UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA VETERINÁRIA

Risk factors for infectious diseases recorded in cats attending a Veterinary Teaching Hospital Isolation Unit in Portugal

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Lastly, but not least important I want to give a really special thank you to my grandmother Juju. Thank you for believing in me. I know you would have been proud to see this moment.

Resumo

Fatores de Risco para Doenças Infeciosas reportadas em gatos hospitalizados na Unidade de Isolamento do Hospital Veterinário Escolar em Portugal

A Unidade de Isolamento e Contenção Biológica (UICB), admite pacientes com suspeita ou confirmação de doença infeciosa. No período de 2013 a 2020, 788 gatos foram hospitalizados, dos quais 405 obtiveram confirmação de doença infeciosa.

Os principais objetivos deste estudo foram caracterizar a população hospitalizada, identificar as doenças infeciosas mais comuns e nesta população efetuar um estudo caso-controlo para identificar possíveis fatores de risco. A informação obtida foi recolhida do sistema informático no dia de admissão, incluindo raça, sexo, castração, idade, estilo de vida, presença de animais coabitantes, vacinação, desordens concomitantes, entre outras.

As principais doenças infeciosas encontradas foram infeções por Retrovírus (48.3%), Doença do Trato Respiratório Superior Felino (DTRSF) (19.9%) e Panleucopénia (14.4%). Para uma melhor análise, os pacientes com Retrovírus foram divididos em infeção pelo vírus da Leucemia Felina (FeLV) e pelo vírus da Imunodeficiência Felina (FIV). Inicialmente, para o estudo de caso-controlo, foi feita uma análise simples de regressão logística. Todas as variáveis que apresentaram um p-value ≤ 0.20 foram incluídas no modelo múltiplo.

Analisando a população infetada por FeLV observou-se que gatos entre 2 e 9 anos (OR=2.5; $CI_{95\%}$=1.4-4.4), domésticos (OR=4.8; $CI_{95\%}$=1.4-18.6), inteiros (OR=1.9; $CI_{95\%}$=1.0-3.4) e com afeções/doenças concomitantes (OR=2.5; $CI_{95\%}$=1.5-4.8) demonstraram um maior risco de serem hospitalizados (p-value <0.05). Para o FIV, gatos domésticos (OR=4.7; $CI_{95\%}$=1.3-30.2), machos (OR=1.9; $CI_{95\%}$=1.1-3.2), entre 2 e 9 anos (OR=3.8; $CI_{95\%}$=1.7-9.4) e ≥10 anos (OR=3.0; $CI_{95\%}$=1.3-7.9), com afeções/doenças concomitantes (OR=2.7; $CI_{95\%}$=1.5-4.8) tiveram também um maior risco de serem hospitalizados (p-value <0.05). Relativamente aos pacientes infetados com DTRSF apenas gatos inteiros (OR=3.0; $CI_{95\%}$=1.6-5.8) e com coabitantes (OR=2.5; $CI_{95\%}$=1.4-4.6) apresentaram maior risco de serem hospitalizados (p-value <0.05). Finalmente, para os pacientes infetados com vírus da Panleucopénia, ausência de uma vacinação correta (OR=50.5; $CI_{95\%}$=11.8- 373.1), sem afeções/doenças concomitantes (OR=7.3; $CI_{95\%}$=2.8-21.0), gatos com <2 anos (OR= 85.0; $CI_{95\%}$=13.1, 1751.1) e entre 2 e 9 anos (OR=10.7; $CI_{95\%}$= 1.7-211.3) tinham um maior risco de serem hospitalizados na UICB (p-value <0.05).

Em conclusão, vários parâmetros na vida de um gato foram comprovados como fatores de risco em concordância com a literatura e o quão importante é prevenirmos estas situações.

Palavras-chave: Fatores de risco, Doenças Infeciosas, Gatos, Epidemiologia, Controlo Biológico.

Abstract

Risk factors for infectious diseases recorded in cats attending a Veterinary Teaching Hospital Isolation Unit in Portugal

The Biological Isolation and Containment Unit (BICU) admits patients with the suspicion or confirmation of an infectious disease. Between 2013 and 2020, 788 cats were admitted, in which 405 cats had an infectious disease.

The main objectives of this study were to characterize the infected population, identify the most frequent infectious diseases and then assembly a case-control study within this population to find possible risk factors.

Information about cases and controls were collected from the hospital's information system on the day of admission, including breed, gender, neuter status, age, lifestyle, cohabitants, vaccination status, concomitant disorders, and others.

The principal infectious diseases recorded at the BICU were Retrovirus (48.3%), Upper Respiratory Tract Disease (19.9%) and Panleukopenia (14.4%). Retrovirus was divided into Feline Leukemia Virus (FeLV) and Feline Immunodeficiency Virus (FIV) for a better analysis.

For the case-control study, a simple logistic regression analysis was assessed for each variable. All variables with a p-value ≤0.20 were included in a multiple regression model for each disease.

Regarding FeLV infected patients, cats aged 2 to 9 years (OR=2.5; $CI_{95\%}$=1.4-4.4), domestic (OR=4.8; $CI_{95\%}$=1.4-18.6), intact (OR=1.9; $CI_{95\%}$=1.0-3.4), presenting concomitant disorders/diseases (OR=2.5; $CI_{95\%}$=1.5-4.8), had a higher risk of being hospitalized (p-values <0.05). Concerning the patients with FIV, domestic cats (OR=4.7; $CI_{95\%}$=1.3-30.2), males (OR=1.9; $CI_{95\%}$=1.1-3.2), cats aged 2 to 9 years (OR=3.8; $CI_{95\%}$=1.7-9.4) and ≥10 years old (OR=3.0; $CI_{95\%}$=1.3-7.9), presenting concomitant disorders/diseases (OR=2.7; $CI_{95\%}$=1.5-4.8), had a higher risk of being hospitalized (p-values <0.05).

For URTD infected patients, only intact cats (OR=3.0; $CI_{95\%}$=1.6-5.8) and living with cohabitants (OR=2.5; $CI_{95\%}$=1.4-4.6) had a higher risk of being hospitalized.

Finally, for the patients with the Panleukopenia virus, absence of correct vaccination (OR=50.5; $CI_{95\%}$=11.8- 373.1), without concomitant disorders/diseases (OR=7.3; $CI_{95\%}$=2.8-21.0), cats aged <2 years old (OR= 85.0; $CI_{95\%}$=13.1, 1751.1) and aged 2 to 9 years (OR=10.7; $CI_{95\%}$= 1.7-211.3), had a higher risk of getting hospitalized at the BICU (p-values <0.5).

In conclusion, several aspects in a cat's life were proved to be risk factors, agreeing with the literature and how important is to be watchful of these situations.

Keywords: Risk Factors, Infectious Diseases, Cat, Epidemiology, Biological Control.

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Abbreviation List

ALT- Alanine Aminotransferase

AST- Aspartate Aminotransferase

AZT- Azidothymidine

BICU- Biological Isolation and Containment Unit

CBC- Complete Blood Count

CD4+- Cluster of Determination

CD8+- Cluster of Determination

CI- Confidence Interval

CK- Creatine Kinase

CMI- Cell Mediated Immune Response

DIC- Disseminated Intravascular Coagulation

ELISA- Enzyme-Linked Immunosorbent Assay

FCoV- Feline Coronavirus Infection

FCV- Feline Calicivirus

FCV-VSD- Feline Calicivirus Virulent Systemic Disease

FECV- Feline Enteric Coronavirus

FeLV- Feline Leukemia Virus

FHV-1- Feline Herpevirus-1

FIP- Feline Infectious Peritonitis

FIV- Feline Immunodeficiency Virus

FMV- Faculty of Medicine Veterinary

FPV- Feline Panleukopenia Virus

HIV- Human Immunodeficiency Virus

ID- Infectious Disease

IFA- Immunofluorescent Antibody

IFN-α- Alfa Interferon

IFN-ω – Omega Interferon

IgM- Immunoglobulin M

MDA- Maternally Derived Antibodies

MDR- Multidrug Resistant

MLV- Modified Live Vaccines

NA- Unknown information

OR- Odds Ratio

PCR- Polymerase Chain Reaction

POC- Point-of-Care

RIM- Rapid Immunomigration Assays

RT-PCR- Reverse Transcriptase Polymerase Chain Reaction

SARVS-COV-2- Severe Acute Respiratory Syndrome Coronavirus 2

UK- United Kingdom

ULisbon- University of Lisbon

URTD- Upper Respiratory Tract Disease

VGG- Vaccination Guidelines Group

VIL- Virology Laboratory

VSD- Virulent Systemic Disease

VTH- Veterinary Teaching Hospital

WSAVA- World Small Animal Veterinary Association

I- Activities developed during the curricular internship

This report concerns the curricular internship that occurred between September 2, 2020 and December 30, 2020 at the Biological Isolation and Containment Unit (BICU), in the University of Lisbon's Faculty of Veterinary Medicine. All the activities took place under the supervision of Professor Solange Gil and the Doctor Inês Machado.

The intern's schedule is in rotation. Therefore, the morning schedule is from 9AM to 4PM, and the afternoon one is from 2:30PM to 9:30PM. There is also rotation on Saturdays between the two interns. In total, 630 hours were made at the BICU.

Every month the interns presented a clinical case about an infectious patient that was admitted. These presentations were made so the intern could correlate the clinical practice to what they have learned about infectious diseases. Additionally, it was a way to prepare for the thesis presentation and enhance oral skills.

During the hours spent in the BICU, there was a chance to follow the progress of the different clinical cases, participating in the animals' clinical monitoring, feeding plan, and drugs preparation and administration. There was also the opportunity to participate in blood sample collection, blood transfusions, peripheral venous catheterization, urethral catheterization, placement of nasogastric tubes, wound cleaning and dressing. Other activities carried out were calculations of fluid therapy and their supplements, accompanying the animals to their ultrasound, radiography and other exams, recording the physical exams of the patients and work on the database of the patients admitted for research studies. Furthermore, checkup calls to the owners, referral appointments, vaccination appointments, discharges, follow-up appointments and how to act during a euthanasia were trained during these months.

Although not medical activities, the interns had the chance to refill the stock. The importance of disinfecting the surfaces, hands, quarantine the cages and the use of individual protection equipment was reinforced. This helps them see how important it is to run an establishment like this and how laborious these tasks are.

Besides other activities, the interns had the chance to help in the third-, fourth- and fifth-year classes.

Overall, it was a very enriching experience, not only in a clinical aspect, but also in a personal aspect, because in every step of the way all doubts could be clarified by the amazing team working at the BICU.

The submitted abstracts during this internship are shown in the first two annexes.

Most frequent infectious diseases in cats

This section intends to review the most frequent infectious diseases of cats recorded in the BICU. Therefore, this section comprises a summary of Feline Leukemia Virus, Feline Immunodeficiency Virus, Upper Respiratory Tract Disease and Feline Panleukopenia diseases. Each disease is divided into etiology, epidemiology, pathogenesis, clinical signs, diagnostic methods, medical and sanitary prophylaxis, treatment and prognostic.

II- Literature Review

1. Feline leukemia virus (FeLV)

Etiology: FeLV is a gammaretrovirus with an enveloped RNA and belongs to the family Retroviridae (Sykes and Hartmann 2013). Isolates of FeLV are divided in different subgroups, which can determine the outcome of FeLV infection (Hartmann and Hofmann-Lehmann 2020). FeLV subgroups are immunologically related but use different cellular receptors (Hartmann 2012). The best-known FeLV subgroups are FeLV-A, FeLV-B, FeLV-C (Hartmann and Hofmann-Lehmann 2020). FeLV-A is contagious and spreads horizontally in nature (Hartmann and Hofmann-Lehmann 2020). The remaining subgroups evolve a FeLV-A-infected cat by mutation or recombination between FeLV-A and cellular or endogenous retroviral sequences contained in feline genomic DNA (Hartmann and Hofmann-Lehmann 2020). FeLV-B and C have higher pathogenicity than FeLV-A. FeLV-B is commonly associated with malignancies, like mediastinal lymphoma (Hartmann and Hofmann-Lehmann 2020). FeLV-C infected cats may show an almost complete lack of erythroid precursors (Hartmann and Hofmann-Lehmann 2020). Other subgroups have been described like FeLV-D and FeLV-T, but it is not clear if both are infectious or pathogenic (Hartmann and Hofmann-Lehmann 2020).

Epidemiology: FeLV infection exists in domestic cats worldwide, but FeLV prevalence varies between geographic regions. In Europe prevalence's can go from 0.7% to 15.6%, while in South America it can go from 3.0% to 28.4% (Hartmann and Hofmann-Lehmann 2020).

The main route of transmission is through close contact between cats. Usually, it is spread horizontally among cats that live together or that fight, and vertically or horizontally from infected queens to their kittens (Little et al. 2020). Iatrogenic transmission can occur by contaminated needles, instruments, or blood transfusions (Hartmann and Hofmann-Lehmann 2020). Kittens have the highest risk of becoming infected. Nevertheless, adult cats can also be infected (Little et al. 2020).

Progressively infected cats shed millions of virus particles in their saliva, and their shedding can occur throughout their life (Hartmann and Hofmann-Lehmann 2020). However, in regressively infected cats, they do not shed the virus through saliva and other excretions, but they can transmit the virus via blood transfusions (Little et al. 2020).

FeLV is easily inactivated, within minutes, in the environment, by disinfectants, soaps, drying and heating (Hartmann 2012; Sykes and Hartmann 2013). There is no risk of infection for single cats who are exclusively indoors. There is also no need for a waiting period when adopting a cat after the removal of a FeLV-infected cat (Hartmann and Hofmann-Lehmann 2020).

FeLV risk factors influence FeLV prevalence, but the exact mechanisms for the different clinical responses are poorly understood. Some of the risk factors for FeLV are shown below:

- Health status: FeLV predisposes cats to certain diseases and secondary infections, so the prevalence is higher in a sick population (Hartmann and Hofmann-Lehmann 2020);
- Behavior: Since transmission requires physical contact, the prevalence is also higher in outdoor cats (Hartmann and Hofmann-Lehmann 2020);
- Gender: Male and intact cats, because of their aggressive behavior, have greater chances for infection (Hartmann and Hofmann-Lehmann 2020);
- Age: Adults cats are more likely to be progressively FeLV infected than juveniles (Hartmann and Hofmann-Lehmann 2020);
- Breed: In purebred cats, FeLV infection is less frequently observed, probably because they are commonly kept indoors (Hartmann and Hofmann-Lehmann 2020);
- Environment: Prevalence can vary among shelters, depending on their testing and hygiene strategies. Living in multicat houses without adequate conditions can increase the risk. Countries with areas of lower purchasing power also have a higher prevalence (Hartmann and Hofmann-Lehmann 2020);

Pathogenesis: Cats typically acquire FeLV via the oronasal route but can also become infected through bite wounds, as well as affiliative social behavior, such as sharing food, water dishes and mutual grooming (Hartmann and Hofmann-Lehmann 2020; Little et al. 2020). FeLV can be detected in the local lymphoid tissues following virus exposure; then spreads via monocytes and lymphocytes and starts the primary viremia, which infects the bone marrow (Little et al. 2020). Secondary viremia can occur after bone marrow infection (Little et al. 2020).

Outcomes of FeLV infection are classified as abortive infection, regressive infection and progressive infection (Hartmann and Hofmann-Lehmann 2020; Little et al. 2020). A ‘battle’ between the immune system of the cat and the virus decides the course of FeLV infection; this is especially true in the early stage of infection, usually within the first 12 weeks of exposure (Hartmann and Hofmann-Lehmann 2020).

Abortive infection is characterized by negative test results from virus cultures, enzyme-linked immunosorbent assays (ELISA) and polymerase chain reaction (PCR) for RNA and

proviral DNA (Hartmann and Hofmann-Lehmann 2020; Little et al. 2020). The only sign of infection of FeLV is that antibodies are present (Little et al. 2020). This likely happens by low-dose exposure to the virus. Abortive infection seems to be more common in cats with natural infection (Hartmann and Hofmann-Lehmann 2020; Little et al. 2020). Cats with an abortive infection can show evidence of FeLV antibodies without clinical signs (Hartmann and Hofmann-Lehmann 2020; Little et al. 2020).

