisse: Endoparasiten wurden bei 11% der Katzen und 33% der Hunde nachgewiesen. Viele Haustiere hatten Kontakt zu Vögeln, Wildtieren, Nutztieren oder anderen Tieren. Die Tierhaltenden lebten in engem Kontakt mit ihren Haustieren. Prophylaktische Massnahmen wie Impfungen und Entwurmungen wurden bei Hunden häufiger und konsequenter durchgeführt als bei Katzen.

Fazit: Diese ersten Ergebnisse verdeutlichen zoonotische Risiken im häuslichen Umfeld. Die Einbeziehung von Haustieren in Kohorten zur Pandemievorbereitung ist zwar herausfordernd, aber wichtig für einen ganzheitlicheren One-Health Ansatz und zur Stärkung zukünftiger Massnahmen im Bereich der öffentlichen Gesundheit.

Stichworte: One Health, Pandemievorbereitung, longitudinale Studie

Bern, 23.07.2025 — Simone Schuller

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1. Introduction

Pandemics in human history – Throughout history, large epidemics and pandemics have been recurring events, and this trend is likely to continue. Infectious diseases have, and still do, greatly affect societies. Examples range from the Black Death, an outbreak of *Yersinia pestis* in the Middle Ages that killed a large part of the European population,[1] to widespread smallpox epidemics in the 16th to 18th centuries. This continued into the 20th century, for example with the Spanish flu, the influenza pandemic with the highest mortality rates to date.[2] In more recent times, the example with the greatest impact on Western societies was SARS-CoV-2, the virus that caused the COVID-19 pandemic. Other diseases of concern include Ebola, MERS (Middle Eastern Respiratory Syndrome), swine flu, monkeypox and Lassa fever.[3]

Pandemics can affect many different aspects of societies. First and foremost, they can have negative effects on the health of the population, mainly by causing clinical symptoms and, depending on the severity of the infection, excess mortality in affected populations.[4] **Even though the number of deaths** attributed to communicable diseases in high-income countries such as Switzerland is decreasing, the coronavirus disease 2019 (COVID-19) pandemic showed how quickly a pandemic can become one of the top causes of death globally.[5]

As a consequence of many people in a population becoming ill, the healthcare system can become overwhelmed, leading to triage of patients and potentially suboptimal quality of care.[6,7] Additionally, there are indirect negative health consequences, such as the effects of restrictions, including social distancing, self-isolation, and lockdowns, on mental health. They can contribute to anxiety, depression and other negative psychological effects.[8,9]

Economies can also suffer greatly. During the COVID-19 pandemic, many countries implemented restrictions that forced shops, restaurants and other businesses to close.[10,11] Social division and political polarization can also increase.[12] Even among family and friends differing views on the situation and on appropriate measures can lead to conflicts and in some cases to a breakdown in relationships. It is also likely that domestic violence increased during this period.[13,14]

One important threat for a future pandemic is influenza. Historical data show that human influenza pandemics reemerge three to four times per century.[15] The one with the highest lethality rate was the Spanish flu in 1918, which most likely derived from avian influenza.[2] The most recent human influenza pandemic was the swine flu in 2009. Avian influenza is also able to infect cats and therefore is a possible source for zoonotic spillover. Before 2023, feline infections with avian influenza were only reported sporadically.[16] However, in June to July 2023, there was a small outbreak of H5N1 clade 2.3.4.4b in cats in Poland.[17] This is also the same clade causing an outbreak of influenza in dairy cows in the United States in summer 2024.[18] Therefore, a systematic literature review in 2025 stated that better surveillance of domestic cats is needed.[16]

The risk of disease emergence is increasing due to various interconnected reasons. One important factor is the rapid population growth and the increasing population density in urban areas. This has led to intensive farming and deforestation, bringing wildlife closer together with humans.[15] Another important factor is climate change, with the expected increase in global temperature creating more optimal conditions for disease vectors, especially arthropod-borne diseases, which are expected to pose an increasing threat.[15,19] A major role is also attributed to the increasing international travel and commerce, which can lead to rapid spread of disease.[15,20]

The term One Health is relatively new, introduced in the early 2000s.[21] However, the concept itself is not new at all, it was already described in the 19th century by well-acknowledged scientists such as Rudolf Virchow and William Osler.[22] The concept is based on the interconnectedness of human, animal, and environmental health.[23] Rooted in this interconnectedness, One Health encompasses the collaborative efforts of multiple disciplines working together to improve knowledge and ultimately enhance the health of people, animals, and the environment.[22] This approach has gained popularity in recent decades. A well-recognized example of a global One Health issue is the challenge of antimicrobial resistance.[24]

One Health principles are also especially important in understanding and managing zoonotic diseases. Of the known infectious diseases, 61% are zoonotic.[25] Special attention should be given to emerging diseases, of these about 75% are zoonotic.[25] Pathogens such as viruses, bacteria, and less commonly

parasites and fungi can spill over from animals to humans, often caused by ecological and environmental factors.[26,27] Recently emerging diseases have shown the major threat that pathogens transmitted from wild animals can pose to humans.[27,28] Therefore, understanding what leads to such spillovers from wild animals to humans is a crucial one health concern. Domestic animals, including cats and dogs, can play a central role in cross-species transmission of zoonotic viruses.[27] This underscores the importance of this approach to pandemic preparedness.

Typically, One Health has focused on agriculture, livestock and wildlife contexts. However, fewer studies have examined household settings and the close contact with companion animals. This presents an opportunity to expand the paradigm to better include the dynamics of human-pet relationships. Further exploring the role of pets in zoonotic disease transmission, as well as their potential role in promoting health, gives the opportunity to explore a less studied aspect of the One Health framework.

The number of households with pets is increasing in Switzerland, as in many other industrialised countries.[29] In 2022, 43% of households in Switzerland owned at least one pet, with 30% owning cats and 12% owning dogs.[30]

Additionally, **the relationship between owners and their animals has been becoming closer.** Many people consider their pets family members, and this number has been increasing over the last years.[31,32] This deepened bond often results in more time spent with pets and more intimate contact. The close contact between pets and their owners can facilitate the interspecies transmission of infectious pathogens. Pet owners also engage in behaviours that can facilitate disease transmission. For example, many pets sleep in the same bed as their owners. A study conducted in the Netherlands showed that 45% of dogs and 60% of cats were allowed on the bed, with 18% of dogs and 30% of cats sleeping in bed with their owner.[33] Other studies reported even higher numbers of pets sleeping in the same bed as their owners.[34–37] Many pets lick their owners' hands and faces and owners regularly clean up their pet's excrement. These behaviours create opportunities for the exchange of pathogens, making it plausible that the likelihood of disease transmission between owners and pets could have increased. Unlike humans, pets do not avoid behaviours that increase their exposure to pathogens. On the contrary, many of their behaviours increase the risk of pathogen acquisition.

For example, they lick their own and other animals' anuses and genitals, as well as their fur, their environment, or even their owners' hands and faces. Dogs often show coprophagia and like to roll in other animals' faeces or carcasses.[38,39] These behaviours and their exposure to outdoor environments and interactions with other animals heighten the risk of acquisition of possibly zoonotic pathogens.

Pet-to-human transmitted diseases - There are many known pathogens which can be transmitted between pets and humans.[37] Examples of such parasitic diseases include giardiasis, echinococcosis, *Strongyloides stercoralis* infection, toxocariasis, and toxoplasmosis. Fungal infections like *Microsporum canis* and *Trichophyton mentagrophytes* are also known to be transmitted between pets and owners.[40] Among bacterial pathogens most frequently transmitted pathogens include campylobacteriosis,[41] salmonellosis,[42] *Clostridium difficile* infections,[43,44] and leptospirosis. In addition, the transfer of antimicrobial resistance genes and resistant bacteria have been documented. Examples include methicillin-resistant *Staphylococcus aureus* (MRSA) and resistant *Enterobacteriaceae.*[45–48] Even healthy pets can carry infectious agents that can pose risks to humans. For example, pets such as dogs, cats, tortoises, and other reptiles are known to be carriers of *Salmonella typhimurium*, several human pathogenic serotypes have been isolated.[42,49–51] Additionally multiple serotypes carrying antibiotic resistance genes have been isolated.[52]

Feeding pets raw meat is another risk factor for zoonotic infections, as raw meat can be contaminated with numerous zoonotic pathogens. Studies that examined commercially available raw meat diets found a wide range of pathogens, including *Salmonella spp*., *Escherichia coli*, *Campylobacter spp.*, *Cryptosporidium spp.*, *Echinococcus spp.*, *Sarcocystis cruzi* and *tenella*, *Listeria monocytogenes*, *Yersinia spp.*, *Giardia spp.*, *Toxoplasma spp.*, *Neospora spp.*, *Clostridium spp.*, and *Staphylococcus aureus.*[53–55] Dogs that eat *Salmonella* contaminated raw feed, especially poultry, often shed *Salmonella* in the faeces. This shedding can lead to environmental contamination and human disease.[56,57]

Positive health aspects of pet ownership - Despite the risk for owners to get infected with pathogens through their pets, there are also well-documented positive effects on human health, which could also affect disease resistance. There is even a term for the human health benefits of companion animals, it is called zooeyia taken

from the Greek words for animal (zoion) and health (hygeia).[58] This topic has been widely studied, with many findings pointing to the positive health effects of companion animals.

Firstly, there is a known association between the presence of pets and reduced stress and blood pressure.[59–61] This can be associated with a reduced risk of cardiovascular diseases such as myocardial infarction.[62] Another aspect where the benefits of companion animals have been widely discussed is their ability to provide a feeling of closeness, which positively impacts psychosocial well-being and mental health. Contact with companion animals is associated not only with reduced stress, but also with alleviated loneliness,[63,64] and a reduced risk of depression.[65] These conditions are known to lead to increased activity of the hypothalamic-pituitary-adrenal (HPA) axis, which raises corticosteroid levels, potentially disrupting the immune system function and can therefore heighten susceptibility to infections.[66] Dog ownership has also been linked to increased physical activity, as most dog owners take their dogs on regular walks. This contributes to different health benefits, such as better cardiovascular fitness with reduced risk of myocardial infarction, stroke, and hypertension; a decreased risk of death from type 2 diabetes, lower obesity rates, and their associated benefits.[67] Regular contact with pets has been associated with reduced stress[68] and a lower risk of depression.[65] It can even be beneficial in recovering from life-threatening cardiovascular illness.[69,70] Exposure to animals, especially dogs, has also been associated with fewer infectious respiratory illnesses and reduced risk for allergies and asthma.[71–73]

Evidence suggests that these positive effects may translate into measurable economic benefits, with fewer doctor visits and, therefore, reduced healthcare costs. A study in Germany and Australia found that pet owners had, on average, 15% fewer doctor visits compared to non-pet owners.[74]

The need for pandemic preparedness - Experts have been warning for decades that epidemics and pandemics will be a significant threat to human health in the 21st century. For example, in the United States, the Institute of Medicine in 2003 already stated the need for innovative systems of surveillance to quickly gather and analyse information to improve the ability to recognise disease outbreaks and track infections.[15] During the COVID-19 pandemic it became clear how unprepared most

countries still were for such an event.[75] Therefore, pandemic preparedness experts recommended to establish cohorts for pandemic preparedness, such as the BEready cohort.[76] Other examples for pandemic preparedness cohorts are the Flu Watch Study focuses on seasonal influenza and other seasonal infectious respiratory illnesses[77] or the RESPIRO Study which focuses on factors influencing infectious community-acquired pneumonia caused by different pathogens.[78] Lifelines, a large cohort study in the Netherlands, pivoted rapidly during COVID-19 to set up a specific COVID-19 cohort to study inter alia potential risk factors for COVID-19.[79]

The benefits of pandemic preparedness cohorts – Such pandemic preparedness cohorts can help to establish ongoing communication and to include the public in infectious disease research. In case of a new pandemic these cohorts can be rapidly mobilised and pre-pandemic samples are available for comparative studies.[76] Such cohorts ensure that asymptomatic individuals and those with milder symptoms can be studied. These cases can significantly contribute to the spread of the infection and can complicate efforts to control outbreaks.[80] Such cohorts are also valuable for identifying populations most at risk for infection.[80] Understanding both human and animal roles in disease spread allows for better-targeted prevention measures.

A household cohort allows researchers to observe how diseases spread in a natural setting where individuals live in close contact. Including as many household members as possible, from different age groups, health statuses, and even pets, improves the understanding of transmission dynamics.[81,82] A risk factor for emerging diseases is contact with wild animals, while most people in Western societies don't have direct contact with wild animals, their pets may.[50]

The longitudinal study design allows for tracking of people and animals over time. This is why longitudinal, also called prospective, cohort studies are a powerful method in epidemiological research for studying how lifestyle and environmental factors influence health.[83,84] These studies follow a cohort over time, collecting repeated data to identify risk factors and monitor outcomes.[85–87] Notable examples of such studies include the Framingham Heart Study, the Avon Longitudinal Study of Parents & Children and the Nurses' Health Studies.[88,89] In veterinary medicine, longitudinal cohort studies are less commonly utilised, most likely because they are

cost- and time-intensive.[84,90] But in recent years there have been more and more cohort studies. Some of them are designed to examine a specific theme for a shorter period, but others are lifelong cohorts open to study different subjects.[91]

Table 1: Examples of cohort studies in veterinary medicine.

Study name	Location(s)	Studied theme	Year of inception	Lead/coordinating institution
Dogslife [83]	Edinburgh (UK)	Diverse, gastrointestinal upset, obesity, health surveillance in Labrador Retrievers	2010	Royal School of Veterinary Studies, University of Edinburgh
Growing dog project [92]	Zürich (CH)	Microbiota, response to vaccines, etc.	-	Vetsuisse faculty Zurich
Golden Retriever lifetime Study [93]	Many in the US	Dietary, genetic and environmental risk factors for cancer and other important diseases in dogs	2012	Morris animal foundation
Generation Pup [94]	UK and Ireland	Influence of environmental and genetic factors on health and behaviour outcomes	2015	Dogs Trust (UK)
MARS Petcare biobank [95]	All Mars Veterinary Health hospitals in the US	Study of health in dogs and cats	2022	Mars Veterinary Health

2. Materials and methods

2.1 Ethical considerations

Ethical approval for the study protocol was granted by the ethics committee of the canton of Bern for human participants (BASEC number 2023-02290) and by the veterinary office of the canton of Bern for pets (approval number BE21/2023).

Participants may withdraw their consent at any time without needing to justify their decision. After withdrawal, their coded data and samples already collected may still be used for the study and, where consent has been provided, for future use. If consent for future use has not been received, samples will be destroyed after analysis. In any case, collected data will remain coded in the database. An individual can withdraw their consent, but the household can remain in the cohort.