Regressive infection is characterized by an immune response that contains, but does not eliminate virus replication. After the first antigenemic phase is over, viral shedding does not occur. However, some PCR assays can detect FeLV proviral DNA in the blood (Little et al. 2020). FeLV integrates into the cat's genome and is unlikely to be completely cleared over time. Cats with regressive infection have reliably high virus-neutralizing antibody titers and are at low risk of contracting FeLV-related diseases (Little et al. 2020). Nevertheless, reactivation can occur in cats with regressive infection, particularly if they are immunosuppressed (Hartmann and Hofmann-Lehmann 2020; Little et al. 2020). The risk of reactivation decreases over time, but it has been shown that reactivation can occur many years after the initial exposure to FeLV (Hartmann and Hofmann-Lehmann 2020; Little et al. 2020).

Progressive infection is not limited to the early stage, and extensive virus replication occurs firstly in the local lymphoid tissues, in the bone marrow, and subsequently in mucosal and glandular epithelial tissues (Hartmann and Hofmann-Lehmann 2020; Little et al. 2020). The last two are associated with the excretion of infectious virus, mainly in saliva but also in other secretions. Cats with progressive infection shed the virus throughout their life's (Hartmann and Hofmann-Lehmann 2020) and have a shorter survival time, because they typically succumb to FeLV-associated diseases after infection (Little et al. 2020).

Clinical signs: Active virus replication occurs in cats with progressive FeLV infection, and is usually responsible for the main clinical signs. A variety of disorders can be associated with progressive FeLV infection, including bone marrow disorders (primarily anemia) and neoplasia (primarily lymphoma) (Hartmann and Hofmann-Lehmann 2020). Furthermore, immunosuppression can lead to susceptibility for secondary infections, and some other clinical syndromes, such as immune-mediated diseases, reproductive disorders, fading kitten syndrome and FeLV-associated neuropathies (Hartmann and Hofmann-Lehmann 2020). FeLV-infected cats may present various co-infections, including feline immunodeficiency virus (FIV) infection, stomatitis, upper respiratory infection, feline infectious peritonitis (FIP), hemotropic mycoplasmosis, followed by leukopenia or thrombocytopenia and leukemia or myeloproliferative disease (Sykes and Hartmann 2013). It is not possible to determine whether concomitant diseases are a consequence of FeLV infection or considered as independent events (Hartmann and Hofmann-Lehmann 2020).

Regressive FeLV infection does not have an impact on life expectancy, except if the infection is reactivated, when that happens, they have the same risk as progressive infected cats (Hartmann and Hofmann-Lehmann 2020). Additionally, there are some clinical syndromes that can be found even without reactivation, such as bone marrow suppression or lymphoma (Hartmann and Hofmann-Lehmann 2020).

Diagnosis: FeLV infection is often diagnosed when healthy cats are screened for infection. While many cats that test positive for FeLV antigen have no clinical signs, or physical examination abnormalities, a complete blood count (CBC), a chemistry panel, and urinalysis should be obtained from these cats, to assess for underlying abnormalities that could indicate the presence of FeLV-associated disorders (Sykes and Hartmann 2013).

FeLV infection diagnosis is typically based on the identification of soluble FeLV p27 antigen by point-of-care (POC) tests, samples from serum, plasma or whole blood can be used (Little et al. 2020). FeLV antigen tests should not be performed on tears or saliva, because of their low sensitivities. Further testing, especially in low-risk and asymptomatic cats should be considered (Little et al. 2020). Besides ELISA or similar immunochromatographic test for soluble FeLV antigen there are other diagnostic methods, such as virus isolation (not widely available), immunofluorescent antibody (IFA) tests (these tests detect a secondary viremia, once bone marrow infection is established), and PCR (Sykes and Hartmann 2013). Quantitative PCR assays for proviral DNA provide additional information to classify a cat's status. While saliva is less sensitive to POC tests than blood or serum, it can be used for reverse transcriptase polymerase chain reaction (RT-PCR) to diagnose FeLV RNA and, thus, FeLV shedding. (Little et al. 2020).

Medical and sanitary prophylaxis: Identification and isolation of infected cats is the most effective procedure for the prevention of FeLV. Implementing testing and vaccination protocols, owner vaccination reminder programs and environmental management can help to contain the spread of these infections (Sykes and Hartmann 2013).

Prevention strategies begin with the recognition of risk factors associated with FeLV infection. For each cat, avoidance or minimization of risk factors that are suitable for management should be determined (e.g., lifestyle, vaccination, and other risk factors previously demonstrated) (Little et al. 2020).

FeLV hospitalized cats should not be allowed to have direct contact with others (Little et al. 2020). They should not be amongst patients carrying other infectious diseases, such as upper respiratory virus or panleukopenia. FeLV-infected cats should receive preventive healthcare checkups at least once every 6 months for prompt detection of changes in their health status (Little et al. 2020). To decrease stress associated with estrus and mating behaviors, sexually intact male and female cats should be neutered. Neutered animals are

also less likely to roam away from home and interact aggressively with other cats (Sykes and Hartmann 2013).

At home, cats infected with FeLV should be confined indoors in order to prevent the infection of other cats and to protect them against other infectious diseases. The best way to avoid transmission to other cats in the household is to avoid direct contact and interaction with the infected cat and its household mates (Little et al. 2020).

Vaccination: Although FeLV vaccine is not considered a core vaccine (Day et al. 2016), vaccination remains an important preventive tool. Combined use of testing and vaccination programs is the cause of the decrease prevalence of the disease. However, it cannot be concluded that FeLV vaccination protects against all outcomes of FeLV infection (Little et al. 2020). Any cat less than 1 year old with an element of outdoor lifestyle should be vaccinated with two doses of the vaccine administered 2–4 weeks apart starting not earlier than 8 weeks of age, or in older cats after testing negative for FeLV, with a booster one year after, followed by revaccinations every 2-3 years (Day et al. 2016).

Treatment and prognosis: An accurate diagnosis is necessary to allow early intervention in FeLV-infected cats (Sykes and Hartmann 2013).

Many FeLV viraemic cats may need fluid therapy and antibiotics, such as doxycycline for secondary bacterial infections. If the cat presents stomatitis/ gingivitis, corticosteroids should be considered to increase food intake (Hans et al. 2009; Little et al. 2020). However, a full teeth extraction may be necessary (Hans et al. 2009; Little et al. 2020). Blood transfusions may be useful in anaemic cats and, in leukopenic cases, a granulocyte colony-stimulating factor can be considered. Some cases of lymphoma respond well to chemotherapy, with remission expected in most cases. Nevertheless, chemotherapy of FeLV-positive lymphomas will not resolve the persistent viraemia (Hans et al. 2009).

Antivirals and immunomodulators are of limited benefit in the long-term treatment of cats with FeLV infections. However, studies prove that the use of recombinant feline interferon omega (IFN-ω) showed higher survival rates after 9 months (Little et al. 2020), and human recombinant interferon alpha (IFN-α) also shows beneficial outcomes (Sykes and Hartmann 2013). Zidovudine (azidothymidine; AZT) is one of the few antiviral compounds used in both FeLV and FIV infections (Little et al. 2020). In naturally and experimentally infected cats with FeLV, AZT improved oral cavity inflammation, decreased antigenemia, and prolonged life span. Antivirals that show promising results include fozivudine and the integrase inhibitor raltegravir, which has been used to treat gammaretrovirus infections in humans and inhibits FeLV replication in cell culture (Sykes and Hartmann 2013).

Considering the prognosis, the survival time of the cats vary depending on the host immunity, the strain of FeLV involved and the stage of infection (Sykes and Hartmann 2013). Many progressively infected cats, especially adult cats, may have a decent quality of life for

several years, so euthanasia is not recommended on the basis of a positive FeLV test. The prognosis is least favorable for cats with leukemia, which generally survive less than a few weeks (Sykes and Hartmann 2013).

2. Feline Immunodeficiency Virus (FIV)

Etiology: Feline immunodeficiency virus is a retrovirus of the genus *Lentivirus* that shares many characteristics of other lentiviruses such as human immunodeficiency virus (HIV) (Sykes 2013b). Lentiviruses are complex retroviruses containing accessory genes in addition to *gag, pol* and *env*. The *gag* gene encodes the capsid protein p24, which is important for diagnosis. The *pol* gene is important for the virulence of FIV (Hosie et al. 2009). The *env* gene has a hypervariable region that allows FIV to split in several subtypes. *Env* properties are also clinically relevant because they determine cell tropism, influence pathogenicity and their proteins are targets of immune responses (Sellon and Hartmann 2012).

Five subtypes have been recognized: subtypes A, B, C, D and E. Additionally, a new subtype has been described in Texas, New Zealand and Portugal (subtype F) (Sellon and Hartmann 2012). Within each region, each subtype has its prevalence; subtype B is more prevalent in European southern countries (e.g., Italy, Portugal) (Sellon and Hartmann 2012). Natural infected cats can harbor multiple subtypes (Sellon and Hartmann 2012).

Epidemiology: FIV is widespread globally, though its prevalence varies between regional areas. Within a given population, the prevalence of FIV in healthy cats is usually lower than in sick cats, this happens because FIV is an immunosuppressive disease, which predisposes these cats to chronic and recurrent infection. Therefore, cats with FIV are more prone for illness (Sellon and Hartmann 2012).

The primary mode of FIV transmission is through bite wounds that introduce saliva containing virus and FIV-infected white blood cells. Infection may also uncommonly occur among cats living together in a household without fighting (Little et al. 2020). Transmission from infected queens to their kittens can also occur in utero or by ingestion of milk, although it tends to be unlikely in naturally infected cats. Level of viremia and viral loads of the queen appear to be key factors for the transmission to their kittens (Colleran 2017). Sexual transmission, which is the most common type of HIV transmission, is unusual for FIV, even though infected cat's semen often contains infectious virus and biting happens during mating. (Little et al. 2020).

Adult and male cats have the highest risk for infection, which is related to the aggressive behavior between these cats. Cats with a history of bite wounds or abscesses and outdoor access are also at greater risk (Sykes 2013b).

The virus is unstable outside their host and is inactivated in a very short time on dry surfaces. Detergents and common hospital disinfectants quickly inactivate FIV (Little et al. 2020).

Pathogenesis: After inoculation, macrophage-rich tissues clear the virus, and viral replication occurs in target cells of lymphoid organs (thymus, spleen, lymph nodes). FIV also infects mononuclear cells of other organs, including kidneys, bone marrow, lung, brain and the intestinal tract (Sykes 2013b).

FIV infection is divided in different stages of infection (Colleran 2017; Little et al. 2020):

- Acute phase: This stage occurs acutely or subacutely after infection (Colleran 2017). It can be associated with transient fever, lymphadenopathy and lymphopenia (Colleran 2017). Within the first few weeks of infection, both CD4+ (helper) and CD8+ (cytotoxic-suppressor) T lymphocyte concentrations decline (Little et al. 2020).
- Subclinical: The initial phase is followed by an immune response with the production of FIV antibodies, suppression of circulating virus leading to a decrease in viral load, and an increase in CD8+ T lymphocytes. These leads to an inversion of the CD4:CD8 ratio that can persist for the rest of the cat's life (Little et al. 2020).
- Acquired immunodeficiency (clinical phase): Over time, both CD4+ and CD8+ lymphocytes numbers continue to gradually decline, and progressive dysfunction of the immune system can occur (Little et al. 2020). Therefore, FIV-infected cats are predisposed to chronic, recurrent infections, neoplasia and immune-mediated diseases (Little et al. 2020).
- Terminal phase: The terminal phase of infection can involve various diseases and death. Survival time is limited to 2-3 months (Colleran 2017).

Clinical signs: Clinical signs of FIV infection are nonspecific (Sellon and Hartmann 2012). In naturally infected cats, most clinical signs of FIV infection are unnoticed. During acute experimental infection, clinical signs are usually transient and mild or even unobserved. Cats exhibit fever, weight loss, anorexia, acute enteritis, dermatitis, conjunctivitis, stomatitis, respiratory tract disease and lymph node enlargement (Sellon and Hartmann 2012). The acute phase can last from several days to several weeks, in which the cats enter a period of clinically healthy appearance (Sellon and Hartmann 2012). Clinical symptoms indicate opportunistic infections, neoplasia, myelosuppression, and neurological illness in the later stages of infection (Sellon and Hartmann 2012; Sykes 2013b).

Stomatitis in FIV-infected cats is a frequent condition and can occur at any phase of infection (Sellon and Hartmann 2012). Neurological symptoms have also been identified (Sellon and Hartmann 2012; Sykes 2013b). Behavioral changes are the most common neurological signs, but seizures, motor abnormalities and disrupted sleep patterns have also

been described (Sellon and Hartmann 2012; Sykes 2013b). FIV-infected cats can also develop ocular diseases, such as anterior uveitis, glaucoma, focal retinal degeneration and retinal hemorrhages (Sellon and Hartmann 2012). Neoplasia, such as lymphoma or leukemia have a higher chance to develop in FIV-infected cats. Most lymphomas in FIV-infected cats are B-cell tumors (Sellon and Hartmann 2012; Sykes 2013b).

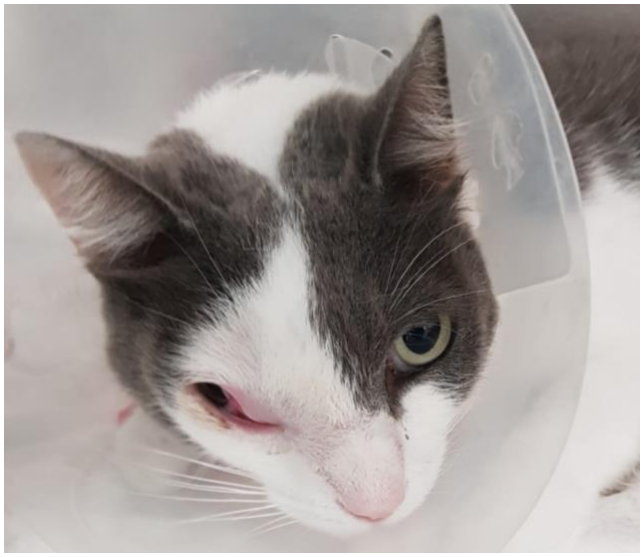


Figure 1- Patient admitted at the BICU with FIV and a neoplasia from the nasal epithelium

Diagnosis: Clinicopathologic anomalies have been identified in FIV-infected cats, but they are not specific or pathognomonic for the infection (Sellon and Hartmann 2012). Regarding CBC, possible abnormalities are anemia, thrombocytopenia, neutropenia and lymphopenia (Sellon and Hartmann 2012). CBC can be normal during the latent infection phase. A biochemistry profile may include hyperglobulinemia. Azotemia can be present in cats with concomitant chronic kidney disease (Sellon and Hartmann 2012). In urinalysis, proteinuria may be noted with concomitant chronic kidney disease, or with glomerulonephritis (Sellon and Hartmann 2012; Sykes 2013b).

FIV infection is most frequently diagnosed through detection of FIV-specific antibody using rapid tests performed on whole blood, serum or plasma (Little et al. 2020). Thus, antibody identification is normally suggestive of FIV infection. Antibodies are usually identified using either ELISAs or rapid immunomigration (RIM) assays (Sellon and Hartmann 2012; Sykes 2013b; Little et al. 2020). Traditionally, western blot is the gold standard diagnostic test for the detection of FIV antibodies (Little et al. 2020) and is used to confirm inconclusive results (Sellon and Hartmann 2012). Detection of FIV proviral DNA or viral RNA (or both) by PCR is commonly used as an additional test (Little et al. 2020). Other diagnostic methods include virus isolation and IFA assays (Sykes 2013b).

It is important to refer that during the initial phase of FIV infection, cats can test negative for antibodies (Little et al. 2020). As recent infection may lead for negative antibody result, testing should not be performed earlier than 60 days after the potential virus exposure (Sykes 2013b; Little et al. 2020). Moreover false negatives can be related to high virus loads that sequester antibodies in antigen-antibody complexes in the terminal stage of infection (Little et al. 2020).

Kittens that tested positive should be carefully interpreted. Antibodies are passively transferred to kittens that nurse on naturally infected or vaccinated queens (Sykes 2013b; Little et al. 2020). Under natural circumstances, if a chronically FIV-infected queen is otherwise healthy, kittens born from that queen rarely acquire FIV in utero or postnatally (Little et al. 2020). Thus, most kittens that have tested positive will test negative when maternal antibodies have waned (Little et al. 2020).

Medical and sanitary prophylaxis: Similarly to FeLV-infected cats, FIV-infected cats have the same medical prophylaxis. All cats should be tested in order to take preventive measures. Cats infected with FIV should receive preventive healthcare checkups at least once every 6 months for prompt detection of changes in their health status (Little et al. 2020). Sexually intact male and female cats should be neutered, to reduce the chance of interaction with other cats (Sykes 2013b). Identical to FeLV-infected cats, FIV-infected cats when hospitalized should not have direct contact with other patients (Little et al. 2020). At home, cats infected with FIV must be kept indoor and only have access to outdoor within secure enclosures. With proper care and environmental management, FIV-infected cats can live many years (Sellon and Hartmann 2012; Little et al. 2020). Vaccination: Although there is a vaccine, it is not available and it does not protect against the most common subtypes in Europe (Little et al. 2020).

Treatment and prognosis: Cats in the terminal phase of FIV infection may require nutritional support, fluid therapy, regular dental prophylaxis, oral gels, dental extractions and antimicrobial drugs with activity against anaerobes for severe stomatitis (Sykes 2013b). For anterior uveitis, cats may require topical glucocorticoids and atropine (Sykes 2013b). Opportunistic infections may respond to appropriate antimicrobial treatment, however, prolonged treatment may be required (Sellon and Hartmann 2012; Sykes 2013b). For nonregenerative anemia it may be useful using the recombinant human erythropoietin or darbepoetin (Sykes 2013b).

Antiviral and immunomodulator drugs, such as oral or subcutaneous AZT in addition to reduce viral load, and improving the clinical health of the infected-cat (Sellon and Hartmann 2012), it also can be used in cats with stomatitis or neurologic disease (Little et al. 2020). However, AZT can cause bone marrow suppression, so the CBC must be monitored weekly (Sellon and Hartmann 2012; Little et al. 2020). Topical lactoferrin has also been associated

with clinical improvement for cats with stomatitis (Sykes 2013b). Fozivudine reduces viremia and may have less hematologic adverse effects (Sykes 2013b). Results of treatment with interferons (human and feline) are lacking or have failed to confirm therapeutic benefits (Little et al. 2020).

Prognostic: The progression of the disease correlates to the virus strain and host immunity. No FIV positive cat should be euthanized as the life span does not show a big difference between FIV-infected cats and noninfected cats (Sellon and Hartmann 2012). Once the terminal phase occurs, cats typically last less than 1 year (Sykes 2013b).

3. Upper Respiratory Tract Disease (URTD)

Etiology: One of the most common cause of morbidity and mortality in cats is infectious feline URTD. Multiple pathogens can contribute to URTD. The most prevalent causes of URTD are feline herpesvirus-1 (FHV-1) and feline calicivirus (FCV) (Sykes 2013d). Primary bacterial causes include *Bordetella bronchiseptica*, *Chlamydia felis*, and *Mycoplasma* spp (Sykes 2013d).

FHV-1 is an alphaherpesvirus, containing double-stranded enveloped DNA (Sykes 2013d). FCV is a member of the *Vesivirus* genus of the calicivirus family, containing a non-enveloped, single-stranded RNA virus (Gaskell et al. 2012). *Bordetella bronchiseptica* is an aerobic, Gram-negative coccobacillus (Sykes 2014). *Chlamydia felis* is a Gram-negative, coccoid, obligatory intracellular bacteria that belongs to the order Chlamydiales (Sykes and Greene 2012). Mycoplasmas are fastidious bacteria that lack a cell wall and belong to the class Mollicute (Sykes 2014).

Epidemiology: URTD is widespread through the cat population, usually with a higher prevalence in multicat households, younger animals and shelters (Gaskell et al. 2012; Sykes 2013d, 2014). The viruses, FHV-1 and FCV, are primarily shed by saliva, nasal, and ocular secretions, and are spread through direct contact with an infected animal (Gaskell et al. 2012). Although infected cats are the most important source of transmission, clinically recovered cats can also be carrier's. Indirect transmission is also possible, contaminated secretions may be present on feeding and cleaning utensils, personnel and cages (Gaskell et al. 2012). Aerosols are not of major importance because cats cannot produce an infectious aerosol during normal breathing. Nevertheless, sneezes may transmit infection if the other cats are less than 1 to 2 meters away (Gaskell et al. 2012).

FHV-1: Virtually, all infected cats develop latent infection (Gaskell et al. 2012; Sykes 2013d), which occurs in the trigeminal ganglia and can also be detected in other tissues (Sykes 2013d). Shedding reactivation, with or without clinical signs of URTD, occurs 4 to 12 days following a stress incident (Sykes 2013d). This stress event could be an exposure to new cats, transportation (e.g., moving to a new house, a trip to the vet or a cat show), lactation,

concomitant diseases or a treatment with immunosuppressive drugs. The duration of shedding can last from 1 to 13 days (Sykes 2013d). FHV-1 survives 18 hours at room temperature and is easily inactivated by drying and by most disinfectants (Sykes 2013d).

FCV: Accounts for 10% to more than 50% of cases (Sykes 2014). Even in the absence of obvious clinical signs, infected cats may develop a persistent infection in the oropharyngeal tissues (Sykes 2013d, 2014). The virus sheds continuously from the oropharynx and the magnitude of shedding varies with time and between cats. Shedding can terminate between weeks to months; but in few cases, it can be lifelong (Sykes 2013d, 2014). Carriers serve as a source of infection for other cats. FCV is more persistent than FHV-1. Susceptibility to disinfectants can vary between FCV strains and survival in the environment can last as long as 28 days (Sykes 2013d, 2014). The virus can persist in a dried state for several months. Therefore, fomites are a important mean of transmission (Sykes 2013d).

B. bronchiseptica: Especially prevalent in shelters, multicat houses, pet stores, where large numbers of potentially stressed animals may be in contact (Sykes 2014). Transmission of this bacterium may occur between dogs and cats, which is important for animals living together. Epidemiologic evidence suggests that cats can be carriers for *B. bronchiseptica* (Gaskell et al. 2012). *B. bronchiseptica* can survive for 10 days in the environment and is able to thrive in water sources but is inactivated by most disinfectants (Sykes 2014).

C. felis: Transmission occurs primarily by direct contact as *C. felis* only survives a few days in the environment and is readily inactivated by most disinfectants. *C. felis* infection usually occurs in multiple cat houses, especially those from breeding catteries. Suboptimal hygiene is a risk factor for infection (Sykes 2014).

Mycoplasma: Stress factors, such as concomitant respiratory viral infections, unhygienic conditions and overcrowding may promote transmission between cats (Sykes 2014). They can be important as secondary pathogens, but their role as primary agents is controversial (Gaskell et al. 2012).

Pathogenesis: FHV-1: The routes of infection are oral, conjunctival and nasal. FHV-1 replicates within the mucosae of the nasal septum, turbinates, nasopharynx and tonsils (Gaskell et al. 2012). Shedding of FHV-1 can be detected as early as 24 hours after infection and generally persists from 1 to 3 weeks. Although viremia is rare, it can be detected in debilitated animals or neonatal kittens (Gaskell et al. 2012).

FCV: The natural routes of infection are conjunctival, nasal and oral. Viral replication occurs principally in the oral and respiratory tissues (Gaskell et al. 2012). FCV strains can have some tropism for different replication sites. FCV can also be found in visceral tissues, feces and in urine. In cases of FCV-associated virulent systemic disease (VSD), the virus gains access to cellular compartments, which are not usually associated with FCV (Gaskell et al. 2012).

Bordetella bronchiseptica: The oronasal cavity seems to be the primary route of infection, where bacteria colonizes the mucosal surfaces. *B. bronchiseptica* uses virulence factors to adhere to cilia of the respiratory epithelium and then causes ciliostasis and their destruction, making it easier for further colonization and persistence of bacteria (Gaskell et al. 2012).

Chlamydia felis: Chlamydia replicates in the mucosal tissues and its principal target is the conjunctiva. The incubation period is about 2-5 days. Shedding generally stops 60 days after infection, although in some cases it can persist (Gruffydd-Jones et al. 2009).

Mycoplasma: By being commonly isolated from upper respiratory tract of healthy cats, their role in URTD has been difficult to determine (Sykes 2014). In order to replicate, mycoplasmas must adhere to host cells. Invasion of deeper tissues and disease occurs as a result of immunosuppression or disruption of normal host barriers (Sykes 2013e).

Clinical signs: The observed clinical signs will depend on different factors, such as the strain of the agent, the infecting dose, environmental and preexisting conditions. Immunosuppressive concomitant diseases like FIV or FeLV may lead to more severe clinical cases (Gaskell et al. 2012).

FHV-1: Early signs include inappetence, sneezing, depression and pyrexia, followed by ocular and nasal serous discharges. FHV-1 infection leads to ocular signs, such as ulcerative keratitis, eosinophilic keratitis, corneal sequester, uveitis and conjunctivitis, which can have severe hyperemia and chemosis (Gaskell et al. 2012; Sykes 2013d). Dyspnea and coughing can occur in more severe cases (Gaskell et al. 2012). Less frequently FHV-1 can cause oral ulceration. In young or debilitated cats, generalized infections and primary viral pneumonia can occur (Gaskell et al. 2012). In some cats, the clinical signs in the acute phase can cause permanent damage of the mucosae and of the turbinates, predisposing the cats to chronic bacterial rhinitis, turbinate osteomyelitis and sinusitis (Sykes 2013d). Clinical signs are usually resolved within 10-20 days (Gaskell et al. 2012).

FCV: Clinical signs of FCV are highly variable because of their different strains, which have different tropism and virulence (Gaskell et al. 2012). A classic FCV infection has early signs such as pyrexia, depression, and the most characteristic one, oral ulceration. Ulceration generally occurs in the tongue, but it can appear on the lips, nose and mouth. Less frequently, sneezing, ocular and nasal discharges, and conjunctivitis may occur (Gaskell et al. 2012). Chronic ulceroproliferative and lymphoplasmacytic stomatitis have been associated with persistent FCV infection. Other FCV strains can cause pneumonia or a febrile disease with lameness (Gaskell et al. 2012; Sykes 2013d). Cats with FCV-VSD develop severe signs including anorexia, fever superior to 40.6ºC, nasal and/or ocular discharge, oral and footpad ulceration and weight loss (Gaskell et al. 2012; Sykes 2013d, 2014). FCV-VSD strains also infect different cell types, including hepatocytes, pneumonocytes, endothelial and pancreatic

acinar cells (Sykes 2013d). Common clinical signs of FCV-VSD include alopecia, crusting, ulceration and cutaneous edema (Sykes 2014). FCV-VSD can also cause severe respiratory distress due to pulmonary edema or pleural effusion, and icteric skin as a result of hepatic necrosis or pancreatitis. Association of the liver, pancreas and gastrointestinal tract may also cause vomiting and or diarrhea. Cats may also develop bleeding abnormalities (Sykes 2013d, 2014).

Bordetella bronchiseptica: A wide range of clinical signs have been reported, namely ocular and nasal discharge, sneezing, coughing (less frequently) (Gaskell et al. 2012). Young kittens are more likely to show severe dyspnea, cyanosis and death caused by bronchopneumonia (Sykes 2014).

Chlamydia felis: Clinical signs include chemosis, conjunctivitis, serous to mucopurulent ocular discharge and blepharospasm. Clinical signs of nasal involvement are stertorous respiration, serous or mucopurulent nasal discharge and sneezing (Sykes 2014).

Mycoplasma: Clinical signs, such as nasal discharge, sneezing, serous to mucopurulent ocular discharge, conjunctival hyperemia and occasionally keratitis, can occur (Sykes 2014).

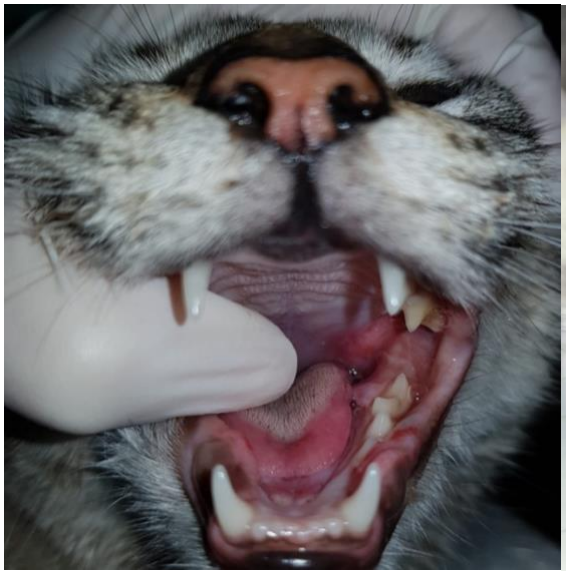


Figure 2- Patient admitted at the BICU presenting oral ulceration and gingivitis

Figure 3- Patient admitted at the BICU with ocular discharge and inflammation

Diagnosis: The etiological agent for transmissible respiratory disease based on clinical signs alone is not always possible because each pathogen produces similar clinical signs (Sykes 2013d, 2014).

Regarding laboratory abnormalities there are no specific changes in CBC, biochemistry panel or urinalysis that can help in the diagnosis of URTD. CBC may sometimes show neutrophilia or lymphopenia in more severe cases. Cats with FCV-VSD can show more abnormalities such as anemia, thrombocytopenia, neutrophilia, lymphopenia,

hypoalbuminemia, hyperbilirubinemia, mildly increase in the activities of creatine kinase (CK), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (Sykes 2013d).

Specific diagnostic tests are generally applied when clinical signs are severe (e.g., pneumonia) or persistent (>7-10 days), or even when multiple cats are infected (Sykes 2013e). Confirmatory diagnosis is generally made using oropharyngeal swabs, though conjunctival or other samples may also be used (Gaskell et al. 2012).

Available assays in order to detect URTD organisms include virus and bacterial culture, histopathology by necropsy or biopsy specimens (Sykes 2014). Serology such as ELISA or serum neutralization assays are not useful unless used to investigate some outbreaks of FCV-VSD (Sykes 2013d, 2014). Lastly, PCR assays are available for all the pathogens of URTD (Sykes 2013d, 2014).

Test results for feline URTD must be interpreted with caution for either result. A positive test can reflect a recent vaccination; or some virus may be shed by healthy cats, and also false-positive PCR results can occur as a result of contamination (Sykes 2013d, 2014). A negative test may indicate that some cats shed undetectable low numbers of organisms, leading to a false negative, or some of the pathogens suffer from degradation of their nucleic acids during transportation (Sykes 2013d, 2014).

Medical and sanitary prophylaxis: Prevention of URTD relies on minimizing stress and overcrowding (Sykes 2013d, 2014). Individual food and water bowls, as well as proper hand washing of the owners and the personnel should be established. Cats should be housed singularly; barriers between cats should be impermeable (Sykes 2013d, 2014). To avoid aerosol transmission, cats should be 1 to 2 meters apart (Sykes 2013d). When entering multicat environments, cats should start a quarantine period of 3 weeks. Disinfection must take place in shelters, boarding facilities and veterinary hospitals to prevent fomite transmission (Sykes 2013d, 2014). Inactivation should be performed by potassium peroxymonosulfate (Trifectant, Virkon S), or sodium hypochlorite (bleach diluted 1:30) and accelerated hydrogen peroxide (Sykes 2013d, 2014).