2.2 Study design

This prospective, population-based cohort study was designed to include 1500 randomly selected households in the canton of Bern. In this thesis, we present the first results focusing on the household pets included in the study.

The study was designed in three parts, an online questionnaire in the target population evaluating willingness to participate, a 12-month pilot study followed by the enrolment of the full cohort. At the end of each stage, results were evaluated and the study protocol was adapted based on the results. In this thesis, the results of the pilot study and the first 9 months of enrolment of the full cohort are presented.

The study was accompanied by a coordinated communication strategy, aiming to raise awareness about pandemic preparedness in the general population, and to inform the public and stakeholders about the study and recruit households.

2.3 Study population

The eligible study population includes all private households in the canton of Bern, Switzerland, including adults, children, and pets. Survey data suggests that approximately 30% of households own a cat and 12% own a dog.[30] We include all animals that people regard as their pets, and that can be registered as distinct individuals for the study. For example, fish that live in a school would not be eligible.

2.4 Pilot study

For the pilot study, 108 households were enrolled from a convenience sample (participants selected based on easy availability rather than through random or systematic sampling) between April and September 2023. The main aim was to assess the feasibility of the main study. The pilot study was time-limited, consisting of a baseline visit and a follow-up questionnaire after one year. Procedures were largely similar to those described below for the main study. Only dogs and cats were eligible for inclusion in the pilot study, no other animals were included.

All baseline visits were conducted by the study veterinarian at the Small Animal Clinic, Vetsuisse Faculty, University of Bern. In contrast to the main study, the baseline assessment included a complete blood count and a biochemistry panel for dogs and cats. No faecal analyses were performed. The pet questionnaire had largely the same structure and covered the same topics as described for the main study. Some questions were subsequently refined, as described in the results section.

In the pilot study, the disease event of interest for dogs and cats was not gastrointestinal symptoms but respiratory symptoms in a household member. In such cases nasal or oropharyngeal swabs of pets were collected by the owners and analysed for respiratory viruses.

2.5 Enrolment of the full cohort

We started enrolment of the full cohort at the end of April 2024 and expect to complete it by the end of 2025. We use various enrolment strategies. We invited households that participated in the pilot study to join the main study. Using the cantonal residents' register, we also invite a random selection of households via postal letter. In each selected household, we randomly designate an adult as the main contact and send an invitation letter for the entire household. We also enrol volunteer households from the general public, using strategies such as “mediators”, defined as individuals who disseminate study information via established social or professional networks. Proactive volunteers are also welcome to enrol. We obtain written informed consent for all participants, including pets.

2.6 Study procedures and visits

Figure 1: Timeline of study visits

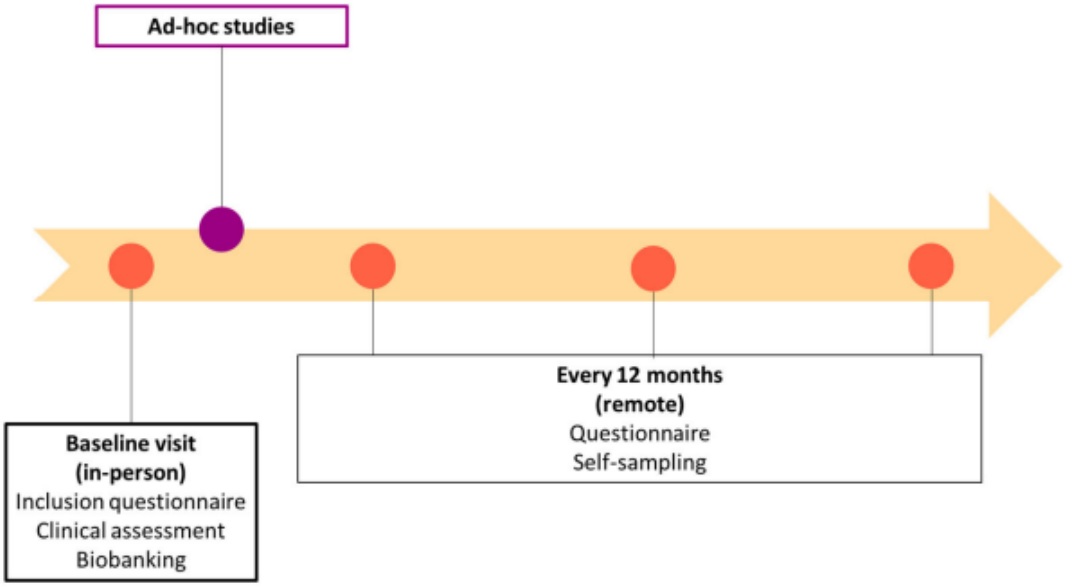


Figure 2: Assessments at each visit

Time	**0**	**Every 52 weeks (±4 weeks)**	**Ad-hoc studies**
Visit	**Baseline**	**Assessment at 12 months**	**Disease event**
Oral and written Information	X		
Written consent	X		
Check inclusion/exclusion criteria	X		
Anthropometric measures (humans)	X		
Blood pressure (humans)	X		
Health check (animals)	X		
Venous sample†	X		
Stool sample (cats and dogs)	X		X
Capillary sample (DBS) (humans)	X	X	
Questionnaire	X	X	X*
Swab	X		X

† Humans, cats and dogs only; * main contact person for the household only; DBS, dried blood spot

2.6.1 Baseline visits

Baseline visits for adults and children usually take place at the Swiss Institute for Translational and Entrepreneurial Medicine (SITEM) in Bern, Switzerland. If participation is not feasible otherwise, we offer home visits. Baseline visits are conducted by a trained study nurse, an informed consent discussion is held, and consent forms are signed. We collect anthropometric measures such as height, weight, hip/waist circumference, and blood pressure. Additionally, a venous blood sample for EDTA-plasma and serum is taken, as well as five to ten drops of capillary blood on filter paper for dried blood spots (DBS). During the visit, the study nurses demonstrate to participants how to collect nasal swabs and capillary blood samples from themselves and their children.

For feasibility reasons, **veterinary visits** are limited to dogs and cats. The initial visit is in-person, either with the study veterinarian or the pet's private veterinarian. This visit includes a general clinical examination and venous blood sampling. The clinical examination includes an estimation of the Body Condition Score (BCS), a widely used system for assessing the nutritional status and body fat of an animal.[96–98] We used the Purina scorecard for dogs[99] and for cats[100], which ranges from 1 (cachectic) to 9 (morbidly obese). A BCS of 4 is considered optimal in cats, and a BCS of 4 or 5 is considered optimal in dogs, considering the regular constitution of the breed. EDTA-plasma and serum are collected for storage at the liquid biobank (https://www.biobankbern.ch/home-de/liquid-biobank-lbb/) in Bern for future use. In the main study, owners bring faecal samples from their pets, collected over the three days prior to the visit. These are analysed for endoparasites using flotation, the Baermann funnel method and the SAF (sodium acetate-acetic acid-formalin) technique.

After the visit, household members receive an automated email invitation to fill in the baseline questionnaire via the electronic data capturing (EDC) system implemented in REDCap (https://www.project-redcap.org/). For children under 14 years, a parent or legal guardian completes the questionnaire, and for pets their owners do. We collect data on socio-demographic characteristics, the number of human-to-human contacts, individual information on gender, quality of life, medical history, comorbidities, allergies, medical treatments, vaccinations, and travel

history. For pets, we collect data about preventive health measures, health status, closeness of contact with their owners, and contact with other animals.

Approximately one year after baseline, there is an annual online assessment. Participants will fill in an online questionnaire focusing on the description of new developments: newly diagnosed illnesses, recent vaccinations, the arrival of new household members, visits to different countries, and any changes concerning their pet(s). Adults and children also collect five to ten drops of capillary blood as DBS on filter paper and post the samples via surface mail to the biobank.

2.6.2 Disease events

Disease events are reported by participants for at least 12 months. For humans, the disease event is focused on symptoms compatible with a respiratory infection, and for animals, we focus on episodes of diarrhoea and/or vomiting. Participants complete a disease event questionnaire. Symptomatic household members collect nasal swabs and send them via surface mail to the Liquid Biobank in Bern for storage at -80°C. We analyse the swabs in batches for a panel of respiratory viruses.

For cats and dogs with acute diarrhoea, the owners collect a faecal sample for detection of parasites. The household sends the sample by surface mail to the Institute of Parasitology at the Vetsuisse Faculty Bern. Samples are analysed using flotation, the Baermann funnel-, the SAF- and Ziehl-Neelsen methods. If fish tapeworm (*Diphyllobothrium latum*) is suspected in dogs, such as when proglottids are observed in the faeces or perineal region, and the dog has consumed raw fish, sedimentation is performed as well. If eggs or oocysts cannot be identified, polymerase chain reaction (PCR) testing is performed for further differentiation.

Pre-packed, barcoded sampling kits for self-sampling are provided to participants. The kits contain all necessary materials for sample collection and shipping, including labelled primary and secondary containers, and a pre-paid return envelope. Pet owners who attend the baseline visit at the small animal clinic in Bern receive an in-person demonstration on how to collect nasal or pharyngeal swabs from their animals. An instructional video is available to all participants on the study homepage.

2.7 Questionnaires

We designed a web-based questionnaire that participants can complete in REDCap. To ensure confidentiality, we assign each pet an anonymous number and store the pets' names and owner information in a separate database. The questionnaire for pets requests information about sex and neuter status, weight, age, and the animal's main function. It also collects information about the animal's lifestyle, such as free roaming, off-leash time, hunting behaviour, raw meat feeding, travel- or import history, and contact with other animals. Additionally, information about known diseases and preventive health measures (vaccinations and antiparasitic treatments) is obtained. We also ask about the closeness of contact between the owner and the pet. We collect data using categorical, binary, and free-text responses. Completing the questionnaires typically takes around ten minutes for most owners. The full pet specific questionnaire can be found in the appendix.

2.8 Data analyses

In this work, data collected until the end of January 2025 are analysed. We performed descriptive statistics on the data regarding the household pets, using basic statistical functions in Microsoft Excel. We examined the number of households with pets, described the demographics of the pets, and assessed whether they engage in behaviours that could pose a risk of obtaining and/or transmitting zoonotic diseases. We also evaluated how closely the pets and their owners live together. We described which parasites were detected and compared the incidence of certain parasites in our study to other studies. In addition, we assessed the vaccination and deworming status of the pets in the study. For this, we used the guidelines of the Swiss Veterinary Association for Small Animals (SVK-ASMPA) for vaccinations,[101] and those of the European Scientific Counsel Companion Animal Parasites (ESCCAP) for endo- and ectoparasite prophylaxis.[102]

3. Results

The results from the pilot and main study are presented separately.

3.1 Pilot study

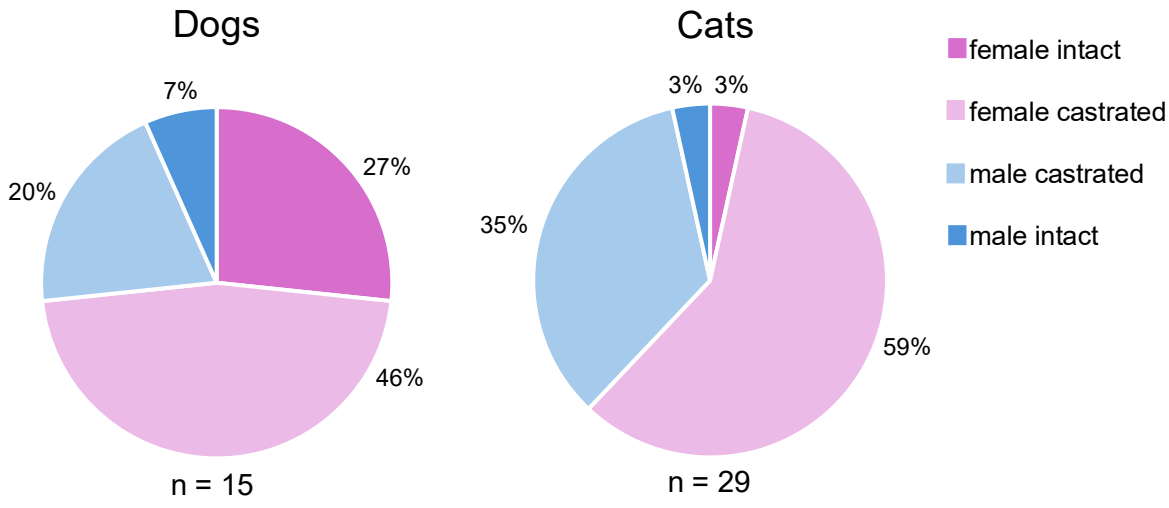
3.1.1 Study population

Between April and September 2023, a total of 108 households were enrolled in the pilot study. Of these, 28 (26%) included at least one pet. In total, 44 animals were enrolled: 15 dogs (34%) and 29 cats (66%). Nine of the 28 pet-owning households (32.1%) included more than one pet. Several households included multiple dogs: one household included two dogs, one included three, and one included four. Consequently, only six of the 15 dogs came from single-dog households. Among cats, 13 households included one cat, and eight households included two.

By the end of the pilot study, only two of the 28 pet-owning households (7.1%) agreed to transition into the main study. These households included two cats and one dog.

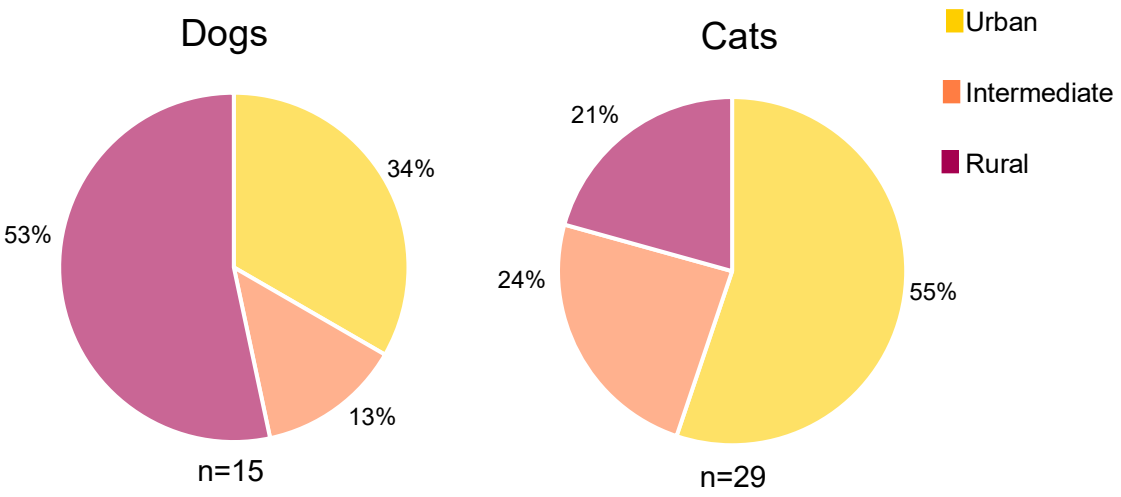
We saw a pronounced overrepresentation of female dogs, which we attribute to one household being a breeder with four female dogs. In contrast, we found no clear reason for the overrepresentation of female cats in the pilot study. The proportion of unneutered cats was very low. The only two intact cats were still too young to be neutered.