Vaccination: FCV and FHV-1 are considered core vaccines, so every cat should receive it (Day et al. 2016). It is vital to understand that the protection given by FCV and FHV-1 vaccines will not grant the same robust protection, nor the duration of immunity as provided by feline panleukopenia vaccines (Day et al. 2016). The vaccination guidelines group (VGG) recommends that vaccination starts for kittens at 6-8 weeks of age and then every 2-4 weeks until 16 weeks of age or older (Day et al.2016). Afterwards, a booster vaccine should be given either at 12 months of age or 12 months after the last of the primary series of kitten vaccines (Day et al. 2016). In adult cats, the VGG recommends for ‘low risk’ cats revaccination at intervals of 3 years or longer. For ‘higher risk’ cats, revaccination should be annually. A low risk cat can be defined as a solitary, indoor cat that does not visit a boarding cattery, and a

high risk cat as an animal that visits regularly a boarding cattery or that lives in a multicat household and has an outdoor lifestyle (Day et al. 2016). For an adult cat with unknown vaccination status the VGG recommends two doses of FHV-1/FCV vaccine, 2-4 weeks apart (Day et al. 2016).

Treatment and prognosis: If acute infections are mild to moderate there is no need for antimicrobial treatment (Sykes 2014). However, if the cats have a more moderate to severe URTD, supportive care must be given. Supportive care includes fluid therapy, antimicrobial drugs for secondary infections, and highly palatable aromatic foods (Sykes 2013d, 2014). If that does not work, enteral nutrition through the use of temporary feeding tubes may be placed (Gaskell et al. 2012). Severe infected cats should be hospitalized and given parental fluids, nebulization and oxygen supplementation (Sykes 2013d). Regarding antimicrobial drugs, broad-spectrum antibacterial that achieve good penetration into the respiratory tract may be given, such as doxycycline (Sykes 2014). Doxycycline is recommended as first choice, principally because of its activity against *Bordetella* and mycoplasmas. If chlamydiosis is suspected or confirmed, treatment should last for 4 weeks. Amoxicillin is a good second choice (Sykes 2014). Acute signs are usually resolved within 2-3 weeks (Sykes 2013d, 2014).

Several antiviral drugs have been considered for use in FHV-1 infection when severe signs such as keratitis, conjunctivitis (Gaskell et al. 2012) and ulcerative facial dermatitis (Sykes 2013d) are present. Clinical improvement in cats with both acute and chronic herpesviral disease occurs with famciclovir and indicates a decrease in viral shedding (Gaskell et al. 2012; Sykes 2013d, 2014). The treatment for herpetic keratitis includes topical ophthalmic preparations that contain idoxuridine, trifluridine, and vidarabine (Sykes 2014). Also, cidofovir shows a great promise as a topical treatment. Studies have shown that human recombinant interferon-α and recombinant feline interferon-ω inhibit FHV-1 in vitro (Gaskell et al. 2012; Sykes 2013d, 2014). The administration of the amino acid lysine has some controversial studies since some show efficacy and others lack apparent efficacy (Sykes 2013d, 2014).

Ribavirin was shown to be effective in cell culture for FCV but was toxic for in vivo application (Gaskell et al. 2012). Additionally, for chronic gingivostomatitis, clinical improvement has been shown in cats with extraction of teeth, and with the use of antimicrobial drugs with activity against anaerobic and gram-positive aerobic bacteria. IFN-ω has also been used to treat caudal stomatitis (Sykes 2013d).

4. Feline Panleukopenia virus (FPV)

Etiology: FPV is a small, non-enveloped single-stranded DNA parvovirus, that infects domestic cats and other *Felidae* (Sykes 2013c; Stuetzer and Hartmann 2014).

Epidemiology: FPV is ubiquitous because of its contagious nature and its capacity for persisting in the environment. FPV is a very stable virus that can live for a year in organic materials or fomites at room temperature (Greene 2012). Parvoviruses in fecal material can survive 5-10 months in the outdoors (Greene 2012). Nonetheless, in the summer months with heat and drying, FPV inactivation is accelerated. Likewise, the virus resists heating till 56ºC for 30 minutes and remains viable for longer periods at lower temperatures (Greene 2012).

Shedding of FPV can occur before the appearance of clinical signs or even in asymptomatic cats (Barrs 2019). In recovered cats shedding in urine and feces can last for up to 6 weeks (Greene 2012; Barrs 2019). However, as already mentioned, FPV has a long environmental persistence which makes indirect contact the most common form of transmission (Greene 2012). Thus fomites, such as contaminated clothing, shoes, hands, infected litter trays or cages play a very effective role on transmission (Greene 2012).

Feline panleukopenia occurs most frequently in unvaccinated or improperly vaccinated cats (Sykes 2013c; Barrs 2019). Age susceptibility is correlated with waning titers of maternally derived antibodies (MDA) as well as “the immunity gap” in improperly vaccinated kittens (Barrs 2019). FPV outbreaks usually occur from Summer to early Autumn, coinciding with the seasonal polyestrus and the birth of kittens (Barrs 2019). Panleukopenia also occurs most regularly in multicat houses, or in shelter environments (Sykes 2013c; Barrs 2019).

Inactivation of FPV is accomplished using bleach, sodium hydroxide, 4% formaldehyde peracetic acid and 1% glutaraldehyde in 10 minutes in room temperature (Greene 2012).

Pathogenesis: FPV spreads by contaminated feces, body fluids, or other fomites, as well as by fleas, through the fecal-oral path (Stuetzer and Hartmann 2014). Less commonly, FPV can be transmitted by the respiratory tract through the inhalation of aerosols (Barrs 2019).

Since the virus needs cellular DNA polymerases to synthesize a complementary DNA strand for replication, it must steal it from the host (Barrs 2019). FPV requires rapidly multiplying cells in the S-phase of division for its replication (Stuetzer and Hartmann 2014). Consequently, it has tropism for lymphoid tissues, bone marrow, and the intestinal mucosa (Greene 2012; Stuetzer and Hartmann 2014; Barrs 2019). In the case of the neonates, FPV replicates in the Purkinje cells of the cerebellum (Barrs 2019).

Initially, the virus replicates in oropharyngeal lymphoid tissue between 18-24 hours after infection, followed by viremia during 2-7 days, which distributes the virus throughout the body (Stuetzer and Hartmann 2014; Barrs 2019). Through infecting the lymphoid tissues, FPV leads to lymphoid tissue necrosis and immunosuppression via cellular depletion (Stuetzer and Hartmann 2014). Infection of the bone marrow affects progenitor cells, which explains the decrease in all myeloid cell populations, such as leukopenia. FPV also damages rapidly replicating cells in the crypt of the intestinal mucosa. Their destruction eventually results in

diarrhea caused by malabsorption and increased permeability (Sykes 2013c; Stuetzer and Hartmann 2014; Barrs 2019).

Transplacental infection can also occur, resulting in fetal death, resorption, abortion and mummified fetuses, in early gestation (Barrs 2019). In late prenatal and early neonatal infection, kittens can have the cerebrum, cerebellum, retina and optic nerves affected (Sykes 2013c; Stuetzer and Hartmann 2014).

FPV severity depends on factors such as immune status, age and concomitant infections with other bacterial or viral pathogens (Sykes 2013c; Stuetzer and Hartmann 2014). Clinical signs generally occur after an incubation period of 2-10 days (Sykes 2013c).

Clinical signs: The incidence of cats showing clinical signs is significantly smaller than the number of cats infected by the virus (Greene 2012; Barrs 2019). FPV can be peracute leading to death within 12 hours, with few or no premonitory clinical signs (Barrs 2019). The most common form of FPV is acute, which include signs such as fever (40-41ºC), lethargy, anorexia, vomiting and diarrhea (Greene 2012; Sykes 2013c; Stuetzer and Hartmann 2014; Barrs 2019). However, some signs may be absent (Barrs 2019). Diarrhea is much less common and it usually shows in a later course of the illness. There may be hypersalivation from nausea (Barrs 2019). Abdominal palpation can be painful and show thickened intestinal loops and/or enlargement of the mesenteric lymph node (Barrs 2019). Some cats show severe dehydration which, when associated with vomiting, anorexia and diarrhea can cause depression and weakness (Greene 2012; Stuetzer and Hartmann 2014). Oral ulceration can be present in severely affected cats, and although rarely, bacteremia may be accompanied by icterus (Sykes 2013c). In the terminal stage of the disease cats can become hypothermic, bradycardic and in a comatose state (Greene 2012, Sykes 2013c).

In newborn kittens, the principal clinical signs of FPV include neurological signs such as ataxia, blindness and hypermetric movements (Stuetzer and Hartmann 2014). Additionally, signs of cerebellar dysfunction like incoordination, tremors and absence of menace response may be present (Stuetzer and Hartmann 2014). Signs of forebrain damage are less common, but include behavioral changes, seizures and normal gait despite postural reaction deficits (Greene 2012; Sykes 2013c; Stuetzer and Hartmann 2014). The severity of the neurological signs varies among littermates (Stuetzer and Hartmann 2014). Examination of the ocular fundus may reveal retinal lesions (Sykes 2013c).

Cats generally die from complications such as circulatory shock, septicemia, and disseminated intravascular coagulation (DIC) (Sykes 2013c; Stuetzer and Hartmann 2014; Barrs 2019).

Diagnosis: A presumptive panleukopenia diagnosis is typically made based on clinical signs and leukopenia involvement. It is common to assume that the severity of leukopenia parallels with the prognosis of the disease (Greene 2012).

The most common abnormality on the CBC is leukopenia, which is characterized by neutropenia and lymphopenia (Sykes 2013c). Leukocytosis can also appear; however it is usually correlated with the recovery of the cat (Barrs 2019). Thrombocytopenia results from megakaryocyte destruction or from DIC (Sykes 2013c; Barrs 2019). Anemia is usually mild, unless there is gastrointestinal blood loss (Greene 2012; Barrs 2019). Serum biochemistry analysis may show hypoalbuminemia, hypoproteinemia, hyponatremia, hypochloridemia, and elevations of AST and ALT (Sykes 2013c; Barrs 2019).

Etiological diagnosis is performed by antigen testing with fecal samples based on ELISA technology (Sykes 2013c). When negative, these tests should never rule out the possibility of FPV. Firstly, because of intermittent viral shedding. Secondly, the test sensitivity can be affected by the presence of antibodies that may bind to viral epitopes and make them inaccessible to the monoclonal antibodies from the test kit (Barrs 2019). Vaccination against FPV using modified live vaccines (MLV) can result in false-positive test results for at least 14 days after vaccination (Barrs 2019). Another confirmatory test is PCR (Sykes 2013c; Barrs 2019). When serological testing is negative, but the cat presents characteristic signs of the disease, specific real-time PCR can be used to confirm the diagnosis of FPV (Barrs 2019). These assays can be used on whole blood, feces or infected tissues. False positives can occur in recently vaccinated cats (Barrs 2019). Other tests for diagnosis that have been superseded by the two tests stated before are hemagglutination assays, virus isolation and electron microscopy (Barrs 2019).

Medical and sanitary prophylaxis: In the event of an outbreak, all clinically healthy cats and kittens older than 4 weeks that were exposed or are at-risk should be urgently vaccinated with MLV and kept for 2 weeks in a quarantine area (Barrs 2019). Passive immunization may be useful when cats are introduced into a shelter where an outbreak is occurring, conferring rapid protection (Greene 2012; Sykes 2013c). Due to the fact that immunoglobulins from a serum of a recently immunized cat can persist for up to 4 weeks, vaccination of passively immunized kittens must be delayed by 2 to 4 weeks (Greene 2012; Sykes 2013c).

All FPV-infected cats should be hospitalized and isolated from other cats. To decrease the risk of fomite transmission, personal protective equipment (e.g. disposable gloves, gowns, shoe covers) and infection prevention preparation protocols should be reviewed (Sykes 2013c; Barrs 2019). Isolation and quarantine areas should each have their own equipment and should be cleaned and disinfected for each animal (Barrs 2019).

Vaccination: FPV is considered a core vaccine, so every cat should receive it (Day et al.2016). The vaccination guidelines group (VGG) recommends that vaccination should start for kittens at 6-8 weeks of age and then repeated every 2-4 weeks until 16 weeks of age or older (Day et al. 2016). A booster vaccine should be given either at 12 months of age or 12

months after the last of the primary series of kitten vaccines (Day et al. 2016). Revaccination should be given every 3 years. For an adult cat with an unknown vaccination status the VGG recommends one dose of FPV, after that revaccination every 3 years (Day et al. 2016).

Treatment and prognostic: Treatment of FPV-infected cats is achieved including supportive care. In order to restore loss of electrolytes, overcome dehydration, and replace daily maintenance needs, parenteral fluid therapy is needed (Greene 2012; Barrs 2019). Fluid therapy should be done with lactated Ringer's solution and potassium supplementation (Greene 2012). Parenteral glucose supplementation may also be needed (Barrs 2019). Plasma or blood transfusion therapy may be required in cats showing severe hypoalbuminemia, anemia, or hypotension (Greene 2012; Barrs 2019).

Early enteral nutrition should be administered through an esophageal or nasogastric tube with highly digestible diets, as soon vomiting is controlled (Barrs 2019). Antiemetic therapy can be prescribed (Greene 2012; Barrs 2019). The antiemetic of choice is maropitant, others such as metoclopramide or ondansetron, can also be used (Greene 2012; Barrs 2019).

Figure 4- Nasogastric tube in a FPV positive cat admitted at the BICU

Antimicrobial therapy is essential to control secondary bacterial infection and sepsis associated with the translocation of gastrointestinal tract bacteria. Antimicrobials should have a broad-spectrum and be effective against Gram-negative, Gram-positive and anaerobic bacteria (Greene 2012; Barrs 2019). A combination of amoxicillin-clavulanate, metronidazole and aminoglycosides may be required for cats that are septic or in a more severe state (Greene 2012). The use of anthelminthics is another important point, since intestinal parasitism is a common comorbidity (Barrs 2019).

Treatment with intravenous IFN-ω is effective in dogs with canine parvovirus, however in cats with FPV the results have been a little lackluster (Greene 2012; Porporato et al. 2018; Barrs 2019). The results did not shown any difference in clinical signs or in the chance of

survival between cats receiving IFN-ω and cats without this treatment (Greene 2012; Porporato et al. 2018). Similar to IFN-ω, human granulocyte colony-stimulating factor needs more prospective studies (Greene 2012; Barrs 2019).

Relatively to prognosis, feline panleukopenia has a high mortality rate (Barrs 2019). Cats with FPV that survive the first 5 days of treatment usually recover (Sykes 2013c). Low leukocyte or platelet counts at presentation, low leukocyte counts during hospitalization, or hypoalbuminemia and hypokalemia at presentation are weak prognostic indicators (Sykes 2013c; Barrs 2019). Cerebellar symptoms usually do not advance in kittens with cerebellar hypoplasia (Sykes 2013c).

III- Risk factors for infectious diseases recorded in cats attending a Veterinary Teaching Hospital Isolation Unit in Portugal

1. Objectives

This retrospective study was divided in two phases. In the first phase the aim was to characterize the patients with infectious diseases admitted in the Veterinary Teaching Hospital Isolation Unit over a 7-year period. For this phase a number of objectives were assessed:

- Establish and divide patients into three groups: cats with infectious diseases, cats with suspicion of infectious diseases and cats without infectious diseases;
- Analyze the group of cats with infectious diseases within different parameters (e.g., Breed, Gender, Lifestyle);
- Define the most frequent infectious diseases in cats hospitalized in the BICU;
- Determine the different types of diagnostic tests performed to reach the etiological diagnosis of the patients infectious diseases;

In the second phase, only the most frequent infectious diseases were analyzed. The following procedures were assessed:

- Assemble of a control group for each infectious disease;
- Analyze the patients with the most frequent infectious diseases and their controls within the parameters observed in phase one;
- Observe possible trends in rising or decreasing of cases throughout the years;
- Determine possible risk factors of getting hospitalized within the main infectious diseases encountered in the BICU;

2. Materials and methods

2.1. Database and data analysis

A previously constructed database in Microsoft® Office Excel 365 for Windows was updated with patients that were hospitalized in the BICU for the last 7 years. This data was gathered from The Veterinary Teaching Hospital's (VTH) management software Guruvet and BICU's medical records.

An exploratory and descriptive analysis on all infectious cat patients hospitalized in the BICU was performed prior to the statistical investigation for potential risk factors with RStudio version 1.3.1093 for Mac.

For the inferential statistics a simple regression model was assessed for each analyzed variable of each disease. All variables with a significance of 0.2 were included in the multiple model for each disease (Hosmer and Lemeshow 2000). The results for the multiple model were considered significant when p-value <0.05. For all the significant values Odds ratios and

their 95% confidence interval were calculated. Covariances between independent variables were tested. For model fit both predictive power (McFadden R-squared and C-statistic) and goodness of fit (Hosmer-Lemeshow statistic test) were used. All inferential statistics was performed with RStudio version 1.3.1093 for Mac.

2.2. Diagnostic tests

The patients presented at the VHT with clinical signs of infectious diseases were subjected to a variety of diagnostic methods:

- Retrovirus (FIV and FeLV) – Detected in practice by rapid immunomigration-type assays or ELISA Viracheck in the virology laboratory of the University of Lisbon in the Faculty of Veterinary Medicine (VIL-FMV-ULisbon), with the detection of antibodies in the case of FIV and antigens for FeLV.
- Panleukopenia – In clinic rapid immunochromatography assay, and real-time PCR made by VIL-FMV-ULisbon.
- Coronavirus
    - Feline enteric coronavirus – Detection by RT-PCR in feces or blood, and antibody titers above 1:400, made in DNAtech, which is the cutoff to consider the patient to be highly suggestive of infection.
    - FIP – Detection with PCR positive for coronavirus in effusion liquid or in PAAF samples and pyrosequencing PCR in order to identify two specific mutations (M1058L and S1060A) in IDEXX laboratories. Compatible histologic findings on necropsy were also included. All diagnostic methods were analyzed in the context of the clinical history and patients clinical signs, like pleural or abdominal effusion and neurological signs.
- URTD:
    - Infectious – Using clinical scores determined by Binns et al. (1999), animals with clinical signs of URTD were included. This clinical score is described in Table 1. Only the animals with a clinical score above 3 points were included for the next step. Patients with unspecific signs, such as anorexia and pyrexia were excluded. According to the Table 2, originally presented by Maggs (2005), the animals who went through the clinical score and passed were submitted to the clinic signs of the table. Only the cats that presented three or more of the most specific clinical signs (+++) of any of the agents were labeled as URTD infectious because each pathogen produces a similar spectrum of signs (Sykes 2014).

Table 1- Clinical Scores to admit a patient with URTD signs (retrieved from Binns et al. 1999)

Clinical signs	Clinic Score
Dyspnea; **Sneezing;** **Coughing;** **Nasal Discharge**	3
Conjunctivitis; **Ocular Discharge;** **Oral Ulceration**	2
Hypersalivation; **Anorexia;** **Pyrexia**	1

Table 2- Clinical signs to determine if the patient has an infectious upper respiratory tract disease adapted from Maggs (2005)

Clinical Signs	FHV-1	FCV	*C. felis*
Anorexia	+++	++	±
Sneezing	+++	+	++
Nasal Discharge	+++	++	++
Oral Ulceration	-	+++	-
Ptyalism	+	+++	±
Ocular Discharge	+++	+	++
Conjunctivitis	+++ Hyperemic	-	+++ Chemotic
Keratitis	+++	-	-

Legend: +++ → Most specific signs; ++ → Specific signs; + → Common signs; ± →This signs sometimes appears; - →It is not a common sign to appear

  - Calicivirus and Herpesvirus – Real time PCR made by VIL-FMV-ULisbon from oropharyngeal swabs, though conjunctival or other samples may sometimes be used.

- MDR – The realization of bacteriological culture and antibiotic sensitivity tests in the Bacteriology Lab of FMV-ULisbon and in the Laboratory of Resistance to Antibiotics and Biocides from different biological samples.

- Dermatophytes – Observation during the appointment of cutanic lesions compatible with the *Wood* lamp (UV 9W, 230V, 50Hz) or mycologic culture in the Mycologic Laboratory of FMV-ULisbon.

2.3. Inclusion criteria

The animals enrolled in this study included all cat patients hospitalized in the BICU of the VHT from October 2013 until September 2020 (n=788).

All cats that entered the BICU for hospitalization in the first phase of the study were grouped in three groups under the classification of confirmed infectious disease (ID), suspected ID or non-ID. The confirmed ID group assembles cats hospitalized with a definitive diagnosis of infectious disease. The suspected ID group gathered all cats that remained suspect due to lack of a conclusive diagnosis test. The non-ID group includes cats that, due to suspicion of ID, were hospitalized at the BICU but had a following negative result from the laboratory tests. In cases where there was more than one hospitalization of the same cat under the same ID condition the date of the first hospitalization was considered for data collection and statistical analysis.

It is important to mention that cats in the BICU may have more than one definitive infectious diagnosis, so the total number of ID is bigger than the total number of cats. For example, a cat with a FeLV infection can also have a upper respiratory tract infection, this means that one cat can have more than one diagnostic result.

In the first phase of the study all infectious cats were considered and an exploratory and descriptive analysis was assessed. A cut-off for the second phase of the study was determined. Only the most frequent infectious diseases were used for a descriptive analysis and then analyzed for potential risk factors. It was determined that the cut-off to be considered one of the most frequent infectious diseases encountered in the BICU had to have at least 50 cases.

To assure a better statistical analysis, control groups were made for each disease. Each case had two controls. The inclusion criteria for controls was assigned in order to make sure that the animals who were consigned to these controls did not have the disease. These inclusion criteria are shown in Table 3. For that reason, some of the control groups were made based on other studies, like Retrovirus and URTD. Because of the lack of studies using control groups for Panleukopenia, this study assessed the control group for Panleukopenia based on characteristic clinical signs depictured in the literature. If the patient did not have any clinical signs corresponding to panleukopenia and neither had leukopenia, then it was eligible to enter the control group.

Table 3: Inclusion criteria for controls

Retrovirus	Cats that tested negative for FIV and FeLV	(Murray et al. 2009) (Macieira et al. 2008)
URTD	Cats without clinical signs of the disease	(Holst et al. 2010)
Panleukopenia	Cats without clinical signs of the disease and without leukopenia	

2.4. Description of the analyzed variables

Unknown variable information was designated as “NA”.

Breed

Cats that had a breed were labeled as “purebred” and cats without breed were labeled as “domestic”.

Gender

All cats were grouped into either male or female.

Neuter status

All cats were intact or neutered.

Age groups

The patients were divided into different ages groups, accordingly to their age: kittens (< 2 years), adults (≥ 2 and < 10 years) and seniors (≥10 years).

Number of animals (Cohabitants)

Cats living with no other animal were designated as “Alone”. Cats living with one or more animals were labeled as “≥ 1”.

Lifestyle

All cats were grouped into 2 groups:

- Indoor: cats that lived exclusively in the house without access to the exterior
- Outdoor: cats that had access to or lived on the street.

Vaccination status

The cat vaccination status was established according to the 2016's recommendations of the *Vaccination Guidelines Group of the World Small Animal Veterinary Association* [WSAVA] (Day et al. 2016).

- Up to date – cats that received the initial core vaccination at 6-8 weeks of age, then every 2-4 weeks until 16 weeks of age or older (primo-vaccination). A booster dose of vaccine given at 12-months of age and thereafter, revaccinations every 3 years. The core vaccines for cats are those that protect against feline panleukopenia (FPV), herpesvirus (FHV-1), and calicivirus (FCV). It is important to point out that cats that have not been vaccinated for FeLV are still considered up to date because it is not a core vaccine (Day et al. 2016).
- Not up to date – this variable contained cats that:
    - Had incomplete vaccination: a cat who had missed one or more vaccines in the primo-vaccination stage.
    - Had delayed vaccines: a cat who had not been vaccinated for at least 3 years.
    - Were unvaccinated: a cat who had not received any vaccines.

Concomitant disorders and diseases (Concomitant Disorders/Diseases)

To understand this variable it is necessary to explain the inclusion criteria to be admitted at the BICU. Only the infectious diseases that can spread easily between animals and are a danger to the public health are necessary to be in the isolation unit (e.g., Zoonotic diseases, URTD, Panleukopenia).

Thus, this variable has all non-infectious diseases and disorders recorded in the patients, such as anemia, neoplasia (e.g., lymphoma), chronic renal disease, among others and infectious diseases that do not need to be isolated, for example, urinary tract infections that are susceptible to antibiotics and thick borne diseases.

Cats with concomitant disorders and diseases were labeled as "Yes". Cats without concomitant disorders and diseases were labeled as "No". These disorders/diseases detected in cats were not the motive of hospitalization in the BICU.

Referrals

All cats were hospitalized in the BICU in sequence to three types of appointments: First opinion; second opinion or referral appointment.

Admission

When the cat was first hospitalized.

Length of hospitalization and Number of hospitalizations

The number of days the cat was in the BICU and the number of hospitalizations.

Diagnostic

After hospitalization and testing, the cat can be found:

- Positive (infectious)- an animal which tested positive for an infectious disease;
- Suspect – if the diagnostic methods were not made, or even if they come through as negative, but there is still a suspicion of an infectious disease;
- Negative non-infectious - an animal which tested negative for an infectious disease;

Type of test performed to reach an etiological diagnostic

Which test was made to confirm such disease, e.g., ELISA for a FeLV positive.

Concomitant Infectious Diseases

Other infectious diseases that were detected in cats, and made them stay in isolation. However, they are not the principal motive of hospitalization in the BICU. Cats with concomitant infectious diseases were labeled as “Yes”, cats without concomitant infectious diseases were labeled as “No”.

Outcome at discharge

When cats left the BICU, they were grouped in 3 categories: Discharge; Euthanasia; or Death.

Follow up

Only cats that survive were eligible for a follow-up, each cat was labeled in one of the following 7 groups:

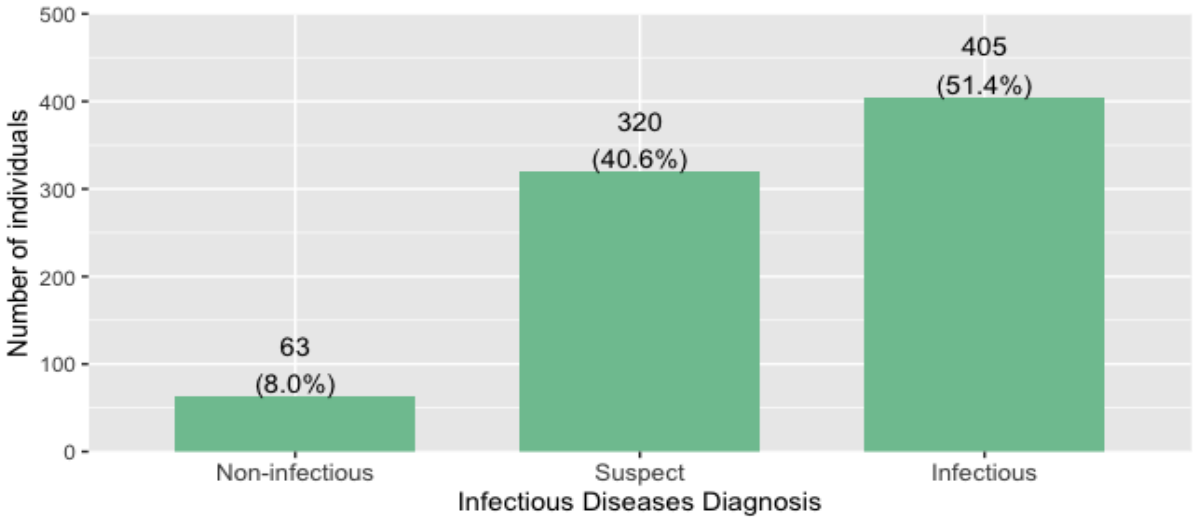
- Chronic- a cat that had a chronic disease;
- Chronic better – cats with less or mild clinical signs;
- Chronic worse – cats that got worse from their chronic disease;
- Better – absence of clinical signs;
- Healthy – absence of clinical signs and clinically healthy;
- Euthanasia – cats that were euthanized;
- Death – cats that died.

3. Results

3.1.1. Infectious diseases status

Since 2013, the total of cats hospitalized were 788, of which 405 (51.4%) had a definitive infectious diagnosis, 320 (40.6%) remained suspected of ID, and 63 (8.0%) were non-infectious. (Graphic 1).

Graphic 1- Infectious Status of cats hospitalized at the BICU

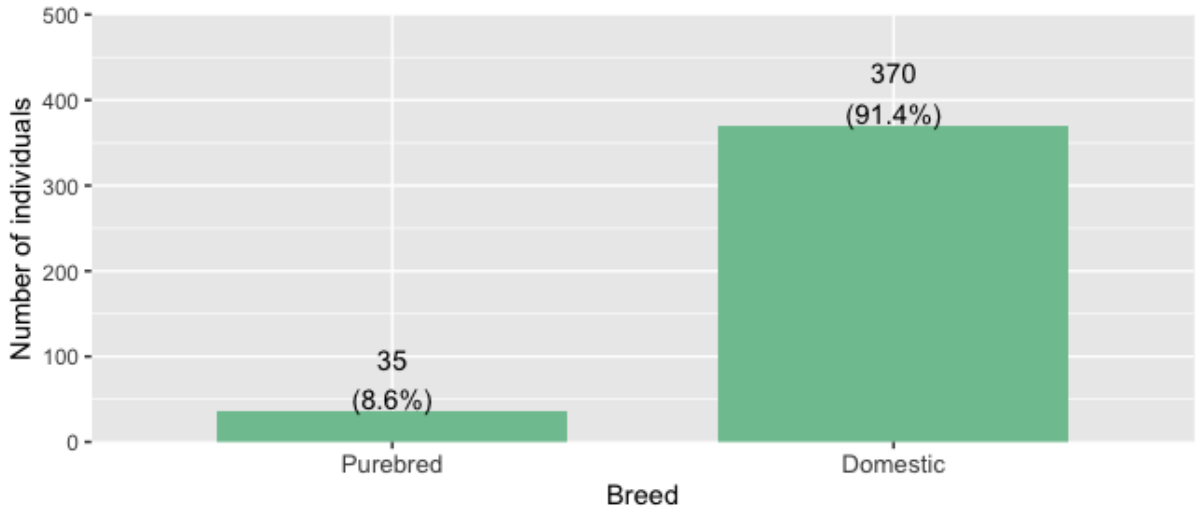


Following this previous infectious status assessment, the descriptive analysis was focused only on the patients with infectious diseases (n=405).