Figure 3: Sex and neuter status of dogs and cats in the pilot study



The distribution of living environments (rural, urban, intermediate) differed between species. More cats lived in urban areas, while more dogs lived in rural areas. However, this pattern was likely biased, as the two households with the highest number of dogs were both located in rural areas.

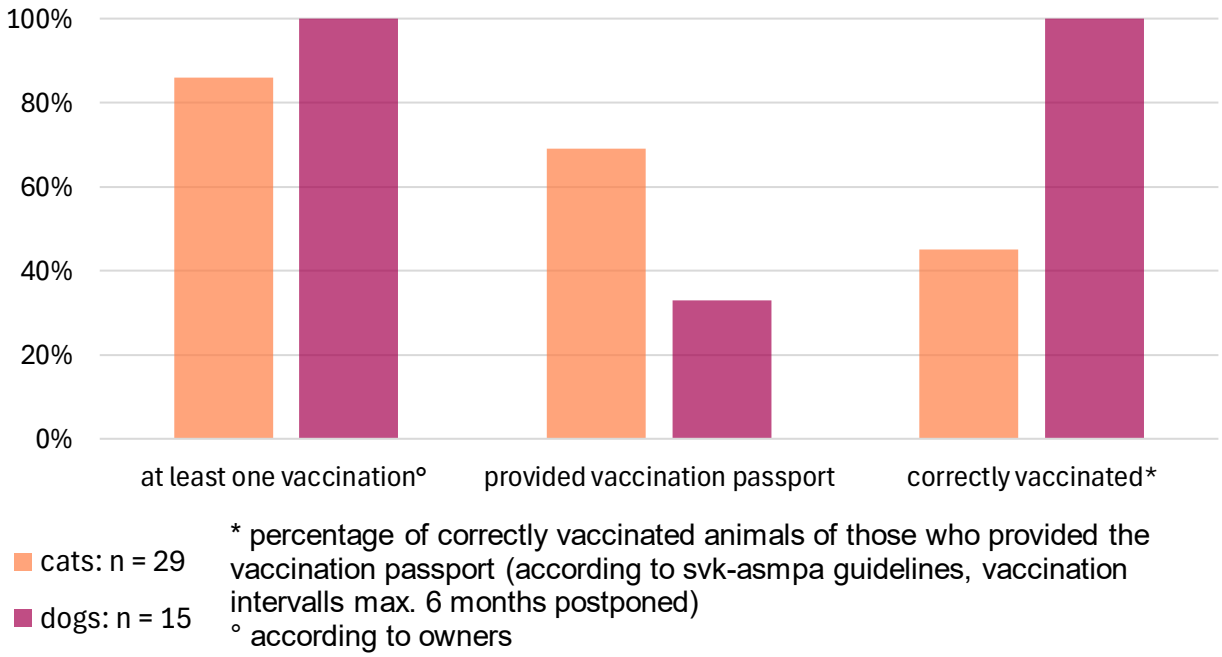
Figure 4: Living environment of dogs and cats in the pilot study



3.1.2 Preventive health measures

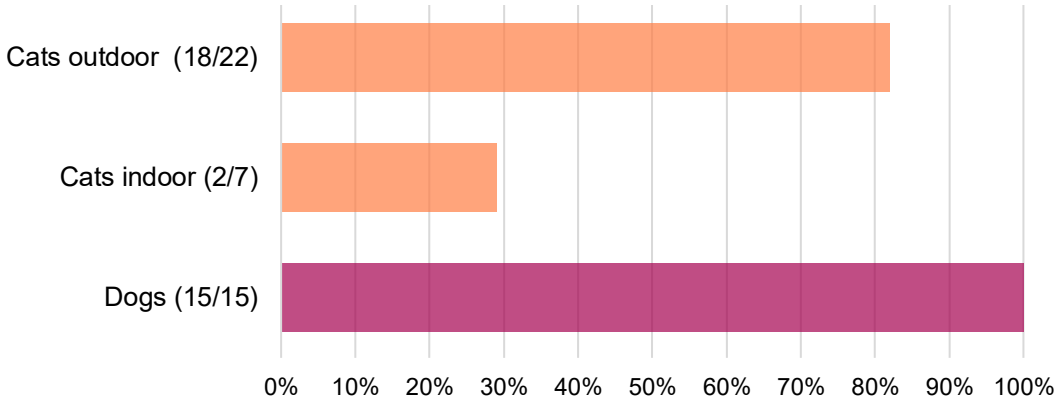
In the pilot study, **vaccination** passports were provided for only five dogs, all of which were vaccinated according to the recommendations. Due to the small number, these data are not representative.

Figure 5: Vaccination of dogs and cats in the pilot study



In the pilot study, we asked owners whether they gave their pets regular antiparasitic treatment. Many owners reported doing so, especially for dogs and outdoor cats. However, the question was too unspecific, with no definition of what "regular" antiparasitic treatment meant.

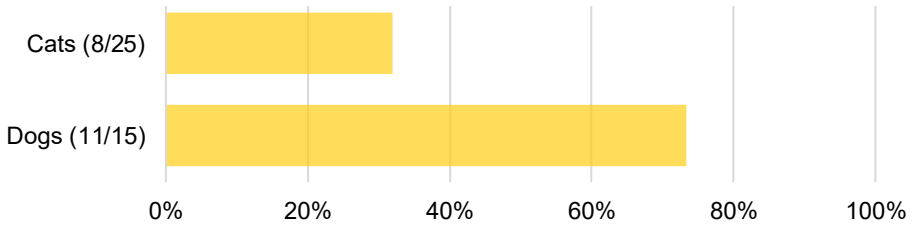
Figure 6: Owner reported regular antiparasitic treatment in the pilot study



3.1.3 Zoonotic risk

In the pilot study, a relatively high number of pets were fed raw meat. Among dogs, many of those living in multi-dog households received raw meat. However, we did not record feeding frequency, so it is possible that some pets were only fed raw meat occasionally.

Figure 7: Feeding of raw meat in the pilot study

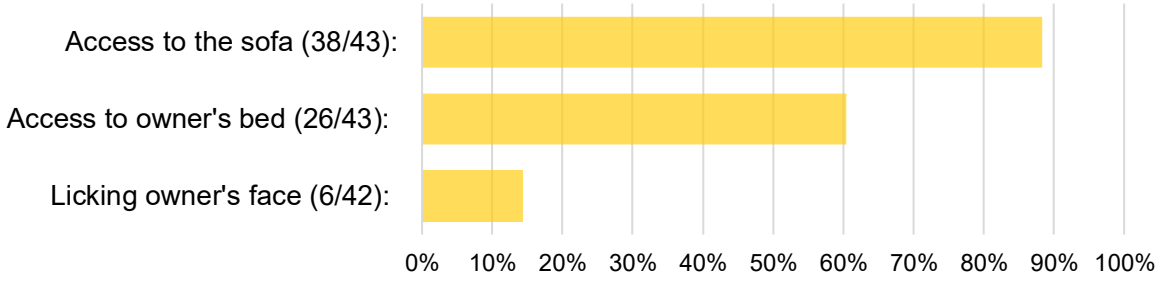


For seven of the 29 cats (24.1%) and 8 of 14 dogs (57.1%), contact with livestock was reported.

3.1.4 Closeness of human-animal contact

Most pets had access to furniture, with nearly all allowed on the sofa and a majority allowed on the owner's bed.

Figure 8: Closeness of contact between pets and owners in the pilot study



3.1.5 Blood samples

In the pilot study, we were able to collect blood samples from 14 dogs and 28 cats. However, some cats reacted adversely to blood sampling, and we were therefore not always able to collect the full set of planned samples. For this reason, only haematology was performed for one cat, and only biochemistry for another.

In the complete blood count (CBC), we found abnormalities in three dogs. All were considered mild and, in the absence of clinical signs, not clinically relevant. We found abnormalities in three cats. One had mild changes, likely due to a cat fight three weeks prior. One showed neutropenia with suspected cyclic neutropenia, and a recheck was recommended. Another had moderate thrombocytopenia and mild neutropenia, for which we suggested follow-up and further investigation.

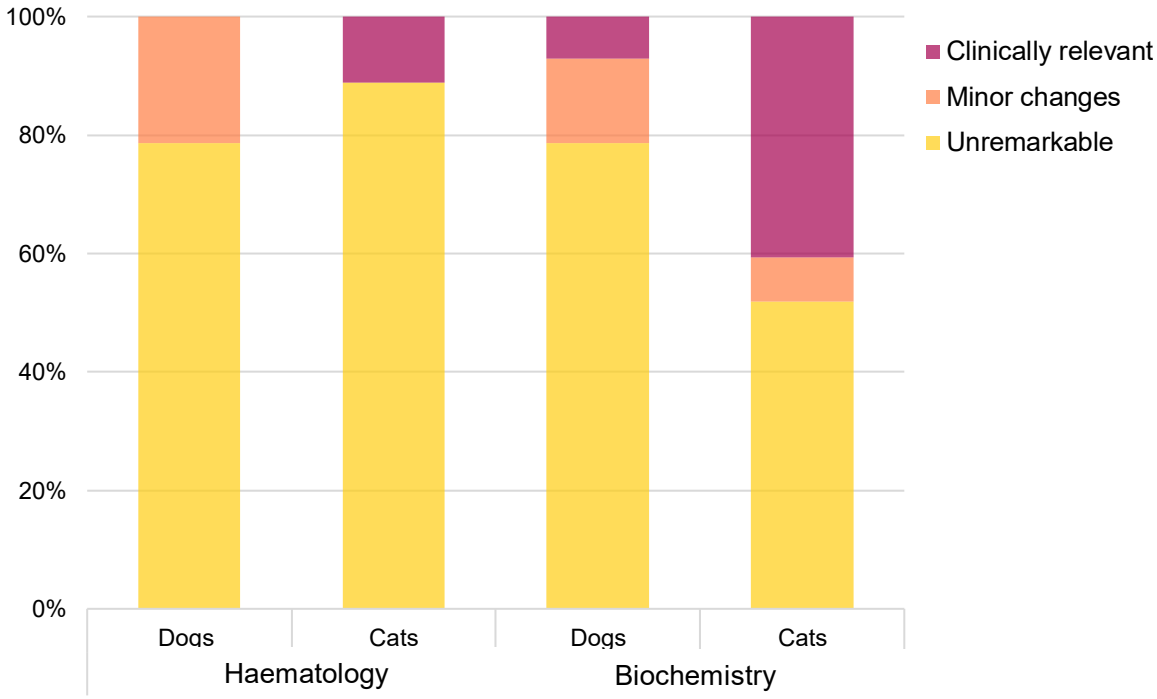
In the biochemistry panel, we found abnormalities in 13 cats. Nine had azotaemia, but chronic kidney disease was known prior in only three of them. The cat previously involved in a fight also had mild hyperglobulinaemia and a mildly increased serum amyloid A (SAA). The cat with suspected cyclic neutropenia showed mild hypokalaemia. In one cat, we found hypokalaemia and increased alanine aminotransferase (ALAT). This cat had no known disease but vomited every 2-3 days and frequently licked its abdomen. Another cat showed mild hypoalbuminaemia and mild hyperglobulinaemia. This was a 12-year-old cat with a

body condition score (BCS) of 2/9, who ate excessively without gaining weight. Total T4 was measured twice and was within the normal range on both occasions.

Abnormalities were found in three dogs, one had mild azotaemia, which was not previously known. Two had hyperproteinaemia due to hyperglobulinaemia, one was considered healthy, and one had a known allergy to dust.

We also analysed samples from two puppies and two kittens, all of whom showed age-related deviations from reference values. These were classified as normal.

Figure 9: Findings from the blood analyses performed in the pilot study



3.1.6 Changes implemented in the main study

After the pilot study, we implemented the following changes in the main study:

- **Blood analyses discontinued:** Not included in the main study due to financial reasons and because owners did not consider them a key motivation for participation.
- **Implementation of faecal analyses**

- **Addition of questions about hunting behaviour:** A new section was added to ask whether the animal hunts or catches other animals, and if so, which species.
- **Revision of the raw meat questions:** The question “Is your animal eating raw meat?” was revised to “Are you feeding raw meat?” to improve clarity.
- **Improved antiparasitic treatment question:** We refined the question to specify treatment frequency, the product used, and the date of last administration. We also introduced a distinction between endo- and ectoparasites during the course of the main study.
- **Refinements of contact with other animals questions:** We improved the answer options in the question about contact with other animals and implemented a specific question about contact with birds.
- **Addition to the closeness of contact section:** One question was added asking about direct contact with the animal.

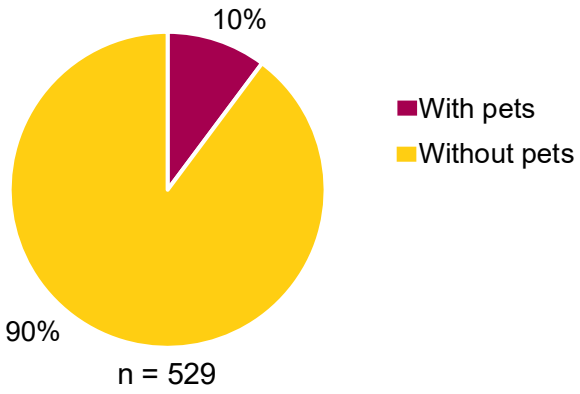
3.2 Main study

3.2.1 Study population

Between April 2024 and January 2025, a total of 529 households were recruited for the main study. Among these, 80 animals from 54 households joined the cohort. These included 33 dogs, 40 cats, three mice, two tortoises, and two horses. For the mice, tortoises and horses each species was kept by only one household.

For 29 of the 33 dogs (88%) and 36 of the 40 cats (90%), at least part of the questionnaire was filled in.

Figure 10: Proportions of households with and without pets in the main study



A larger proportion of cats in the main cohort were neutered compared to the dogs. As in the pilot study, there was an overrepresentation of female dogs in the main study. The two horses, as well as the three mice and one of the tortoises, were intact males; the other tortoise was an intact female.