3.1.2. Breed

Regarding the 405 cats investigated, the majority of them were domestic (n=370, 91.4%) and only 35 cats were purebred (8.6%). (Graphic 2)

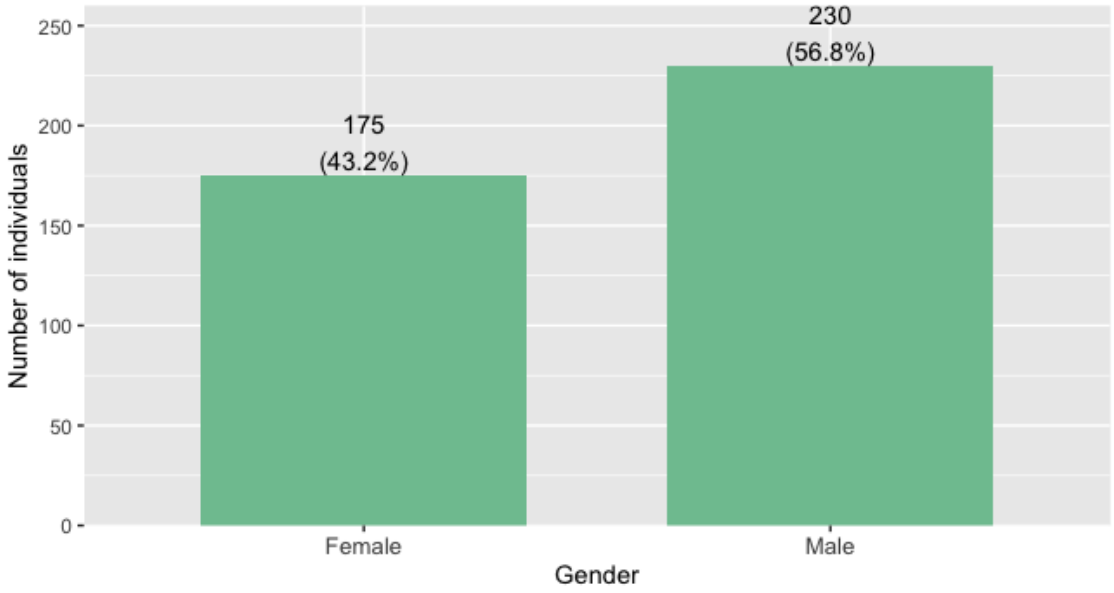
Graphic 2- Breed of cats



3.1.3. Gender

Considering gender, male cats represented 230 of the 405 cats (56.8%) and female cats 175 of the 405 (43.2%). (Graphic 3)

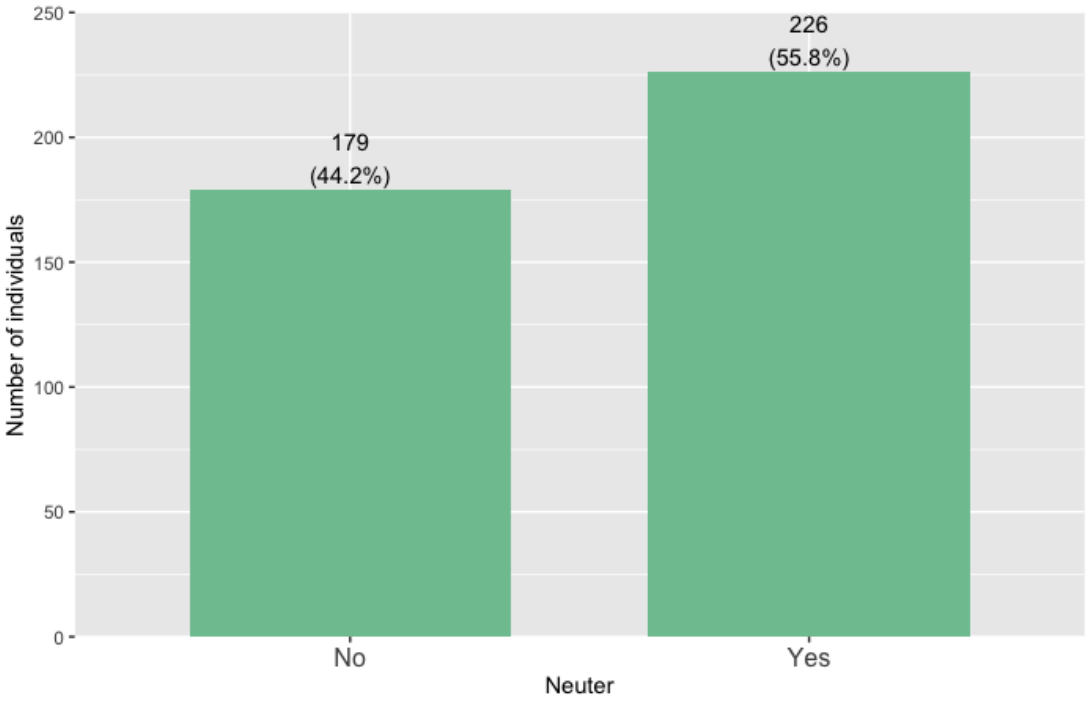
Graphic 3- Gender of the cats



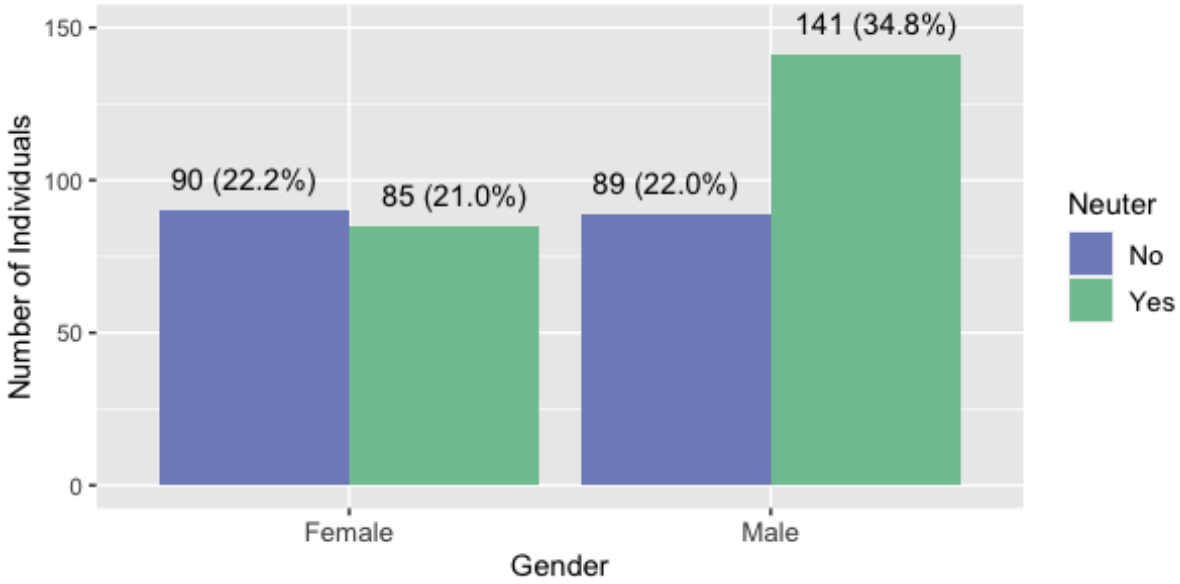
3.1.4. Neuter status

The majority of cats were neutered (n=226, 55.8%), intact cats represented 179 of the cats (44.2%) (Graphic 4). From the neutered pool, 141 cats (34.8%) were male, and 85 (21.0%) were female. Regarding the intact cats 90 were female (22.25%) and 89 were male (22.0%). (Graphic 5)

Graphic 4- Neuter status of the cats



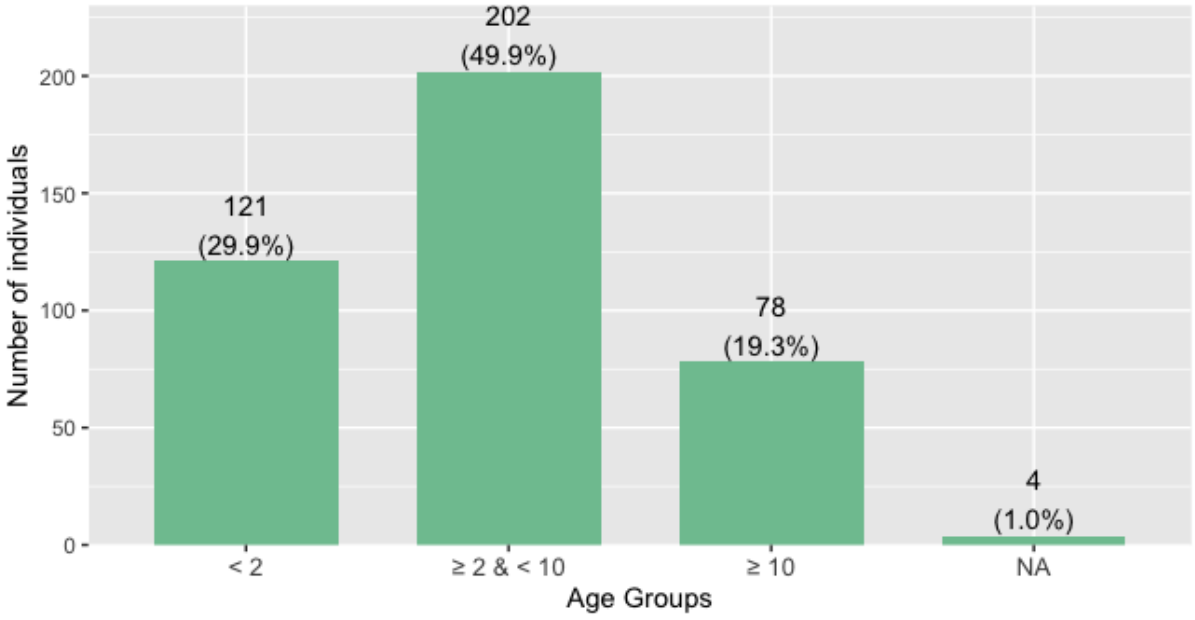
Graphic 5- Reproductive status per gender



3.1.5. Age groups

The median age for cats was 4 years old, ranging from 1 month to 19 years. Cats were divided into 3 groups: kittens (< 2 years), adults (≥ 2 and < 10 years) and seniors (≥ 10 years). Most cats were in the adult group (n=202, 49.9%). The second most common group was kittens (n=121, 29.9%), followed by seniors (n=78, 19.3%). From the 405 cats, 4 did not have information about age (1.0%). (Graphic 6)

Graphic 6- Age groups of the cats



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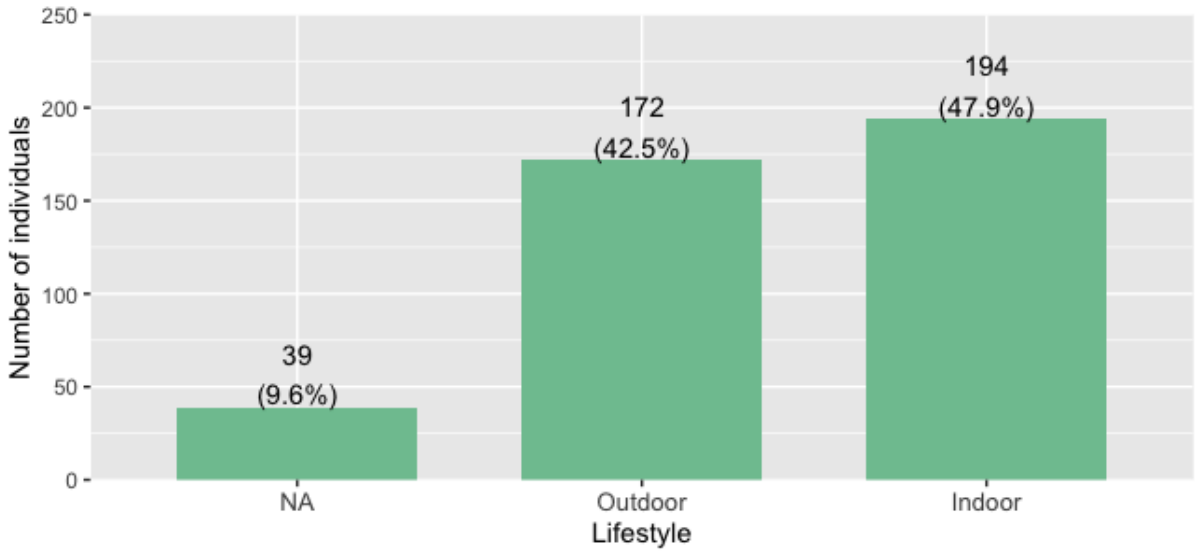
3.1.6. Lifestyle

Concerning lifestyle, 194 cats lived strictly indoors (47.9%), 172 had access to outdoors or lived in the outdoors (42.5%). There was no information about the lifestyle of 39 cats (9.6%) (Graphic 7).

Graphic 7- Lifestyle status of the cats



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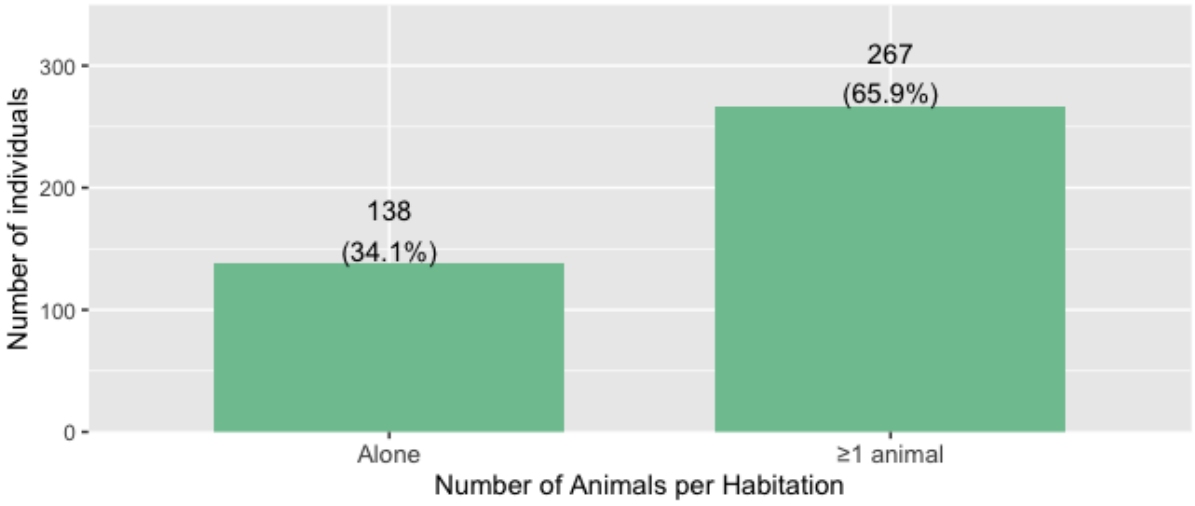
3.1.7. Number of animals (Cohabitants)

A large percentage of cats lived with one or more animals (n=267, 65.9%), these could be other cats, dogs or other animals. Only 138 cats (34.1%) did not live with other animals (Graphic 8).

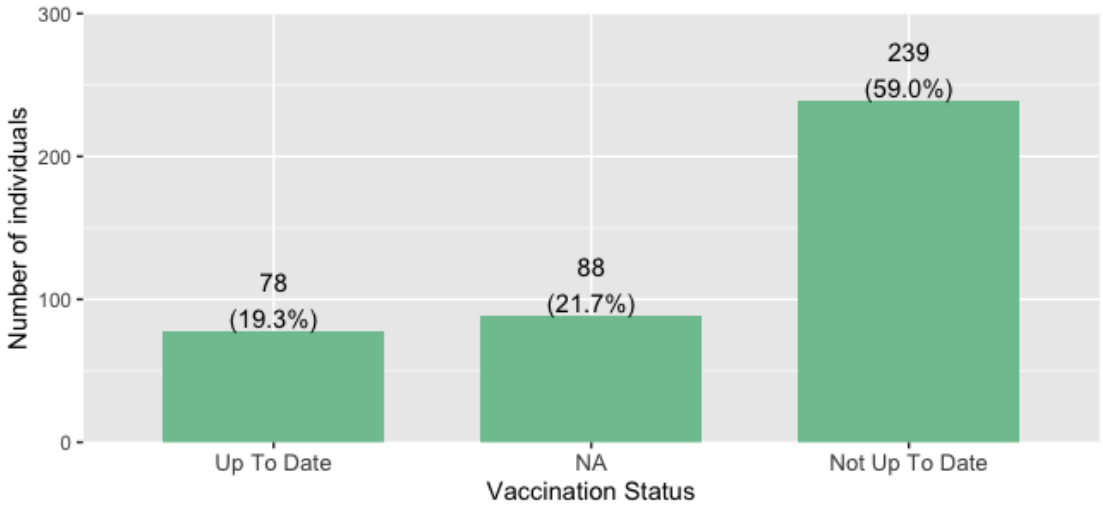
Graphic 8- Number of animals per habitation



3.1.8. Vaccination status

Accordingly to the vaccination guidelines the majority of the cats (n=239, 59.0%) did not have their vaccines up to date. As previously stated, not up to date vaccines could mean that the cats had an incomplete vaccination, had delayed vaccines or had never been vaccinated. Only 78 cats (19.3%) had updated vaccines. Finally, 88 cats (21.7%) had no information about their vaccination status (Graphic 9).