Figure 11: Sex and neuter status of dogs and cats in the main study

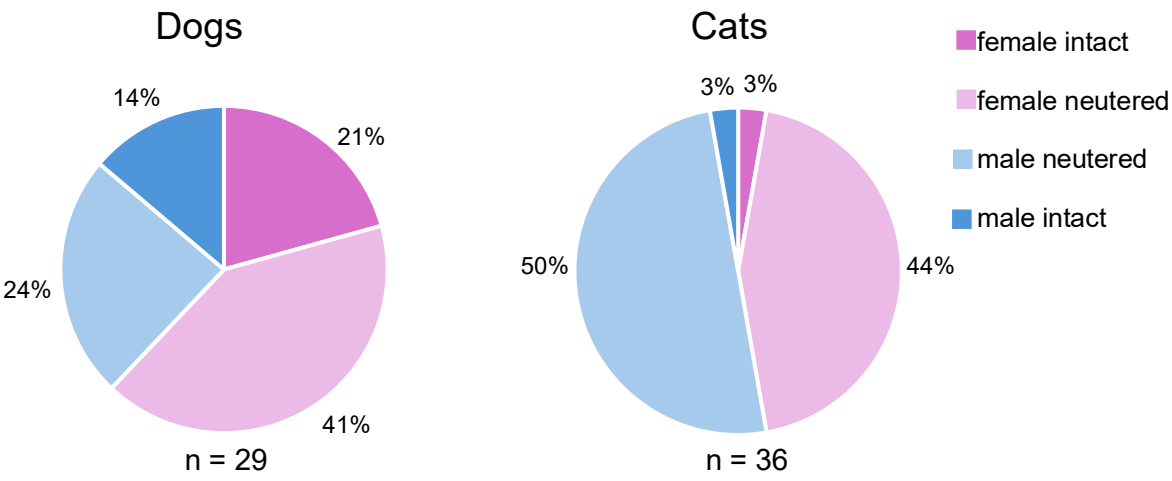
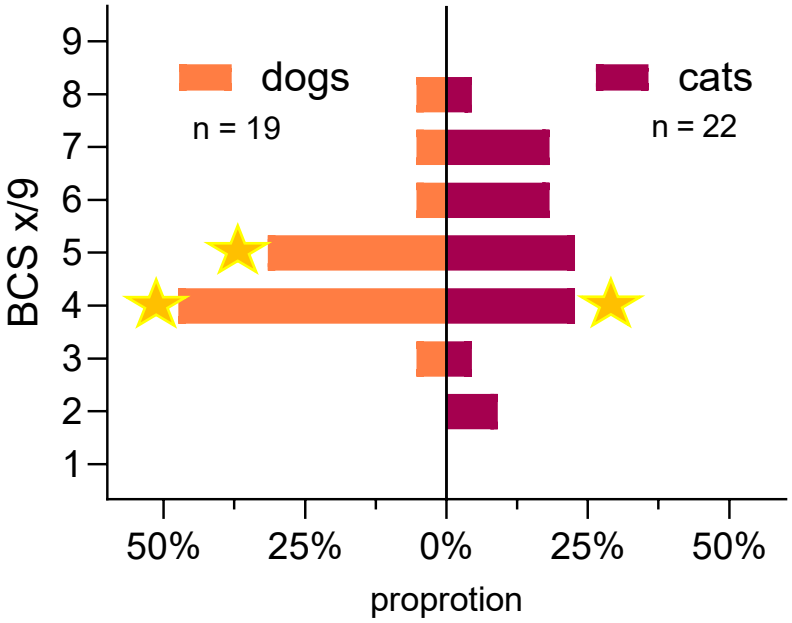


Table 2: Age distribution of dogs and cats [103]

Age group	Dogs (n=29)	Cats (n=36)
≤ 1 year	2 (7%)	5 (14%)
2–8 years (dogs) / 2–11 years (cats)	20 (69%)	18 (50%)
≥ 10 years (dogs) / ≥ 12 years (cats)	7 (24%)	13 (36%)

In our cohort, more cats deviated from the optimal body condition score compared to dogs, especially in the direction of obesity.

Figure 12: Distribution of Body condition scores in cats and dogs in the main study cohort. The optimal Body condition score is marked with an asterix.



Of the 29 dogs with reported roles, all were companion animals, with two dogs' main task being a service dog. Two dogs were also used for hunting, and three for breeding. All except one dog (27/28) were sometimes off-leash outdoors. Ten cats (28%) were strictly indoor pets, while 26 (72%) had outdoor access.

Nine of the 29 dogs (31%) were imported, primarily from southern or south-eastern Europe. One originated from Austria, and one from the United States. Twelve dogs (41%) had travelled to southern Europe or outside Europe. Six of the 36 cats (17%) were imported, all from neighbouring countries, and one cat had travelled to southern Europe or outside Europe.

Of the 54 households that included pets, nine (17%) were located in the countryside, 28 (52%) in urban areas, and 17 (31%) in intermediate areas.[104] Multipet households made up 29.6% of pet-owning households. Cats were more likely to live

in a multipet household, with 72.5% (29/40) living with other cats or, in one case with a dog. In contrast, only 18.2% (6/33) of dogs lived with other dogs or a cat.

Figure 13: Living environments of dogs and cats in the main study

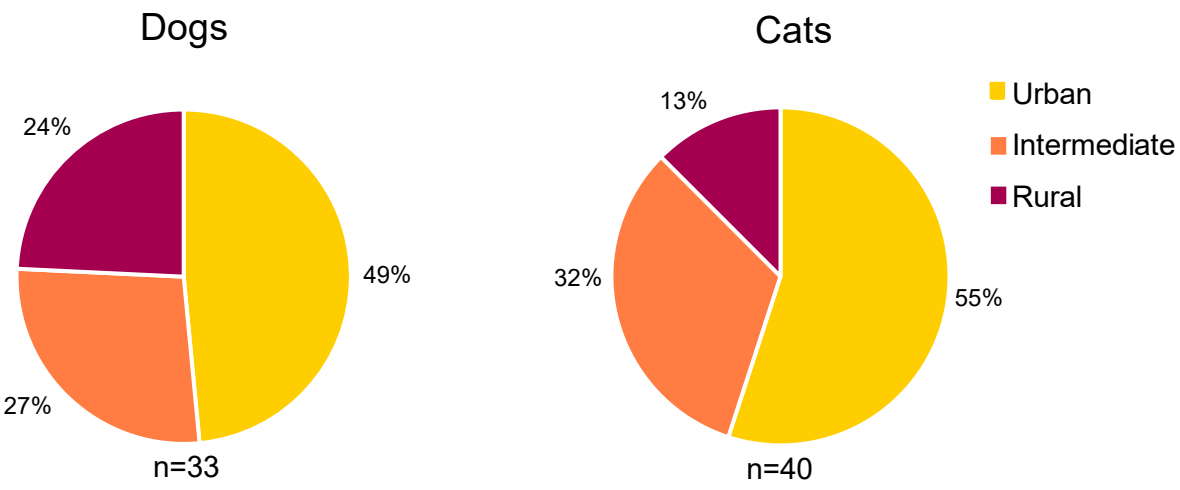
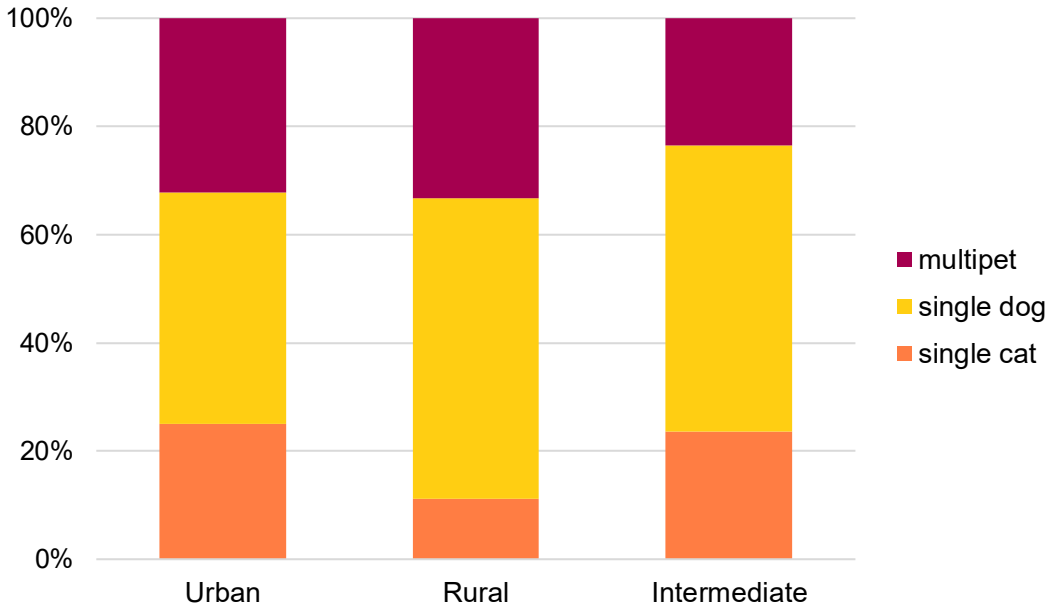


Figure 14: Pet ownership by living environment in the main study

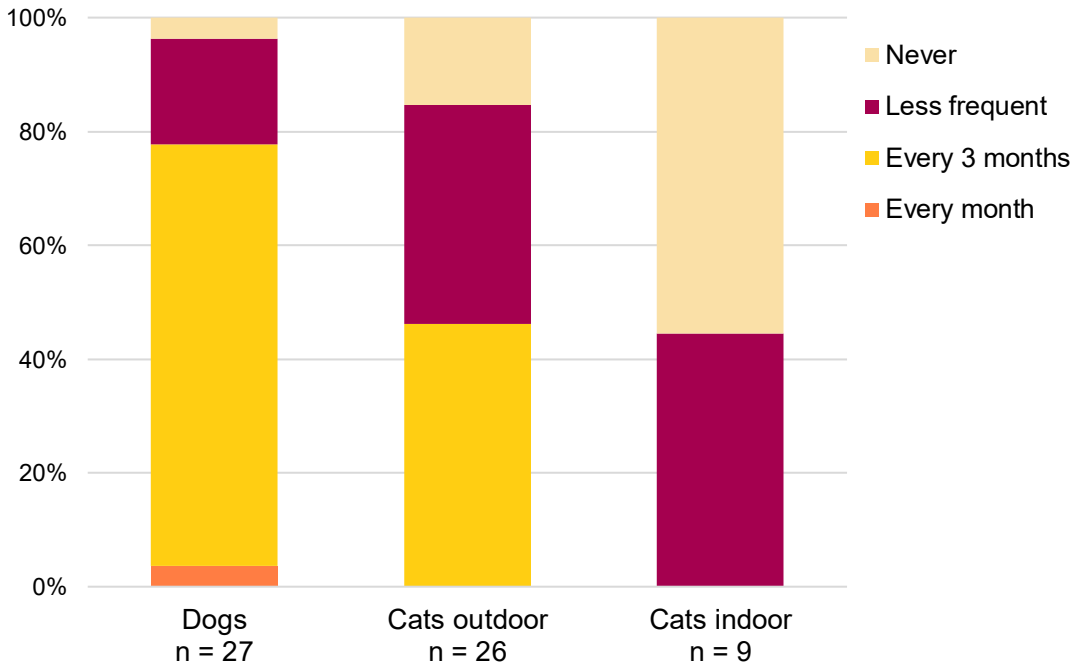


3.2.2 Preventive health measures

3.2.2.1 Parasite prophylaxis

Indoor cats are dewormed less frequently than outdoor cats or dogs. However, the frequency at which indoor and outdoor cats are dewormed according to recommendations is comparable. Dogs are more often dewormed according to recommendations than cats. Deworming of the tortoises was performed less frequently than every three months using fenbendazole. The horses were also dewormed less than every three months, but the product used was not reported. The mice were not treated for parasites.

Figure 15: Deworming frequency of dogs and cats in the main study



As the question on ectoparasite treatment was introduced later, we received responses for only 14 dogs. One of these dogs had never received treatment, seven dogs (50%) were treated every three months, and six dogs (43%) less frequently. We collected data on ectoparasite prophylaxis for 13 cats. Four (31%) had never been treated, two (15%) were treated more than once a month, two (15%) every three months, and five cats (38%) less frequently.

Table 3: Used products for parasitic prophylaxis

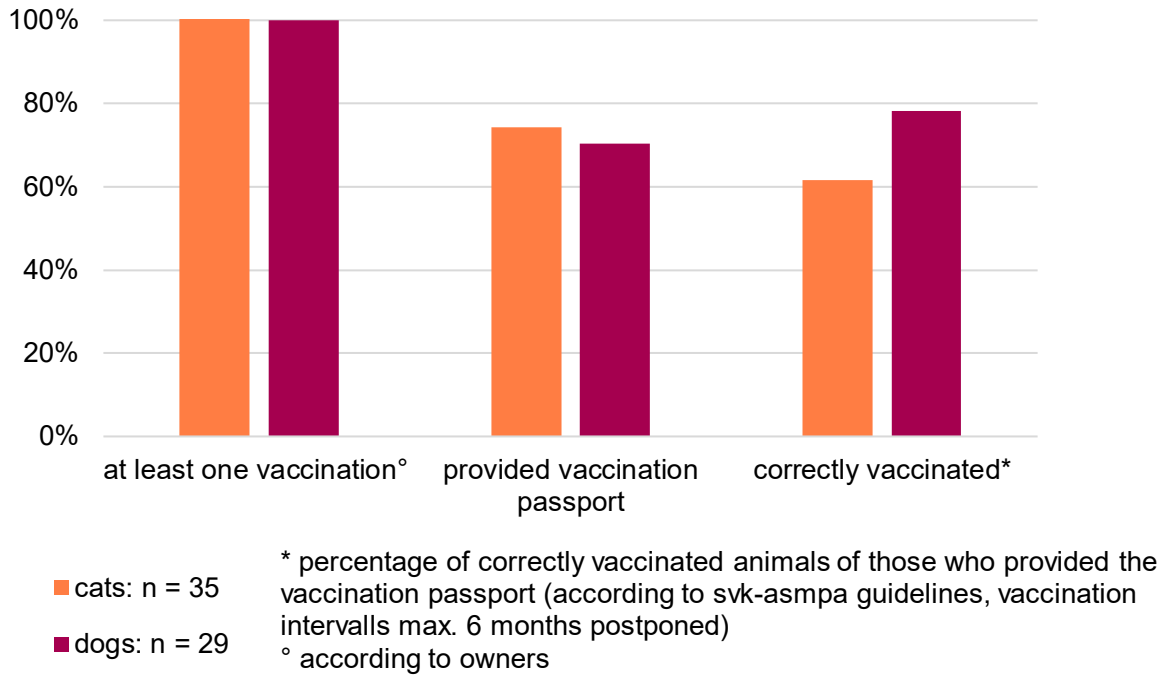
Used product	Dogs	Cats
Endoparasiticides		
Milbemycin oxime + Praziquantel	20	12
Fenbendazole	1	0
Emodepside + Praziquantel	0	1
Combination products		
Eprinomectin, Esafoxolaner, Praziquantel	0	3
Eprinomectin, Fipronil, Methoprene, Praziquantel	0	1
Imidacloprid, Moxidectin	0	2
Ectoparasiticides		
Fipronil	0	6
Flumethrin + Imidacloprid	1	1
Deltamethrin	1	0
Lotilaner	2	0
Fluralaner	7	0
Sarolaner	1	0

red = not approved or available for use in the respective species

3.2.2.2 Vaccination

The five dogs that were not vaccinated according to current recommendations had completed their primary immunisation, but the recommended yearly revaccination was delayed by more than six months. Among the ten incorrectly vaccinated cats, three had not received the primary immunisation, three were not vaccinated against feline leukaemia virus despite outdoor access, and the remaining four had vaccination intervals that were too long. Both horses were vaccinated, but no passport was provided. The tortoises and mice were not vaccinated.

Figure 16: Vaccination of dogs and cats in the main study



3.2.3 Zoonotic risk

Of the 29 dogs, 28 had contact with other dogs, 13 (45%) with cats, four (14%) with horses, six (21%) with farm animals, and seven (24%) with wild animals, and two (7%) with other unspecified animals. Only one had no contact with animals outside its household.

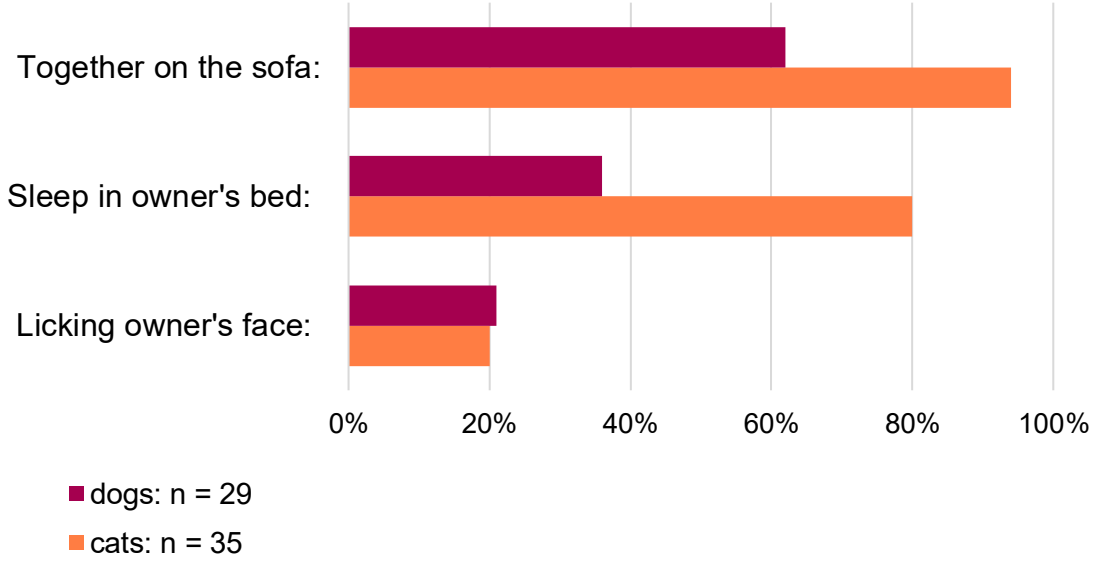
Among the 35 cats, 10 (29%) had contact with dogs, 22 (63%) with other cats, two (6%) with horses, nine (26%) with farm animals, and 16 (46%) with wild animals, and one (3%) with another unspecified animal. Thirteen cats (37%) had no contact

with other animals outside their household. Eleven dogs (38%) and 26 cats (74%) had contact with birds.

Five of the 29 dogs (17%) and 16 of the 35 cats (46%) consumed raw meat.

For 2/12 dogs (17%) the owners reported that the dogs caught animals, while 8/16 (50%) chased animals. This question was updated during the study to improve clarity. Among the 26 outdoor cats, 12 of 15 (80%) chased and 8 of 11 (73%) caught animals. Of the ten indoor cats 2/7 (29%) chased animals, and none of the three indoor cats whose owners answered the updated question caught anything.

Figure 17: Closeness of contact in the main study



3.2.4 Closeness of human-animal contact

Many of the cats and dogs spent time in the owner's bed or on the sofa, with a higher proportion of cats than dogs doing so. Roughly the same proportion of dog and cat owners reported that their pet licked their face. None of the pets shared eating or drinking dishes with their owners, nor did they drink from toilets.

Twenty-two of 29 dogs (76%) and 31 of 35 cats (89%) had skin-to-skin contact with their owners or contact via saliva, faeces, or urine. All dog owners collected faeces, while six of the 35 cat's owners reported collecting faeces from the garden.

Almost all participants (28 dog's owners and all 35 cat's owners) reported washing their hands after removing faeces.

3.2.5 Blood samples

In the main study so far, we successfully collected venous blood samples from 12 dogs and 11 cats.

3.2.6 Parasitological examination

As of 31 January 2025, we analysed stool samples from 21 dogs and 18 cats. Of the cats, seven (39%) lived indoors only, while 11 (61%) had outdoor access. We detected parasites in two of 18 cats (11%) and in seven of the 21 dogs (33%). Both cats with detected parasites had outdoor access. One cat was reported to chase animals and the other to catch animals (different question). In one of the cats we found three different types of parasites. In two dogs, we found parasites from other species in intestinal passage, probably due to coprophagia. When excluding those dogs, five dogs (23.8%) tested positive for parasites. One was dewormed every three months, while the others received treatment less frequently.

Table 4: Parasite findings in dogs, *suspected intestinal passage due to coprophagia

Parasites found	Number of dogs	Prevalence
Toxocara canis	1	4.8%
*Toxocara cati**	1	4.8%
Neospora caninum	1	4.8%
Cystoisospora ohioensis	1	4.8%
*Spirurida**	1	4.8%
Giardia	2	9.5%

In the dog with *Neospora caninum*, PCR testing was performed to differentiate the oocysts, as they appear similar to those of other species under microscopical

examination. Serological testing was negative. Re-examination of the faeces 14 days later showed no oocysts present. The suspected source of infection was the feeding of raw beef liver.

Table 5: Parasite findings in cats

Parasites found	Number of cats	Prevalence
Toxocara cati	2	11.1%
Capillaria eggs	1	5.6%
Taenia (PCR confirmed)	1	5.6%

We found no parasites via the Baermann funnel technique, including no evidence of lungworm infections such as *Angiostrongylus vasorum* or *Aelurostrongylus abstrusus*. Additionally, we detected no *Strongyloides stercoralis*, a parasite of special interest, due to its potential emergence in Europe.

Due to low case numbers, we did not conduct statistical analysis of risk factors. However, we will discuss potential associations with age, outdoor access, and hunting behaviour.

3.2.7 Disease event

By the end of January, only one disease event in a dog had been reported. No parasites were found in the faecal analysis.

3.3 Differences between pilot and main study

In the pilot study, we were able to enrol a higher proportion of households with pets, with 26% including at least one pet. This was expected, as we had intentionally invited more pet-owning households. In contrast, the main study included fewer households with pets (10%), but we were able to achieve a more balanced distribution between dogs and cats.

Demographic differences were most notable among dogs. This is at least partly explained by the fact that two large households in the pilot study accounted for

nearly half of the dog population and contributed to a higher average number of pets per household. The main study included no such large households, although the overall number of multi-pet households was similar between the cohorts.

Both cohorts showed an overrepresentation of female dogs, which was more pronounced in the pilot study, possibly due to one large household that was a breeder with four female dogs. Additionally, a larger proportion of dogs in the pilot study lived in rural areas, a finding likely influenced by the two large multi-dog households, both located in rural areas.

The level of closeness between pets and owners was comparable across the two cohorts. Reported raw meat consumption varied slightly. For dogs, this difference may again reflect the influence of the large households in the pilot study, whereas no clear pattern was observed for cats.

The number of cats reported to have contact with livestock was nearly identical in both cohorts. In contrast, substantially more dogs had reported livestock contact in the pilot study, again likely due to the two large rural households reporting this.

In the main study, we revised the question about deworming to include specific intervals, which led to lower rates of deworming in accordance with current guidelines.

4. Discussion

The BEready cohort is, to our knowledge, one of the first pandemic preparedness cohorts that includes both human participants and household pets, while using self-sampling as a method for collecting data on disease events. By integrating pets into the study design, we gain a valuable opportunity to look more closely at the human-animal interface in the context of infectious diseases. So far, our study has included primarily dogs and cats, with only a few other pet species. Due to the limited data available for these other pets, they are not discussed further in this thesis.

4.1 Biases and limitations

As with many longitudinal studies, the BEready cohort is likely affected by sampling bias due to its time-intensive nature. Participants may be more motivated, have more spare time, and potentially a higher socio-economic status than the general population.[105] This may influence the relationship between owners and pets, if they spend more time together, they may form closer bonds and possibly invest more in preventative health measures. However, this remains speculative, as to our knowledge, no studies have systematically analysed this relationship.

It is more difficult to assess whether the pets included in the cohort are representative of the broader pet population. Comparisons of breed distribution and mixed-breed versus pedigree status between the study cohort and the dogs registered in the national dog database (Amicus, https://www.amicus.ch/) were not performed but could be informative in future studies. For cats this analysis is more difficult, as there is currently no legal requirement to officially register cats living in Switzerland.

To avoid selection bias, we employed various recruitment strategies (see Chapter 2.5). However, it has been argued that enrolling motivated participants may be preferable, as they are more likely to comply with the study protocol, and the impact of selection bias may be limited.[105]

Since we used questionnaires as one of the primary methods of data collection, common questionnaire-related biases must be considered, including acquiescence bias, recall bias, and response fatigue.[86,106] Another relevant example is social

desirability bias, where respondents give answers they perceive as more socially acceptable, for example when asked whether they always wash their hands after contact with their animal or its faeces.

Only 10.4% of households in our main cohort included a pet. This is low compared to the 43% of Swiss households that own a pet.[30] Unfortunately, we did not collect data on how many study households owned pets but chose not to enrol them in the study. Reasons for not including pets may vary. Many pets are afraid of veterinary visits, and cats often dislike being transported, which could discourage owners from enrolling them.

For the pets, and especially in the current work presenting first results, the small sample size limits the significance of the findings.

4.2 Sampling of dogs and cats

We were able to show that faecal sampling of dogs and cats by their owners is a feasible approach in a cohort study like BEready. It offered several advantages such as reduced stress for the animals, as they are handled by trusted individuals and do not need to travel to a veterinary practice. Another advantage is the possibility of timely sample collection without waiting for a suitable appointment. In the event of a disease outbreak, transmission risks can be minimised if the pet and owner do not need travel to a veterinary practice.

Owner-collected faecal samples are a well-established and widely used method, especially in dogs and cats with gastrointestinal symptoms. Since most cases of diarrhoea and vomiting do not go to see a veterinarian, studies based on veterinary practice data miss those cases.[84] With our study, we have the opportunity to also catch these cases, which highlights the value of self-sampling. While it is usually simple, some people may experience feelings of disgust. However, most pet owners are used to cleaning up after their pets and therefore experience less discomfort. For cats that have outdoor access or live in multi-cat households, it can be more difficult or not feasible.

Taking oropharyngeal or nasal swabs from pets is more challenging for most people than collecting faecal samples. However, due to the COVID-19 pandemic and the

widespread use of at-home sampling, people are more used to taking swabs. Nevertheless, collecting swabs from pets remains challenging, as many animals find the process uncomfortable. Pets often need to be restrained to prevent them from moving during sample collection, and in most cases, a second person is needed to assist with the sampling.[107] Cats, in particular, may show adverse reactions such as scratching or, less frequently, biting. Dogs may also attempt to bite, but most dogs will not bite their owners, who are usually able to assess their dog's behaviour well.

The feasibility of sampling cats and dogs by their owners has been looked at and applied in previous studies. For example, a study conducted by researchers associated with the German National Cohort (GNC) examined nasal and buccal swabs, faecal samples, and fur samples. At enrolment, a study veterinarian collected nasal and buccal swabs. After receiving instructions, participants were asked to collect samples at home and send them to the study institute. These samples were bacteriologically cultured, and the study concluded that owner-collected samples from dogs and cats are feasible and appropriate for zoonotic disease research in population-based studies.[107] However, in that study, samples were collected shortly after participants received instruction from veterinary professionals on proper sampling techniques. Whereas in our study, there may be a significant delay between instruction and the need for sampling. Collection of rectal and oropharyngeal swabs by pet owners has also been successfully used in a Swiss study investigating methicillin-resistant bacteria in pets and their owners.[108]

4.3 Parasitic findings

Although our sample size is small, with faecal parasitological examinations performed for 18 cats and 21 dogs, the preliminary findings offer insight into potential zoonotic risks. We identified infections with *Toxocara cati*, *Toxocara canis*, and *Giardia* all of which can potentially be zoonotic. We also compared our results with those of larger studies to see whether the findings from our faecal parasitological examinations to date align with existing data.

4.3.1 Cats

We found endoparasites in 2 out of 18 cats (11%), both of which had outdoor access. Deworming was reported every three months for one cat and less frequently

than every three months for the other, however, the exact date of the last deworming is not known. One cat was reported to chase animals, and the other to catch animals (based on responses to different questions). Compared to other studies, this is a slightly lower prevalence of endoparasites in our cohort. Other studies have reported prevalences between 22.8% and 39.6%.[109–112] Some of these studies excluded cats that were recently dewormed, whereas we did not, which may explain to the lower prevalence in our cohort.

We found *Toxocara cati* in both cats, and in one of the two we found co-infection with *Taenia* and *Capillaria spp*. Other studies also reported *Toxocara cati* as the most common endoparasite found in cats.[110–112] Co-infection appears to be common, with more than one-third of infected cats carrying multiple endoparasites.[111,112] With climate change and increasing temperatures, conditions for parasites such as *Toxocara cati* are becoming more optimal, and prevalence may increase.[113] This is especially concerning because *Toxocara cati* is a parasite which has zoonotic potential, particularly for children.[114]

Our sample size is currently too small to make valid assumptions about risk factors. Other studies have identified age, outdoor lifestyle, geographical location, and a lack of antiparasitic treatment as risk factors in cats.[112]

4.3.2 Dogs

We detected parasites in seven out of 21 dogs (33%). Excluding cases attributed to suspected coprophagia, the prevalence was five out of 21 (23.8%). *Toxocara canis* was found in one dog (4.8%), and *Giardia* in two (9.6%). These values fall within the lower range of prevalences reported in previous European studies, which reported endoparasite prevalences of around 20–30% and *Giardia* between 7–9%.[115,116]

Asymptomatic dogs are usually not tested for *Giardia*, as treatment is not always recommended due to difficulty of treatment and concerns about resistance.[117] The most commonly used deworming agents (milbemycin oxime and praziquantel) are not effective against *Giardia*. However, some types of *Giardia* are zoonotic. If children or immunocompromised individuals live in close contact with the pet, treatment and possibly routine testing should be considered.