Graphic 9- Vaccination status of the cats



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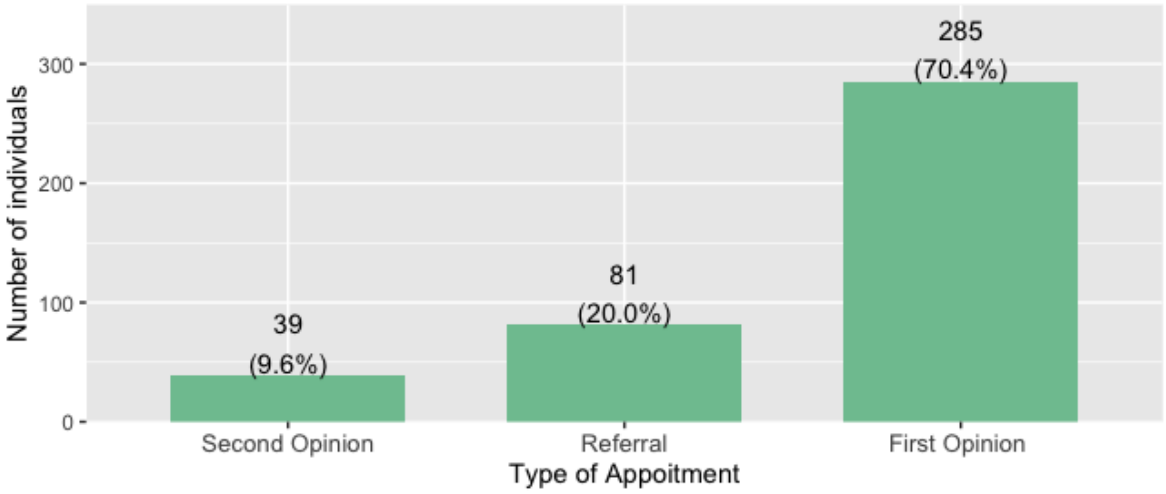
3.1.9. Referrals

First opinion appointments were the most frequent type of admission to the BICU (n=285, 70.4%). 81 cats (20.0%) were referenced to the BICU, and 39 cats (9.6%) were second opinion appointments. (Graphic 10)

Graphic 10- Which type of appointment



3.1.10. Concomitant Disorders and Diseases

Upon admission in the BICU, 272 cats (67.2%) presented concomitant disorders/diseases. The most frequent findings were neoplasia (e.g., lymphoma),

exterior/interior parasites (e.g., fleas) and urinary disorders (e.g., chronic renal disease). While 133 cats (32.8%) only had the infectious disease that made them stay at the BICU.

3.1.11. Length of the hospitalization

The mean hospitalization period was 3.5± 2.8 days. And the median hospitalization was 3 days, ranging from 1 to 21 days. The majority of cats were hospitalized only for 1 day (n= 103, 25.4%). 84 cats were hospitalized for 2 days (20.7%). 66 cats were hospitalized for 3 days (16.3%), 40 for 4 days (9.9%), 30 for 5 days (7.4%), 38 for 6 days (9.4%), 17 for 7 days (4.2%), 9 for 8 days (2.2%), 3 for 9 days (0.7%). Regarding 10 and 11 days of hospitalization, both had 4 cats in that time (1.0%). Only one cat stayed 12 and another 13 days (0.2%). 2 cats stayed 14 days (0.5%). Finally, only 1 cat stayed 20 and another 21 days (0.2%).

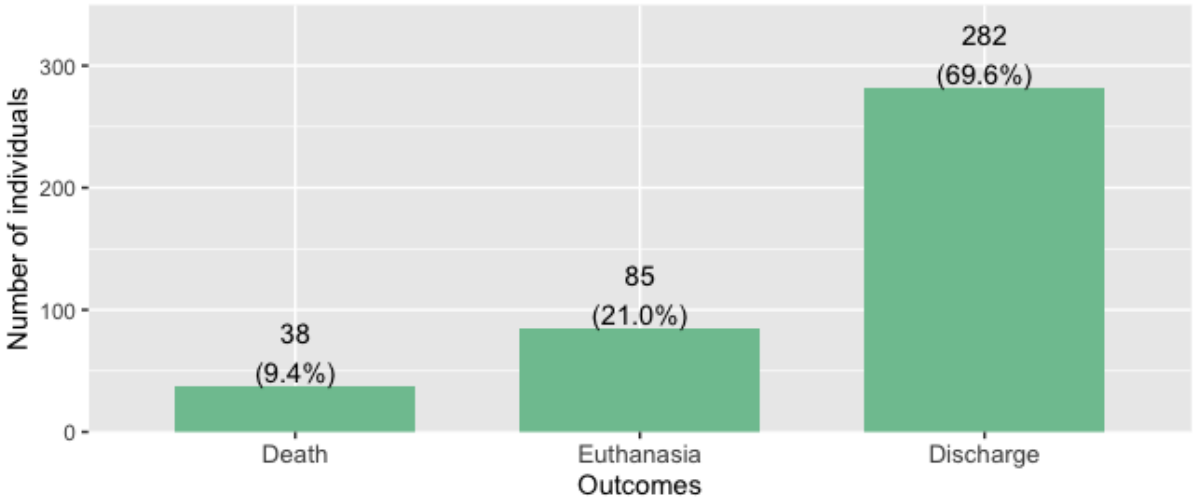
3.1.12. Number of hospitalizations

The median number of hospitalizations was 1, ranging from 1 to 7 hospitalizations. The majority of the cats were only hospitalized once (n=349, 86.2%), 43 cats were hospitalized twice (10.6%), 7 were hospitalized three times (1.7%) and 4 hospitalized four times (1.0%). Only 1 cat was hospitalized 5 times (0.2%) and another one 7 times (0.2%).

3.1.13. Outcome at discharge

In regard to the 405 hospitalized cats, 282 (69.6%, $CI_{95\%}$=64.9-73.9) were discharged, 85 (21.0%, $CI_{95\%}$=17.3-25.1) were euthanized, 38 (9.38%, $CI_{95\%}$=6.91-12.6) died during the hospitalization. (Graphic 11)

Graphic 11- Possible outcomes at discharge

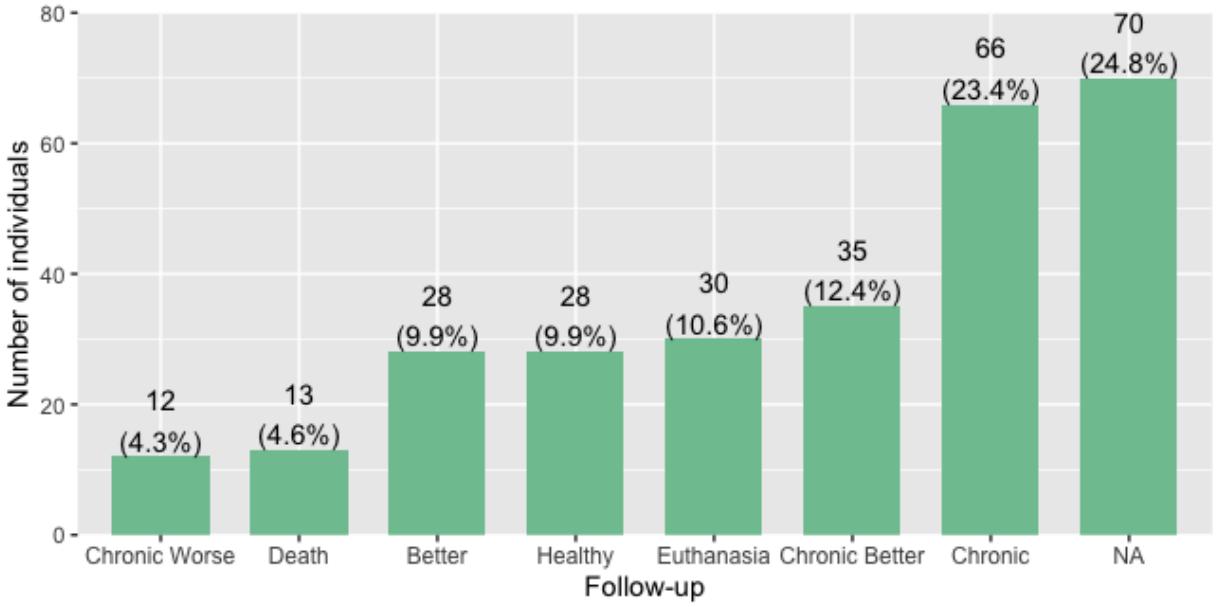


3.1.14. Follow-up

This parameter was only considered for the animals who had a discharge as an outcome. Therefore, the total of animals that had follow-up were 282.

All owners were advised to return with their animals for an appointment after one week from discharge at the BICU. Part of these animals returned and some of them were accompanied by VHT, which allowed a follow-up of the cases. 70 cats did not have a follow-up (24.8%). 66 cats (23.4%) maintained a chronic disease. Additionally, it was considered that the chronic disease of 35 cats (12.4%) was improved. 30 cats (10.6%) were euthanatized during their follow-up. 28 cats (9,9%) were considered healthy. In addition, 28 cats (9.9%) improved, but not enough to consider them healthy. 13 cats (4.6%) died. The chronic diseases were worse in 12 cats (4.3%) (Graphic 12).

Graphic 12- Follow-Up from cats hospitalized at the BICU



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3.1.15. Infectious Concomitant Diseases

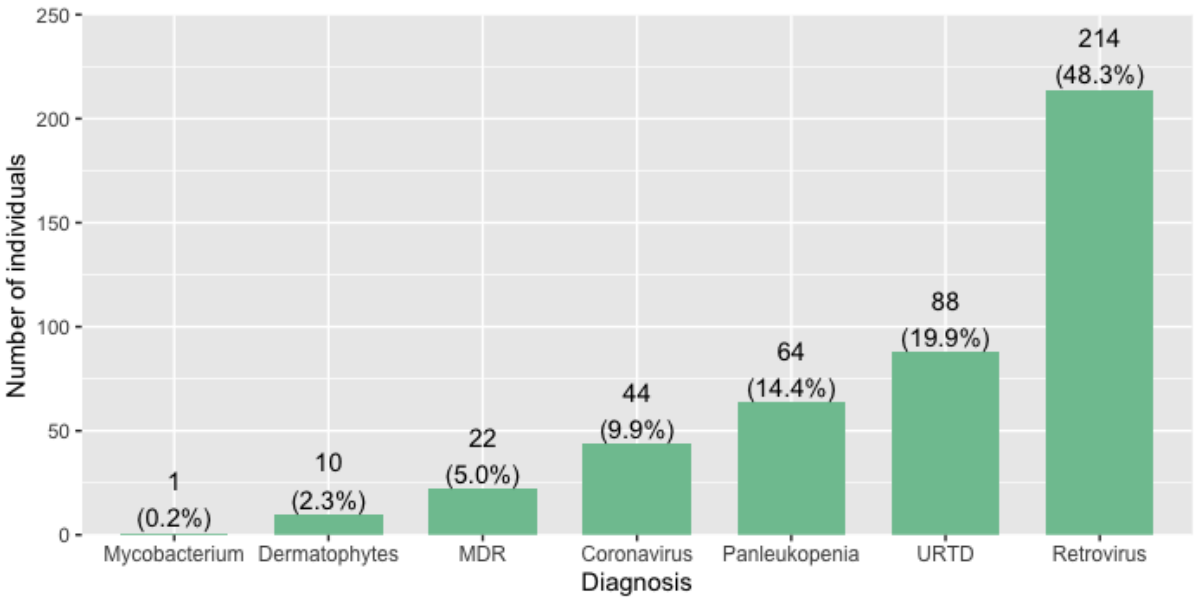
The majority of the cats hospitalized at BICU had only one infectious disease at the moment of hospitalization (n=367, 90.6%). Only 38 cats (9.4%) had another infectious disease at admission. As previously stated, these cats by having more than one infectious disease were counted for more than one final diagnose. This leads to a total of diagnosed cats with infectious diseases greater than the total number of cats admitted at the BICU.

3.1.16. Diagnostic

Of all infectious cats, the most diagnosed disease was Retrovirus (n=214, 48.3%), followed up by URTD (n=88, 19.9%), and then Panleukopenia (n=64, 14.4%). In fourth place

was Coronavirus (n=44, 9.9%), and with less causality was MDR (n=22, 5.0%), dermatophytes (n=10, 2.3%), and finally mycobacterium (n=1, 0.2%). (Graphic 13)

Graphic 13- Confirmed Diseases of cats at the BICU



3.1.17. Type of test performed to reach an etiological diagnostic

Different tests were performed to confirm an infectious disease, Table 4 shows which type of test was assessed for each infection. For Coronavirus, 22 cats were diagnosed through PCR (55%), 12 cats through antibody titers (27.2%), 7 through PCR for specific mutation detection (16%) and 3 cats through necropsy (6.8%). Culture was the only method of testing for Dermatophytes, MDR and Mycobacterium.

For Panleukopenia, 60 cats were diagnosed through PCR (93.8%), 2 through rapid immunochromatography (3.1%) and also 2 cats through Immunoglobulin M (IgM) serology (3.1%).

Retrovirus confirmation was made by ELISA (n=140, 66.3%), rapid immunochromatography (n=44, 20.6%) and PCR (n=1, 0.5%). However, there was no information about what type of test was performed in 27 cats (12.6%).

Finally, for URTD, 45 cats were confirmed by PCR (51.13%). 39 cats were diagnosed through clinical signs already mentioned in the materials and methods (44.32%) and 4 through culture (4.55%).

Table 4- Different tests performed for each etiological diagnosis

	Coronavirus, N = 44 Cats (%)	Dermatophytes, N = 10 Cats (%)	MDR, N = 22 Cats (%)	Mycobacterium, N = 1 Cats (%)	Panleukopenia, N = 64 Cats (%)	Retrovirus, N= 214 Cats (%)	URTD, N = 88 Cats (%)
Antibody Titers	12 (27,2%)	-	-	-	-	-	-
Clinic	-	-	-	-	-	-	39 (44.32%)
Culture	-	10 (100%)	22 (100%)	1 (100%)	-	-	4 (4.55%)
ELISA	-	-	-	-	-	140 (66.3%)	-
Rapid Immunochromatography	-	-	-	-	2 (3.1%)	44 (20.6%)	-
NA (Unknown Information)	-	-	-	-	-	27 (12.6%)	-
Necropsy	3 (6.8%)	-	-	-	-	-	-
PCR	22 (50%)	-	-	-	60 (93.8%)	1 (0.5%)	45 (51.13%)
PCR For Mutation Detection	7 (16%)	-	-	-	-	-	-
IgM Serology	-	-	-	-	2 (3.1%)	-	-

3.2. Descriptive analysis of the most frequent infectious diseases

As stated previously, in the second phase of the study a cut-off was determined. Diseases with more than 50 cases were explored individually and then analyzed for potential risk factors.

The diseases with more than 50 cases were Retrovirus, URTD, Panleukopenia, as previously shown in Graphic 13. For a better analysis, infection with Retrovirus was divided in FIV and FeLV infection.

In the first phase of the study a general characterization was performed, and it was considered relevant to show the percentages of the unknown information in the graphics or tables. However, in the second phase, as the key point is to identify possible risk factor and, because the unknown information is minimal, it was decided that this information would not have percentages attached to them.

3.2.1. FIV

Throughout the 7 years of this study, 115 cats were diagnosed with FIV. Accordingly to the materials and methods, the FIV controls were cats that tested negative for FIV and FeLV

infection. For a better understanding, Table 5 contains the descriptive analysis of the cases and controls for FIV.