The dog with *T. canis* was dewormed less frequently than the recommended interval of every three months. The other parasites detected (*Giardia*, *Neospora caninum* and *Cystoisospora ohioensis*) are not targeted by standard preventative treatments.

4.4 Preventive health measures

In our cohort so far, dog owners appear to be more consistent than cat owners with preventive health measures such as vaccination and deworming. A study conducted in Brazil reported similar findings.[118]

In our cohort, 81% of dogs, 46% of outdoor cats, and 44% of indoor cats were dewormed according to the guidelines of the ESCCAP.[102] In a Dutch study, the deworming rates were even lower, with only 25% of outdoor cats being dewormed according to the guidelines. In the same study, they also asked about the reasons for deworming, and only 11% of owners mentioned that they also dewormed their cats for public health reasons.[119] This low number is most likely due to a lack of awareness. This is concerning, especially since the most prevalent parasite, *Toxocara cati,* is zoonotic, and its eggs can remain infectious for years in the soil. It is known that cats often defecate in children's sandpits.[120]

In the previously mentioned Swiss study, 73% of dogs were dewormed once or twice per year, and only 14.2% more frequently.[115] This may have improved over time as awareness increased or guidelines changed.

Regarding vaccination, 78% of the dogs and 62% of the cats were vaccinated according to guidelines of the SVK-ASMPA.[101] The vaccination data for the cats in our cohort were comparable to those in a UK study, where 69% of cats had been vaccinated in the previous year.[121]

Our results indicate that owners are less consistent with preventive health measures in cats than in dogs. The low deworming rates in indoor cats are likely due to limited knowledge about the need for deworming. Lower vaccination rates in cats may also have different reasons, one might be a gap in veterinary advice, as three cats were regularly vaccinated but did not receive the FeLV vaccine despite being outdoor cats. Among the four cats whose vaccination intervals were too long, the reasons may include lack of knowledge or motivation, either for cost or time reasons, or

because it is too stressful for owners and cats to visit the veterinarian.[121] It is well known that veterinary visits can be stressful for cats. This may be because cats are not used to being handled by strangers or dislike their carriers. However, we did not ask owners for their reasons, so these remain speculative — but it would be an interesting topic for further investigation.

4.5 Zoonotic risk

Of the cats in our study, 46% consume raw meat at least occasionally, compared to 17% of dogs. The practice of feeding raw meat has also been reported as common in other studies.[115,122] Despite recommendations from many veterinary associations advising against the feeding of raw meat due to safety concerns, such as bacterial and parasitic infections, antimicrobial-resistant bacteria, and nutritional imbalances when fed as the main diet, many owners are either unaware of the risks or choose to ignore them.[123–126] Arguments made by supporters of raw feeding are often based on comparisons with the diets of wolves or wild cats, they claim nutritional superiority or health benefits such as cleaner teeth and shinier coats. However, these benefits have not been demonstrated in any scientific studies and are mostly based on anecdotal reports.[127]

The pets in our study have contact with a wide range of animals, including other dogs and cats, livestock such as cows, and wild animals. Each contact offers the possibility to transmit infectious diseases. For biosecurity reasons, it is generally recommended to keep livestock and pets separate.[128]

As in the general cat population, many cats in our cohort engage in hunting, mostly targeting birds, small mammals, or reptiles. While this greatly enriches cats' lives, it poses a significant threat to biodiversity.[129] If cats eat birds or mice, this can pose a risk of infection with parasites and other infectious diseases that can be zoonotic, such as avian influenza, toxoplasmosis, or *Coxiella burnetii.*[130,131] Dogs that hunt and eat mice can become infected with *Echinococcus*, which is also zoonotic and can be fatal for both dogs and humans.[132]

4.6 Closeness of contact

We found that many owners in our cohort live in close contact with their cats and dogs, including skin-to-skin contact, sharing the sofa, and sleeping in the same bed. Such close contact may increase the risk of pathogen transmission.

In our study, only about 20% of owners reported that their cat or dog **licks their face**. This is a natural behaviour signalling submission.[133] In other studies, this has been reported at significantly higher rates. For example, in a Dutch study 50% of dog and cat owners allowed face licking,[33] and in another study 60% of UK participants reported that their dogs lick their face at least occasionally.[134] The lower proportion in our study may have several explanations. For one, it is possible that owners participating in our study are aware that, among other topics, it focuses on zoonoses. Therefore, they may either be more aware of the risks and more careful, or be subject to a social desirability bias. Another factor could be that our question did not specify the frequency of the behaviour, which may have led to underreporting if the behaviour occurred only occasionally.

No owner reported that their pet **drinks from the toilet**. Although we found no published data on the prevalence of this behaviour, its frequent mention in online articles and forums suggests it is not rare. The absence of reports in our study could be influenced by social desirability bias, or because it is not observed.

We asked participants whether they **wash their hands** after contact with their pet's urine or faeces, and almost all participants responded affirmatively. However, this result should be interpreted with caution. Firstly, we did not ask how soon after contact they wash their hands. Especially for dog owners, when animals defecate during walks, there is a risk of getting faecal particles on their hands without realising it while picking up the faeces (which all dog owners reported doing), and it is usually not possible to wash hands immediately. It is also likely that social desirability bias played a role in these responses. We did not ask about general handwashing after contact with pets. A study in the Netherlands found that only 15% of dog owners and 8% of cat owners always washed their hands after touching their pets.[33] The same study also demonstrated that dogs and cats can carry parasitic eggs in their fur.

We also asked owners whether they have **skin-to-skin contact with their pets** or contact via saliva, faeces, or urine. The formulation of this question was probably not ideal, as nearly all pet owners have regular skin-to-skin contact with their pets, and many also have contact with saliva, but far fewer are likely to have contact with faeces or urine. This may explain why 76% of dog owners and 89% of cat owners responded affirmatively.

As in other studies,[33–37] many owners in our cohort reported that their **pets sleep in their bed or share the sofa** with them. These behaviours were more commonly reported in cats than in dogs. Such close contact increases the opportunities for zoonotic transmission, especially when combined with other risk factors such as licking, poor hand hygiene, or immunocompromised household members.

4.7 Conclusion

To summarise, we would like to underscore again that epidemics and pandemics are becoming more frequent, with the majority of emerging diseases being zoonotic. While zoonotic research has primarily focused on wildlife and livestock, comparatively little attention has been paid to companion animals, despite their close contact with humans. By including household pets in the cohort, the BEready study addresses this gap by enabling research on this often overlooked aspect of the One Health paradigm. Additionally, there is limited population-level data on zoonoses, another research gap that BEready seeks to fill.

Quickly understanding how emerging pandemics spread, which populations are at risk, and whether pets could play a role is important for tailoring effective measures to prevent the spread of pathogens.[135] To help determine this, it is necessary to identify whether pets are susceptible to infection, the extent and direction of transmission between humans and animals, and the possible transmission routes.[80]

Our results show that pets in the BEready cohort live in close contact with their owners and often have direct or indirect contact with other animals, including livestock, birds, and rodents. This may pose a risk for acquiring zoonotic pathogens and transmitting them to humans. This makes our cohort a valuable resource for investigating the role of household pets in the (re-)emergence of an infectious

disease in Switzerland. It thereby contributes to improving pandemic responses by helping to improve the understanding of disease epidemiology.

On the other hand, the close contact between the pets and their owners also reflects a strong human-animal bond, which likely enriches the owner's life and may offer protective effects.

At present, the cohort is still too small to allow significant associations between parasitic findings and potential risk factors. Such analyses should be performed once enrolment is complete. It will also be valuable to monitor disease events such as diarrhoea and vomiting in cats and dogs. Many cases of mild diarrhoea may never be presented to a veterinarian, so examining these cases could help determine the relevance of parasitic infections in such animals.

Given the increasing number of feline infections with avian influenza in other countries, we have prepared a study protocol to assess potential household transmission and sources of infection in Switzerland, should cases emerge. The draft version of this protocol can be found in the appendix.

Further projects are in development, focusing not only on the animal aspect but also on the human component of the BEready study. The cohort remains open to collaborations.

In conclusion, BEready provides a unique platform for studying emerging infectious disease threats with epidemic or pandemic potential. The integration of entire households, including pets, into a longitudinal cohort represents a valuable contribution to One Health research. Ultimately, the project aims to support evidence-based improvements in both human and veterinary public health policy, and to enhance preparedness for future outbreaks.

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6. Appendix

On our study homepage (https://www.beready.unibe.ch/) many more information can be found.

6.1 Questionnaire Baseline Pet main study

General details:

Sex: (single choice)

- Spayed, female
- Not spayed, female
- Neutered, male
- Not neutered, male
- Not known

Weight [kg] (if known): _____ (with one decimal)

Age [Years]: ____

DOG: What is the main function of your pet: (multiple choice)

- Companion animal
- Assisting dog
- Hunting dog
- Guard dog
- Police dog
- Rescue dog
- Breeding
- Other (describe other function: ____)

CAT: What is the main function of your pet: (multiple choice)

- Companion animal
- Breeding
- Other (describe other function: _____)

CAT: Is your pet allowed outside: (single choice)

- Yes
- No

DOG: My pet is outside: (single choice)

- Always on lead
- Sometimes off-lead

Have you noticed whether your pet hunts prey: (single choice)

- Yes
- No

OLD: Whether it catches prey: (single choice)

- Yes
- No

Which prey: (multiple choice)

- Rodents (e.g. Mice, rats)
- Birds
- Other

Does your pet wear a GPS Tracker for real time tracking via an app (not to be confused with the microchip under the skin, which is used for identification): (Yes/No)

Diet:

OLD: Does your pet eat raw meat? (Yes/No)

NEW: Do you feed raw meat to your pet?

How often do you feed raw meat to your pet:

- Daily as main feed
- Daily or several times a week as supplement
- Several times a month
- Once a month or less often

What raw meat do you feed to your pet? (multiple choice)

- Beef
- Poultry
- Game
- Pork
- Horse
- Other (-> Please specify: _____)

Stays abroad:

Was the pet brought in from abroad? (Yes/No)

If so, from which country? _____

How long has it been living in Switzerland? [Year] _____

Has your pet ever been in southern Europe or outside Europe? (Yes/No)

Vaccines, Parasites

Has your pet ever received a vaccine? (Yes/No)

Does your pet have a vaccine passport? (Yes/No)

Please upload a photo of your pet's vaccine passport. In the process, make sure that your name or your pet's name cannot be seen so that your/your pet's information remains encrypted.

➔ Space for 4 files

OLD: How often do you treat your pet for parasites? (e.g. Worms, Fleas) (single choice)

- More than once a month
- Once a month
- Once every 3months
- Less than once every 3months
- Never

OLD: What product(s) do you use to treat for parasites? _____

OLD: When was the last time your pet was treated against parasites? _____

NEW: How often do you treat your pet for ectoparasites (e.g., ticks, fleas)? (single choice)

- More than once a month
- Once a month
- Once every 3months
- Less than once every 3months
- Never

NEW: What product(s) do you use to treat for ectoparasites (e.g., ticks, fleas)?

NEW: When was the last time your pet was treated against ectoparasites (e.g., ticks, fleas)?

NEW: How often do you treat your pet for worms?

NEW: What product(s) do you use to treat for worms?

- More than once a month
- Once a month
- Once every 3months
- Less than once every 3months
- Never

NEW: Last time: ____

Diseases:

Is your pet healthy? (Yes/No)

What diseases does your pet have? _____

Contact with other animals:

What animals does your pet have contact with outside of your home? (multiple choice)

- Dogs
- Cats
- Horses
- Farm animals
- Wild animals
- Other
- None

Does your pet have contact with birds? (e.g., on the balcony, in the garden, with other pets that are birds in the same household): (single choice)

- Yes
- No

Contact between human and animal:

Does your pet come into your bed? (Yes/No)

Does the pet lick your face? (Yes/No)

Does the pet sit with you on the sofa? (Yes/No)

Does the dog eat out of your plate? (Yes/No)

Does the dog drink out of the toilet? (Yes/No)

Do you have direct skin contact with your pet, its saliva, pee and/or poo? (Yes/No)

Do you pick up your pet's poo? (Yes/No)

Do you wash your hands after you have removed the urine or stool from your pet? (Yes/No)

6.2 Study protocol avian influenza in cats – draft version

Bern, get ready (BEready) population-based cohort study for pandemic preparedness: avian influenza in cats sub-study

Study Protocol

Research legislation:	Swiss Ordinance on Human Research with the Exception of Clinical Trials (HRO)[1]
Type of Research Project:	Research project involving human subjects, risk category A
Study Identifier:	BEready avian influenza in cats sub-study
Sponsor:	University of Bern
	represented by: Prof. Dr. med. Nicola Low Head of Sexual and Reproductive Health Research Group University of Bern Institute of Social and Preventive Medicine (ISPM) Mittelstrasse 43 3012 Bern +41 31 684 30 92 nicola.low@ispm.unibe.ch
Protocol Version & Date:	2.0, 22.05.2025

PROTOCOL SIGNATURE FORM

Study Title: BEready avian influenza in cats sub-study

By her signature, the sponsor, who also acts as project leader, approves this protocol version, and confirms hereby to conduct the project according to the protocol, the Swiss legal requirements[1,2] the ICH-E6 (GCP) guidelines[3] (as far as they apply), the current version of the World Medical Association Declaration of Helsinki [4] and the principles and procedures for integrity in scientific research involving human beings.

Sponsor & Project Leader:

University of Bern, Institute of Social and Preventive Medicine (ISPM), Mittelstrasse 43, 3012 Bern

Name: Prof. Dr. med. Nicola Low

Date: Signature:

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GLOSSARY OF ABBREVATIONS

BASEC	Business Administration System for Ethical Committees
BLV	Bundesamt für Lebensmittelsicherheit und Veterinärwesen
CRF	Case Report Form
eCRF	Electronic Case Report Form
EDC	Electronic Data Capturing
GCP	Good Clinical Practice
H	hemagglutinin
HPAI	Highly pathogenic avian Influenza
HRA	Human Research Act
HRO	Human Research Ordinance
ICH	International Council for Harmonisation of technical requirements for pharmaceuticals for human use
MCID	Multidisciplinary Center for Infectious Diseases
N	Neuraminidase

REVISION HISTORY

Version no. & date	Chapter changed	Description of change	Reason for the change
1.0, 07.03.2025	N/A – first version	N/A – first version	N/A – first version

1 BACKGROUND AND PROJECT RATIONALE

1.1 Background

Highly pathogenic avian influenza (HPAI) was first detected in 1996 in Guangdong, China. It is caused by the influenza A Virus. These viruses are specified by their surface proteins, hemagglutinin (H) and neuraminidase (N). Since 2020, globally, the most successful clade has been H5N1 clade 2.3.4.4b. As the name indicates, HPAI infects mainly avian species, especially aquatic birds and causes devastating outbreaks in domestic poultry. Since winter 2021-2022 more interspecies transmission have been noted[5]. Until October 2023, there were infections in over 48 species of mammals reported[6]. **[PLEASE UPDATE, ALSO USE** https://doi.org/10.1093/ofid/ofaf261 **!]**

In cats, H5N1 first was described in 2004, since then, experts are concerned that the virus may mutate into a more dangerous strain with the potential to cause a pandemic[7]. While for H5N1 no direct transmission between humans and cats has been proven, recent reports[8] suggest so and it has been reported for influenza strain H7N2[9].

In June of 2023, there was a disease outbreak of the 2.3.4.4b clade in 24 cats in Poland[10,11]. In the same year there was also an outbreak in two South Korean cat shelters[12]. In early 2024, there was an uptake of cases in sea lions in South America. In March of the same year an outbreak in U.S. dairy farms occurred. Not only were high numbers of cattle infected for the first time, but on these farms also cats and mice were affected[13]. There are also several reports of infected cats that didn't live on a farm and even in some indoor cats[8,14]. Clinical signs in cats included primarily neurological symptoms such as a depressed mental state, stiffness, ataxia, blindness, and circling; some also showed oculonasal discharge. Neurological examinations revealed the absence of menace reflexes and pupillary light responses with a weak blink response[13].

So far, only few human cases with clade 2.3.4.4b have been described, with highly varying severity, from mild to fatal[15–17]. In the 2024 outbreak in cows, some farm workers had confirmed disease, with mild respiratory symptoms and conjunctivitis[18,19]. To date, transmission of avian influenza H5N1 between humans appears to be rare and very limited.[20,21] Between January 2003 and November 2024, there have been 939 reported human H5N1 cases globally, of these 464 have been fatal[22]. **[PLEASE UPDATE]**

Clade 2.3.4.4b H5N1 viruses have caused ongoing multistate dairy cattle outbreaks in the United States, which involved H5N1 cases in farm workers.[23] In most cases, those affected developed conjunctivitis and mild respiratory symptoms. However, one death of a woman infected with H5N1 in Louisiana who had been in contact with poultry was also reported.[24]

Influenza viruses have a high mutation rate, creating a constant risk of attaining a higher human pathogenicity and more efficient human-to-human transmission. The tendency to infect more and more mammalian species raises concerns about the potential for a human epi- or pandemic[22].

1.2 Justification

The recent uptake in feline cases of H5N1 and the high mortality rate of those cases raise concerns. Still, not much is known about how H5N1 circulates within domestic cat

populations or how it can be transmitted to and from other species. Given these gaps further investigation is necessary to gain more understanding about the risk to cats and humans.

This proposed sub-study would be implemented as part of the BEready cohort study (Bern, get ready', BASEC number 2023-02290). This is a longitudinal household study that includes cats and other household pets from enrolled households. This covers cats living in various environments (e.g. urban vs. rural) and lifestyles (e.g. indoor versus outdoor). Data on cats' contact with birds, raw meat consumption and closeness of contact with their owners is collected at baseline and annually thereafter.

While the likelihood of detecting avian influenza in the cats of this cohort is currently considered low, its early detection would be highly beneficial for both owners and cats. On the one hand, it would allow for appropriate biosecurity measures, such as restricted contact with the cat and isolation from other cats, to be implemented. On the other hand, knowing the cause of the symptoms early would enable more precise veterinary care, ensuring the cat receives appropriate treatment if needed.

Not only in the context of the current outbreaks in the USA, transmissions from animals to humans have been described. Although the symptoms were mild and self-limiting in most of those affected, severe courses of the disease are also possible with serious complications such as severe bilateral pneumonia, multi-organ failure and death.[25] It is therefore crucial to recognise animal-to-human transmission quickly, inform the population and take appropriate preventive measures.

The proposed sub-study would only be implemented in case of increased risk, see also 2.2.

2 PROJECT OBJECTIVES AND DESIGN

2.1 Overall aim

The aim of the proposed sub-study is to see whether domestic cats in the BEready cohort are infected with influenza A viruses and whether there are transmissions to their human household contacts. We will assess the prevalence in our cohort and determine possible risk factors. We will also gather information about possible sources of infection and possible transmission pathways at the animal-animal and at the animal-human interface. We will assess the potential need for protective measures for cat owners.

Primary endpoint:

Proportion of influenza A **(H5N1)** among households with cats by one year. **[discuss what interval makes sense]** Measured through PCR **[specify what kind of PCR, likely real-time]** analysis of oropharyngeal swabs of participating cats.

Secondary endpoints:

Serum antibody titers against influenza A hemagglutinin H5 in cats and human household contacts at baseline. Measurements of baseline serum antibodies to assess if prior exposure occurred.

Assessment of clinical signs and symptoms of affected cats. In case of symptomatic cats in the household, assessment of possible characteristic symptoms in their human household contacts.

Transmission pathways, testing humans and other household pets of affected cats: Detection of Influenza A H5N1 via PCR in human household contacts in case of an affected cat in the household.

Identification of potential risk factors for infections in cats. Analysis of various factors such as demographics, lifestyle factors, contact patterns, nutrition and current symptoms.

Analysis of demographics in affected human household contacts and style of contact to their cats.

Pathology of deceased cats with unclear cause of death. To assess for influenza A as a potential cause of death.

2.2 Project design

In Switzerland, the Federal Office for Food Safety and Veterinary Affairs (BLV), in cooperation with the Friedrich-Loeffler-Institute in Germany, publishes the monthly "Radar Bulletin". This is a newsletter that provides updates about the status of infectious animal diseases and the risk to animal health in Switzerland. This includes updates about avian influenza. The risk assessment includes a traffic light system. We will regularly control the "Radar Bulletin", and in case the alert level goes to red, we will start to screen literature and news for cases of avian influenza in cats in Europe and cases in birds in Switzerland.

The trigger point for the implementation of this study is once there are disease cases in cats in Europe **and** cases in birds in the canton of Bern or neighbouring cantons. **[discuss if this is still adequate in current situation]** At this point, we will start to inform cat owners about possible symptoms and ask them to report disease events in their cats. In case of disease with symptoms consistent with avian influenza, owners will be asked to perform an at-home oropharyngeal swab in their cat. In multi-cat households this would be performed in all cats.

In the event of the first confirmed cases of avian influenza in cats in Switzerland **[or in Berne]**, we may consider swabbing **[must be discussed based on epidemiological situation and the chances of finding positive cats]** all cats in the cohort.

Cat owners who are had their baseline visit for BEready at the small animal clinic in Bern (Länggassstrasse 128, 3012 Bern) received an introduction on how to perform oropharyngeal swabs in cats. For all owners, including those that had their cat's baseline visit at their local veterinary practice, there is an instruction video available on the study homepage on how to correctly and safely perform oropharyngeal swabs in cats.

At the time of swabbing, owners will be asked to fill in supplementary questionnaires about symptoms and possible contact with waterfowl, birds, and poultry.

In the case of a cat in a household having symptoms consistent with an infection with HPAI H5N1, we will screen the human household members by questionnaire for typical symptoms of avian influenza (conjunctivitis, fever, cough, sore throat, nasal congestion, fatigue, myalgia, arthralgia, headache, diarrhoea). As the incubation period is variable and ranges

from 3 to 10 days[20,21], this questionnaire is initially collected when the case of illness is reported and 10 days later.

Additionally, we will instruct all household members to perform swabs on themselves. During the baseline visit at the beginning of the study, participants were instructed on how to correctly and

safely perform a nasal swab on themselves. There is also a corresponding instruction video on the study website for performing nasal swabs on yourself. If potential influenza symptoms are detected in the owners in the second questionnaire 10 days after diagnosis of HPAI H5N1 infection in the domestic cat, the nasal swabs are repeated in these individuals.

We will analyse serum samples collected at baseline in the main BEready study (BASEC number 2023-02290) for serum antibody titers against influenza A (H5).

In case a cat dies with unclear cause of death and matching symptoms, we will offer voluntary post-mortem examination of the cat to the owners free of charge. **[depending on available funding]**

3 PROJECT POPULATION AND STUDY PROCEDURES

3.1 Project population, eligibility criteria

BEready ('Bern, get ready') is a population-based 'pandemic preparedness cohort' in the canton of Bern (BASEC-Nr. 2023-02290). It is designed to specifically address research questions on emerging infectious disease threats. As structured data-collection platform, it provides capacity for additional data collection for nested studies aimed at answering specific research questions related to infectious diseases and pandemic preparedness. The current study will be a nested sub-study within the BEready main study.

We will invite households that have included at least one cat to participate in this avian influenza study. At start of the study, we will also inform all households about the study and ask them if they have cats that are not part of the BEready cohort but that they would be willing to include in the avian influenza sub-study.

In addition, people in BEready households with cats who are not participating in the BEready main study but are interested in the avian influenza study can also be included.

Inclusion criteria for cats:

- Cats participating in the BEready main study
- Cats of participating households that are not part of the main study

Inclusion criteria for humans:

- Persons who are participating in the BEready main study and have at least one cat in the household

- Persons living in BEready households with cats who are not participating in the main study but show interest in the avian influenza substudy

3.2 Recruitment, screening and informed consent procedure

Once the criteria for the implementation of this sub-study are met, we will send an email **[email has to be drafted for ethics]** to cat owners of the BEready main study. In this email we will inform the owners about the increasing risk of influenza A in cats and will ask if they would like to participate with their cats in this nested sub-study. The email will contain the participant information sheets and a personalised link to the e-consent form. **[E-consent is currently not yet available in our electronic data capture system, alternatively send a letter]** Another email will be sent to all households asking if they own cats that could participate in this sub-study.

Because the study design is very simple and the study takes places in the context of the BEready study, there will be no direct contact with the participants. No consent discussion will be scheduled, and only written information will be provided. However, household members will be provided with a contact telephone number and email to get in touch with the study team should they have any questions.

3.3 Study procedures

Table 1 lists the assessments at each visit.

Table 1: Schedule of assessments

Time	**At least -1 day**	**0**	**Unscheduled**
Visit	**Information**	**Baseline**	**Disease event**
Written information	X		
Written consent	X		
Swab			X
Questionnaire		X*	X*
Pathology			X†

* Main contact person for the household only

† Only in fatal event with owner's permission

Baseline assessment (Month 0)

The main contact person for the household will receive an automated invitation to complete a questionnaire that collects information regarding the cat. We will collect data on animal lifestyle (e.g. indoor vs outdoor, hunting, contact with other animals), the closeness of contact to humans and preventive health measures (e.g. deworming and vaccinating). Serology to assess antibody titers against hemagglutinin H5 (ID Screen® Influenza H5 Antibody Competition 3.0 Multi-species) **[this is currently the only commercially available one for mammals also – as far as written not validated for cats]** will be done on biobanked blood samples from the baseline visit at the diagnostic lab (Institute for Infectious Diseases, Friedbühlstrasse 51, 3010 Bern). **[confirm laboratory]**

Disease event

Every time when a cat experiences symptoms in line with influenza A (i.e. bloody diarrhea, fever, dyspnoea, apathy, oculonasal discharge, neurological symptoms such as altered mental state, stiffness, ataxia, blindness, seizures) **[check if these symptoms are also currently the ones seen]**, the owner will fill in a disease event questionnaire.

This will notify the study veterinarian, who will telephone the main contact person in the household within one working day **[check what is feasible for the current study vet]** for a telemedicine consultation for the cat with the symptoms. The study veterinarian will assess the symptoms and advise on treatment, e.g., symptomatic treatment at home, referral to a veterinarian, or referral to the emergency department.

The study veterinarian will ask for a swab of the cat to be taken for detection of influenza A. The household will post samples to the laboratory for testing and biobanking.

Respiratory samples (swabs) will be stored at the Inselspital Liquid Biobank and analysed at the diagnostic lab (Institute for Infectious Diseases, Friedbühlstrasse 51, 3010 Bern) in batches for respiratory viruses. **[Respiratory Viruses or influenza A – batches, is it more urgent?]**

In the case of a fatal event in a cat, a pathological examination of the cadaver at the animal hospital (Kleintierklinik Vetsuisse, Länggassstrasse 128, 3012 Bern) will be offered to the pet owner **[depending on available funding]** (Institute for animal pathology, Länggassstrasse 122, 3012 Bern).

If a cat develops symptoms consistent with an infection with avian influenza H5N1, the study veterinarian will order swabs for the other household members, too. In addition, electronic questionnaires are sent out asking about typical symptoms of avian influenza in humans (conjunctivitis, fever, cough, sore throat, nasal congestion, fatigue, myalgia, arthralgia, headache, diarrhoea) at the time of reporting the case of illness in the cat and 10 days later. Participants reporting symptoms 10 days later will be asked to repeat the nasal swab. The nasal swabs will be stored in the Liquid Biobank as described above. First, the swabs from the cats will be analysed. In the households in which there were actually cats with positive PCR for avian influenza H5N1, the remaining swabs from the contact persons will also be analysed for avian influenza H5N1 via PCR. The remaining swabs will continue to be stored for the time being.

3.4 Withdrawal and discontinuation

In line with the BEready main study, participants are entitled to withdraw their consent at any time without having to justify their decision. After withdrawal, their coded data and samples already collected can still be used for the study and where consent has been received for future use. If consent for future use has not been received, samples will be destroyed after analysis. Collected data will remain coded in the database in any case.

Based on general expertise regarding the significance of the accumulating data or other important reasons such as accumulating external evidence, quality concerns, budget constraints etc., the sponsor may terminate the study at any time.

4 STATISTICS AND METHODOLOGY

4.1 Statistical analysis plan

Baseline and demographic characteristics of cats enrolled will be summarised by standard descriptive summaries (e.g., means and standard deviations or medians and quartiles for continuous variables such as age and percentages for categorical variables such as gender).

The primary outcome is the proportion of influenza A infections in cats amongst all households with cats by one year. We will summarise the distribution of influenza A in index cases (the first cat in the household to experience symptoms) by age, sex, household size and month, taking clustering at household level into account.

The secondary endpoints are: proportion of positive serum antibody titers against influenza A in cats at baseline, symptoms of affected cats and a description of pathology findings in deceased cats with matching symptoms. Proportions will be calculated as: number of cats with positive antibody titers divided by the number of cats enrolled. We will use descriptive statistics and regression-based modelling approaches to describe the relationship between the probability of having a positive antibody titer and demographic and behavioural variables (sex, age, location of residence, access to outdoor space, eating habits, contacts to birds). Another secondary endpoint is the number of human household contacts who become infected with HPAI H5N1 when a cat in their household falls ill. Proportions will be calculated as number of human household contacts with positive PCR for HPAI H5N1 divided by the total number of human household contacts. We will take clustering at household level into account.

4.2 Handling of missing data

We will not use imputation or other statistical methods to account for missing data. Number and proportion of missing data will be shown descriptively.

5 REGULATORY ASPECTS AND SAFETY

5.1 Local regulations / Declaration of Helsinki

This research project will be conducted in accordance with the protocol, the Declaration of Helsinki[3], the ICH-E6 (GCP) guidelines (as far as they apply), the Swiss Human Research Act (HRA)[2] and the Human Research Ordinance (HRO)[1] as well as other locally relevant regulations. The sponsor acknowledges her responsibilities as both the sponsor and the project leader.

5.2 Notification of safety and protective measures

If, during the research project, circumstances arise which could jeopardise the safety or health of the participants or lead to a disproportionate relationship between the risks and burdens and the benefits, all the measures required to ensure protection are to be taken without delay (HRA, Art. 15).

The sponsor is promptly notified (within 24 hours) if immediate safety and protective measures have to be taken during the conduct of the research project. The Ethics Committee will be notified of these measures and of the circumstances necessitating them within 7 days (HRO, Art. 20).

5.3 Serious events (HRO Art. 21)

A serious event is defined as any adverse event where it cannot be excluded that the event is attributable to the sampling of biological material and/or the collection of health-related personal data, and which:

a. requires inpatient treatment not envisaged in the protocol or extends a current hospital stay.

b. results in permanent or significant incapacity or disability; or

c. is life-threatening or results in death.

If a serious event occurs, the research project will be interrupted, and the Ethics Committee notified on the circumstances within 7 days (HRO Art. 21).

5.4 Amendments

Significant changes as defined in HRO Art. 18 will be submitted to the Ethics Committee for approval before implementation. Exceptions are measures that have to be taken immediately in order to protect the participants (HRO, Art. 18).

5.5 End of project

Upon project completion or discontinuation, the Ethics Committee will be notified within 90 days (HRO, Art. 22).

5.6 Insurance

In the event of project-related damage or injuries, the sponsor (University of Bern) will be liable, except for damages that are only slight and temporary and for which the extent of the damage is no greater than would be expected in the current state of scientific knowledge (HRO, Art. 12, 13).

6 FURTHER ASPECTS

6.1 Overall ethical considerations

The proposed sub-study requires only minor additional interventions (oropharyngeal swabs) in cats and for owners a small effort with an additional questionnaire. Owners will only be asked questions about their cats, so it should not be uncomfortable for them to answer.

Social value of the BEready project

Epidemics and pandemics are leading threats to global health security[28]. Pandemics affect not only people's health and well-being, but they can also have an impact on all aspects of

society and the economy. BEready collects data about infectious disease threats that contribute to preparedness for a future pandemic can make a difference to response measures, which could reduce future suffering. With the proposed avian influenza sub-study, we aim to gather early information about a potential new threat.

Scientific value of the project

BEready is designed specifically to address research questions on emerging infectious disease threats. The overall goal is to establish BEready as a 'pandemic preparedness cohort', which means a cohort with a well-characterised study population of households, which has an infrastructure to conduct studies about infectious diseases, and which can be rapidly mobilised for example to gather information about a potentially new pandemic pathogen like influenza A(H5N1) virus.

Justification of the study design

A population-based household cohort study is appropriate for the study of infectious diseases. The study procedures are designed to minimise the burden for participants. The advantage of electronic data capture is that the quality of the data entered can be enhanced by (formatting, skipping rules, checks, warning messages). The additional online questionnaires should take about 5 minutes per pet to complete. The self-sampling is relatively non-invasive, and usually less stressful than a veterinary visit.

The additional questionnaire for humane household contacts should also only take a maximum of 5 minutes per person. Here too, self-sampling is non-invasive and easy to carry out. The majority of our participants in the BEready pilot study agreed with the statement that the swab was not unpleasant and was easy to perform.

Incidental findings

In this sub-study, only respiratory viral panels and serology for influenza A will be performed. No further analyses are planned. With these examinations no incidental findings are expected.

If owners agree for pathological examination of their cat, incidental findings are expected to be found. Owners can choose whether they want a report or not.

Inclusion of pets

Including pets into the cohort as part of a One Health approach is crucial to investigate household transmission of infectious diseases. The virus that causes COVID-19 has been detected in cats, mostly after close contact with people with COVID-19[29] and cat to human transmission has been reported [30]. Influenza A can infect cats and cause an often-deadly disease[11]. Procedures for pets are minimally invasive and not considered problematic. Approval for research in animals has been approved from the cantonal authorities (BE21/2023).

6.2 Risk-Benefit Assessment

Benefits to study participants

The cohort aims to enrol a representative sample of the cat population. Most cats are expected to be in good health, and symptoms of disease events are expected to be relatively mild. The benefits from the telemedicine consultation will therefore be small to moderate. Cat owners might benefit from better disease awareness for avian influenza in their cats which could lead to better care for their pets. The main benefits for owners and cats will be societal, i.e., by contributing to better pandemic preparedness for themselves and their communities.

In human cases of avian influenza H5N1, symptoms are also generally expected to be mild. Since the nasal swabs are analysed with a time delay for logistical reasons, the participants themselves do not benefit directly from early diagnosis. The benefits are more at the societal level, in terms of identifying human cases early on and taking appropriate precautions in the interests of pandemic preparedness.

Risks of filling in questionnaires

Most questions asked in the questionnaire are about symptoms and pose no risk for the owners. Certain questions on behaviour could lead to mild discomfort and embarrassment.

Risks of sampling in pets

Oropharyngeal swabs in cats are needed for diagnosis and characterization of influenza A infection. The risk of injury from taking oropharyngeal swabs is very low. Possible complications for the cats are discomfort, pain, fear, and swab fracture resulting in a retained foreign body. Participants who visit the small animal clinic in Bern with their cats receive instruction from the study veterinarian on appropriate techniques to reduce the risk of injury to the pet and human.

Risk of pet sampling for humans

Since the taking of oropharyngeal swabs in cats can cause discomfort for them, adverse reactions are possible. This might include scratching or biting. This could lead to disease transmission, or wound infection. Participants will be informed about this risk and asked to stop in case of adverse reactions and to only attempt the swabs if they think their cat is cooperative enough. Owners usually know their cats very well, so the risk is minimal.

Another risk to consider is the possibility of contracting avian influenza during the swabbing process. However, since cat owners already live in close contact with their cats, the additional risk appears to be minimal.

Risk of unauthorised data access and/or unwanted identification of participants

Participant data will be handled with uttermost discretion and is only accessible to authorised personnel who require the data to fulfil their duties within the scope of the research project. For more details on confidentiality and coding see **Section 7.3**. Sampling kits are sent to participants in a neutral envelope.

Risk of sampling in humans

The risk of injury from nasal swabbing is very low. Complications include discomfort, pain, fear and phobia, swab fracture resulting in retained foreign body, epistaxis, and headache. Participants receive training from a research nurse or junior research assistant on appropriate technique to reduce the risk of injury.

6.3 Rationale for the inclusion of vulnerable participants

An understanding of household transmission of infectious diseases is still evolving, and studies need to include all household members, including children.

7 QUALITY CONTROL AND DATA PROTECTION

7.1 Quality measures

Personnel will be trained on all project related aspects.

An information security and data protection concept has been implemented for BEready.

The Case Report Forms (CRFs) in this study are implemented electronically using a dedicated Electronic Data Capturing (EDC) system (REDCap, https://www.project-redcap.org/). The EDC system is activated for the study only after successfully passing a formal test procedure. All data entered in the CRFs are stored on a Linux server in a dedicated mySQL database. The responsibility for hosting the EDC system and the database lies with CTU Bern (the clinical trials unit of the University of Bern). The quality of the data entered using REDCap will be supported by the formatting of specific fields (e.g., specific format for dates, age etc.). Data is checked by the EDC system for completeness and plausibility. Warning messages will appear within the questionnaires when answers are identified as missing or incomplete. It will be decided during the pilot study whether a central data monitoring will be required. This would then be described in a dedicated central data monitoring plan.

Before database lock the project-leader will validate the collected data with her signature.

Pre-packed sampling kits for self-sampling are already barcoded and are given to participants. The kits contain all required materials for sample collection, labelled primary and secondary receptacle, and a pre-paid return envelope. Once the sample has been taken, the barcode in the kit is entered into the REDCap database, where it will be linked with the unique participant identifier.

Swabs for storage will be sent directly to the Biobank Bern **[needs to be discussed if analyses in batches or directly].** The Biobank Bern complies with professional standards (e.g. ISO 20387:2018) and it performs its daily biobanking activities according to Good Biobanking Practices. The Biobank Bern has the VITA, NORMA and OPTIMA label which demonstrates compliance with the Swiss Biobanking Platform (SBP) requirements for the implementation of the highest standards of quality assurance measures. The BEready Cohort biobank has the VITA label for compliance with legal and ethical standards.

Swabs will be sent in batches to the diagnostic lab (Institute for Infectious Diseases, Friedbühlstrasse 51, 3010 Bern) for PCR analysis for detection of respiratory viruses. **[needs to be discussed if analyses in batches or directly].**

For quality assurance the Ethics Committee may visit the research site. Direct access to the source data and all project related files and documents will be granted on such occasions. All involved parties keep the participant data strictly confidential.

7.2 Data recording and source data

Most of the data will be directly recorded in the electronic CRFs (eCRFs) in REDCap, i.e., for these data, the eCRF is the source. Only few data are initially recorded elsewhere, i.e., serious event form and laboratory reports. For analysis, data from the avian influenza study will be merged with data from the BEready main study.

7.3 Confidentiality and coding

Project data will be handled with utmost discretion and is only accessible to authorised personnel who require the data to fulfil their duties within the scope of the project. On the CRFs and other project specific documents, participants are only identified by a unique participant ID (unique, randomly attributed). Study-related data of participants will be collected in a coded manner (participant ID for genetic or non-genetic data, sample ID for samples), not containing any (parts) of date of birth, initials or the like. The only exception is the email address in the main study database, which may contain the participant's name (or parts of it). This must be stored in the database so that the requests to complete the questionnaires can be sent to them automatically. Participants will be encouraged to use a non-identifying email address where possible. The email address is only visible to the study personnel who enters it into the database and to technical personnel who are responsible for setting up the database. The email address will not be exported in the analysis files for this study. The participant identification list (the key) will be stored in a separate database.

Access to the REDCap database will be restricted to authorised persons with a personalised login. Unauthorised or accidental disclosure, alteration, deletion and copying will be prevented by control of access levels in REDCap. Each data point has attributes attached to it identifying the user who entered it with the exact time and date. Retrospective alterations of data in the database are recorded in an audit table. Time, table, data field and altered value, and the person are recorded (audit trail).

The server hosting the EDC system and the database is kept in a locked server-room. Only the system administrators have direct access to the server and back-up tapes. A role concept with personal passwords (sponsor/project leader, statistician, monitor, administrator etc.) regulates permission for each user to use the system and database as he/she requires. All data entered into the CRFs are transferred to the database using Transport Layer Security encryption. A multi-level back-up system is implemented. Back-ups of the whole system including the database are run internally several times per day and on external tapes once a day. The back-up tapes are stored in a secure place in a different building.

Biological material for this sub-study is labelled only with a sample ID. When taking a sample, the participant will enter the sample number into the REDCap database when filling in the disease event questionnaire. The main REDCap database will link the participant ID to the sample ID number. For transport to the biobank, samples are shipped by participants in suitable packaging at ambient temperature directly to the Biobank Bern, where it is appropriately stored in a restricted area only accessible to authorised personnel. The Biobank Bern meets the requirements of the HRA in terms of sample collection and storage. The address of the Biobank Bern is: INSELSPITAL, Universitätsspital Bern, Zentrum für Labormedizin, INO-F, Freiburgstrasse 10, 3010 Bern. General Contact: +41 31 632 22 01, biobank@insel.ch.

Biological material or genetic data can only be sent abroad in the scope of the research project, if the participant involved has given his/her consent to do so upon having been sufficiently informed (HRO, Section 2).

7.4 Retention and destruction of study data and biological material

There is no predefined end date for the main study for storage samples in the Biobank Bern and corresponding data with the sponsor. At final analyses, data files will be extracted from the database into statistical packages to be analysed. After database lock, the status of the database is recorded in special archive tables. The sponsor will keep the extracted data, the meta data and final reports for at least 10 years.

The data and samples will be stored according to the protocol of the main cohort study. If participants agree to future use of samples and data, there is no predefined end date for storage of samples in the Biobank Bern and corresponding data with the sponsor.

8 FUNDING / PUBLICATION / DECLARATION OF INTEREST

This research is funded by the Multidisciplinary Center for Infectious Diseases (MCID) at the University of Bern **[update if additional funding becomes available]**. The MCID is funded by the Vinetum Foundation. This funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data or decision to submit results. The sponsor and project leader has no conflict of interests to declare. Publications arising from this study will be submitted to open-access journals. Co-authors will fulfil the criteria of the International Committee of Medical Journal Editors. Data used in publications will be available on reasonable request to the investigators.

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APPENDIX

Things that have to be reconsidered before implementation of the protocol:

- Inclusion of dogs, currently there were few seropositive dogs (December 2024)
- Cite the latest templates from Swiss ethics for HRO, human research act, and declaration of Helsinki
- In case of emerging influenza in cats is it justifiable to only do testing of swabs in batches periodically?
- Control all the citations
- Update numbers of enrolment / cats

Link to the ELISA for H5: ID Screen® Influenza H5 Antibody Competition 3.0 Multi-species - Innovative Diagnostics

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8. Eigenständigkeitserklärung

Ich, erkläre hiermit, dass ich die vorliegende Dissertation selbständig verfasst habe und keine anderen als die angegebenen Quellen benutzt habe. Alle Stellen, die wörtlich oder sinngemäss aus Quellen entnommen wurden, habe ich als solche gekennzeichnet.

Mir ist bekannt, dass andernfalls der Senat gemäss Artikel 36 Absatz 1 Buchstabe r des Gesetzes über die Universität vom 5. September 1996 und Artikel 69 des Universitätsstatuts vom 7. Juni 2011 zum Entzug des Doktortitels berechtigt ist. Für die Zwecke der Begutachtung und der Überprüfung der Einhaltung der Selbständigkeitserklärung bzw. der Reglemente betreffend Plagiate erteile ich der Universität Bern das Recht, die dazu erforderlichen Personendaten zu bearbeiten und Nutzungshandlungen vorzunehmen, insbesondere die Dissertation zu vervielfältigen und dauerhaft in einer Datenbank zu speichern sowie diese zur Überprüfung von Arbeiten Dritter zu verwenden oder hierzu zur Verfügung zu stellen.

Bern, 27.7.2025

Ort, Datum

Unterschrift Doktorand*in