Table 5- Descriptive analysis of FIV

Variables	Categories	Case, n = 115 Cats (%)	Control, n = 230 Cats (%)
Breed	Purebred	2 (1.7%)	25 (11%)
	Domestic	113 (98%)	205 (89%)
Gender	Female	36 (31%)	105 (46%)
	Male	79 (69%)	125 (54%)
Neuter	No	38 (33%)	75 (33%)
	Yes	77 (67%)	155 (67%)
Number of Animals	Alone	45 (39%)	86 (37%)
	≥1 Animal	70 (61%)	144 (63%)
Lifestyle	Indoor	35 (34%)	136 (59%)
	Outdoor	67 (66%)	94 (41%)
	Unknown	13	0
Vaccination Status	Not Up To Date	60 (79%)	183 (80%)
	Up To Date	16 (21%)	47 (20%)
	Unknown	39	0
Concomitant Disorders/ Diseases	No	20 (17%)	84 (37%)
	Yes	95 (83%)	146 (63%)
Age Groups (Years)	< 2	9 (7.9%)	64 (28%)
	≥ 2 & <10	69 (61%)	102 (44%)
	≥ 10	36 (32%)	64 (28%)
	Unknown	1	0
Survival at Discharge	% [$CI_{95\%}$]	70.4 [61.5-78.0]	-
Length of hospitalization (Days)	Median [Min, Max]	2.00 [1.00-10.00]	-
Number of hospitalizations	Median [Min, Max]	1.00 [1.00-5.00]	-

The distribution of FIV cases can be seen in Graphic 14. The bar plots represent how many animals were admitted in each month. It can be observed that in the majority of each

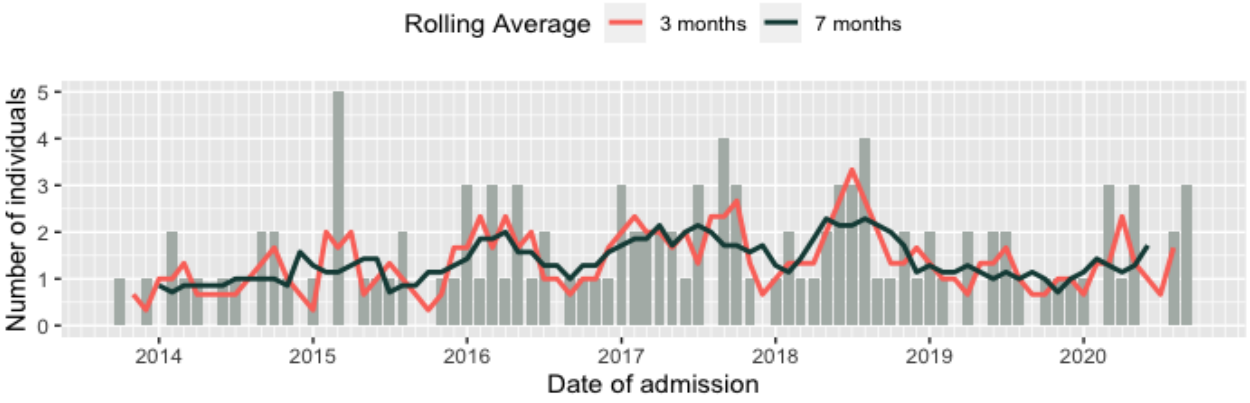
month, throughout the 7 years, there was at least one animal hospitalized with FIV. It was also shown observations between 0 and 5 animals per month.

A rolling average calculates a series of averages of different subsets of the full group of measurements (Thrusfield 2018), in this case the full group is the number of cases in each month, between 2013 and 2020. While the subsets are 3 months and 7 months. For example to construct a 3-month rolling average, sets of three consecutive months are averaged.

The combination of two rolling averages with different time frames helps to show trends that could not be visible using only one rolling average. In this study two rolling averages were designed, one with 3 months and another with 7 months. When the 3-month rolling average (short-term) crosses the rolling average of 7 months (long-term), an uptrend is expected. This means that the number of cases are expected to rise. On the other hand, if the 3-month rolling average is crossed by the 7-month rolling average, a downtrend might be expected, therefore the number of cases are expected to decrease.

The temporal distribution of FIV hospitalized cats in Graphic 14 showed that that every time the rolling average of 3-month went down and crossed the 7-month rolling average, the number of infected cases of FIV decreased. In opposition, when the rolling average of 7-month went up and crossed the 3 months rolling average, the numbers of FIV infected cats increased. Two trends can be observed in the graphic. Firstly, it seemed that the majority of FIV cases appeared in the first semester of every year. Secondly, since 2019, the number of cases seemed to decreased.

Graphic 14- Temporal Distribution of FIV hospitalized cats



Regarding the statistical analysis both simple and multiple regressions were performed in order to investigate possible risk factors for FIV.

As for the simple logistic model, showed in Table 6, domestic cats, male cats, those with access to the outdoors, with concomitant disorders/diseases and between the ages of ≥ 2 & < 10 and ≥ 10 years were more at risk of being hospitalized with FIV (p-value ≤ 0.20).

Likewise, the multiple regression model in the Table 6 showed that the same variables were significant (p-value < 0.05). Domestic cats (OR=4.70; $CI_{95\%}$=1.30-30.23), male cats (OR=1.85; $CI_{95\%}$=1.08-3.19), outdoor living (OR=2.80; $CI_{95\%}$=1.66-4.80), cats with concomitant disorders and diseases (OR=2.72; $CI_{95\%}$=1.45-5.30) and finally cats between the ages of ≥ 2 & < 10 years (OR=3.80; $CI_{95\%}$=1.71-9.41) and ≥ 10 years (OR=3.03; $CI_{95\%}$=1.27-7.92) were more likely to be hospitalized with FIV.

Table 6- Simple and Multiple regression models for FIV

Variables	Categories	Simple Logistic Regression			Multiple Logistic Regression		
		OR[1]	95% CI[1]	p-value	OR[1]	95% CI[1]	p-value
Breed n=345	Purebred	—	—		—	—	
	Domestic	6.89	2.00, 43.3	0.009	4.70	1.30, 30.2	0.042
Gender n=345	Female	—	—		—	—	
	Male	1.88	1.18, 3.03	0.009	1.85	1.08, 3.19	0.026
Neuter n=345	No	—	—				
	Yes	1.00	0.62, 1.62	>0.9			
Number of animals n=345	Alone	—	—				
	≥1 Animal	0.95	0.60, 1.50	0.8			
Lifestyle n=331	Indoor	—	—		—	—	
	Outdoor	2.80	1.73, 4.59	<0.001	2.80	1.66, 4.80	<0.001
Vaccination Status n=306	Up To Date	—	—				
	Not Up to Date	0.96	0.52, 1.87	>0.9			
Concomitant Disorders/ Diseases n=345	No	—	—		—	—	
	Yes	2.68	1.57, 4.76	<0.001	2.72	1.45, 5.30	0.002
Age Groups (Years) n=344	< 2	—	—		—	—	
	≥ 2 & < 10	4.86	2.37, 11.0	<0.001	3.80	1.71, 9.41	0.002
	≥ 10	3.94	1.82, 9.31	<0.001	3.03	1.27, 7.92	0.017
	[1] OR = Odds Ratio, CI = Confidence Interval						

3.2.2. FeLV

During the 7 years of this study, 119 cats were diagnosed with FeLV. As previously established the controls for FeLV needed to be negative when tested for FIV and FeLV infection. Table 7 is a descriptive summary of the FeLV infected cats and their controls.

Table 7- Descriptive analysis of FeLV

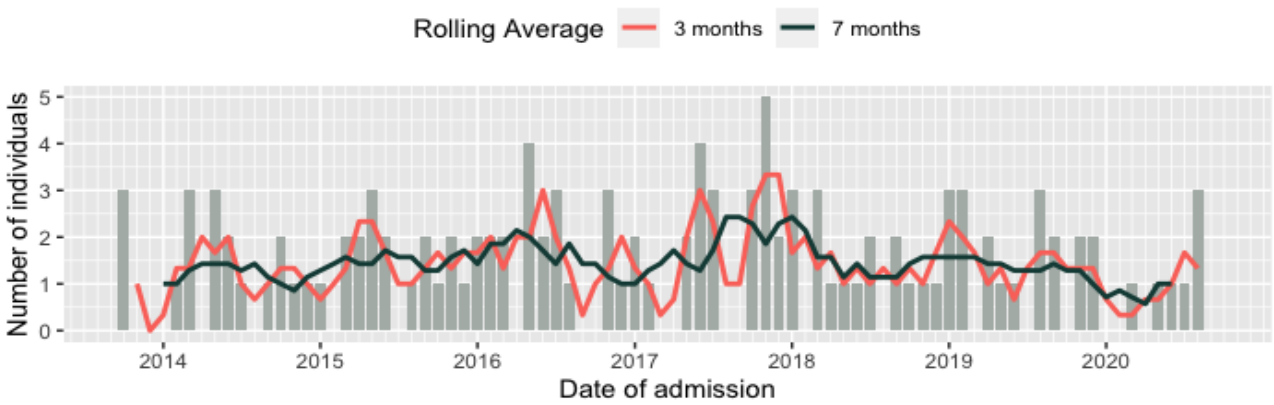
Variables	Categories	Case, n = 119 Cats (%)	Control, n = 238 Cats (%)
Breed	Purebred	3 (2.5%)	27 (11%)
	Domestic	116 (97%)	211 (89%)
Gender	Female	56 (47%)	110 (46%)
	Male	63 (53%)	128 (54%)
Neuter	No	51 (43%)	80 (34%)
	Yes	68 (57%)	158 (66%)
Number of Animals	Alone	54 (45%)	90 (38%)
	≥1 Animal	65 (55%)	148 (62%)
Lifestyle	Indoor	53 (52%)	140 (59%)
	Outdoor	49 (48%)	98 (41%)
	Unknown	17	0
Vaccination Status	Not Up To Date	57 (68%)	190 (80%)
	Up To Date	27 (32%)	48 (20%)
	Unknown	35	0
Concomitant Disorders/ Diseases	No	28 (24%)	88 (37%)
	Yes	91 (76%)	150 (63%)
Age Groups (Years)	< 2	22 (19%)	68 (29%)
	≥ 2 & < 10	83 (70%)	104 (44%)
	≥ 10	13 (11%)	66 (28%)
	Unknown	1	0
Survival at Discharge	% [$CI_{95\%}$]	57.9 [49.0-66.5]	-
Length of hospitalization (Days)	Median [Min, Max]	2.00 [1.00-10.00]	-
Number of hospitalizations	Median [Min, Max]	1.00 [1.00-4.00]	-

The distribution of FeLV cases throughout the years are presented in Graphic 15. There was at least one animal hospitalized with FeLV in the majority of each month as is shown in the graphic. The number of cases per month varied between 0 and 5 animals.

The temporal distribution of FeLV hospitalized cats demonstrated in Graphic 15 showed that every time the rolling average of 3-month decreased and crossed the 7 months rolling average, the number of FeLV infected cats decreased. In contrast, when the rolling average of 7-month increased and crossed the 3 months rolling average, the number of cats hospitalized with FeLV increased .

Another finding exhibited in Graphic 15 was that in the last 2 years the numbers of FeLV cases were slowing down. Both rolling averages had their pick at the end of 2017.

Graphic 15- Temporal Distribution of FeLV hospitalized cats



Regarding the statistical analysis, both simple and multiple regressions were assessed in order to investigate possible risk factors for FeLV.

When using the simple model, in Table 8, it showed a significant association for FeLV hospitalized cats with domestic, intact, living alone, vaccinations up to date, concomitant disorders/ diseases, and ages between ≥ 2 & < 10 and ≥ 10, traits (p-value ≤ 0.20).

Similarly, in Table 8, the multiple regression model showed that some but not all variables were significant (p-value <0.05). In this case, living alone, having vaccines up to date and being 10 years or older were not significant traits (p-value > 0.05).

There was a significant association showed in Table 8 with being domestic (OR=4.22; $CI_{95\%}$=1.37-18.58), intact (OR=1.90; $CI_{95\%}$=1.05-3.56), with concomitant disorders and diseases (OR=2.44; $CI_{95\%}$=1.33-4.60), between the ages of ≥ 2 & < 10 years (OR= 2.01; $CI_{95\%}$=1.04-3.99) and being admitted at the BICU for FeLV.

Table 8- Simple and Multiple regression models for FeLV

Variables	Categories	Simple Logistic Regression			Multiple Logistic Regression		
		OR[1]	95% CI[1]	p-value	OR[1]	95% CI[1]	p-value
Breed n=357	Purebred	—	—		—	—	
	Domestic	4.95	1.70, 21.0	0.010	4.22	1.37, 18.58	0.025
Gender n=357	Female	—	—				
	Male	0.97	0.62, 1.50	0.90			
Neuter n=357	Yes	—	—		—	—	
	No	1.48	0.94, 2.33	0.088	1.90	1.05, 3.46	0.034
Number of Animals n=357	≥1 Animal	—	—		—	—	
	Alone	1.37	0.87, 2.13	0.20	1.29	0.75, 2.21	0.4
Lifestyle n=340	Indoor	—	—				
	Outdoor	1.32	0.83, 2.11	0.24			
Vaccination Status n=322	Not Up To Date	—	—		—	—	
	Up To Date	1.87	1.07, 3.26	0.027	1.73	0.95, 3.14	0.071
Concomitant Disorders/ Diseases n=357	No	—	—		—	—	
	Yes	1.91	1.17, 3.18	0.011	2.44	1.33, 4.60	0.005
Age Groups (Years) n=356	≤ 2	—	—		—	—	
	≥ 2 & < 10	2.47	1.43, 4.39	0.002	2.01	1.04, 3.99	0.040
	≥ 10	0.61	0.28, 1.29	0.2	0.46	0.17, 1.16	0.11
	[1] OR = Odds Ratio, CI = Confidence Interval						

3.2.3. URTD

Between October 2013 and September 2020, 88 cats were diagnosed with infectious URTD. To assess the controls of URTD the patients needed to not show any clinical signs of the disease. Table 9 shows a descriptive analysis of these cases and their controls.

Table 9- Descriptive analysis of URTD

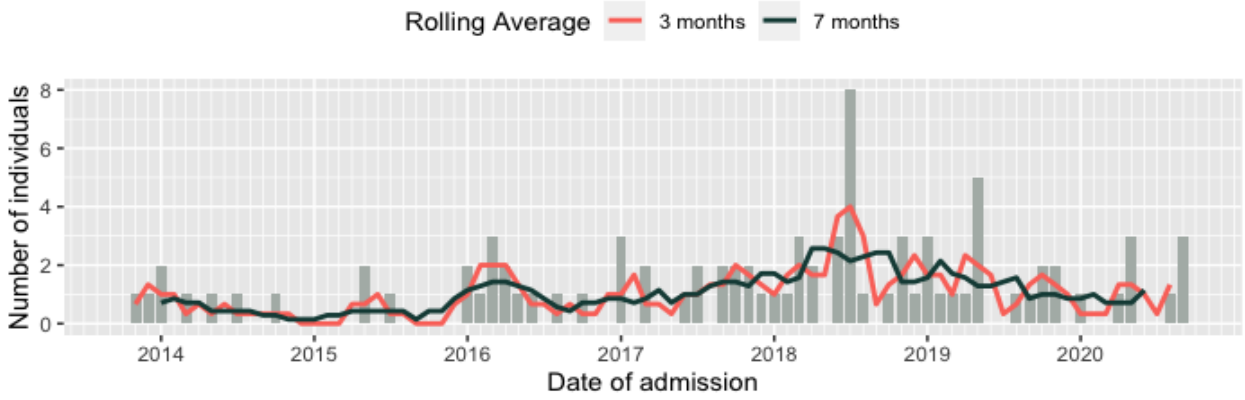
Variables	Categories	Case, n = 88 Cats (%)	Control, n = 176 Cats (%)
Breed	Purebred	11 (12%)	10 (5.7%)
	Domestic	77 (88%)	166 (94%)
Gender	Female	42 (48%)	81 (46%)
	Male	46 (52%)	95 (54%)
Neuter	No	46 (52%)	44 (25%)
	Yes	42 (48%)	132 (75%)
Number of Animals	Alone	22 (25%)	73 (41%)
	≥1 Animal	66 (75%)	103 (59%)
Lifestyle	Indoor	46 (55%)	101 (57%)
	Outdoor	37 (45%)	75 (43%)
	Unknown	5	0
Vaccination Status	Not Up To Date	57 (81%)	144 (82%)
	Up to Date	13 (19%)	32 (18%)
	Unknown	18	0
Concomitant Disorders/ Diseases	No	27 (31%)	39 (22%)
	Yes	61 (69%)	137 (78%)
Age Groups (Years)	< 2	29 (34%)	37 (21%)
	≥ 2 & < 10	35 (41%)	75 (43%)
	≥ 10	22 (26%)	64 (36%)
	Unknown	2	0
Survival at Discharge	% [$CI_{95\%}$]	76.1 [66.3-83.8]	-
Length of hospitalization (Days)	Median [Min, Max]	3.00 [1.00-14.00]	-
Number of hospitalizations	Median [Min, Max]	1.00 [1.00-3.00]	-

Since the beginning of 2016, the temporal distribution exhibited in graphic 16, showed that most months had at least one animal hospitalized with URTD. The graphic also showed that the number of cats admitted at the BICU varied between 0 and 8 cats per month.

Based on the temporal distribution of URTD hospitalized cats, demonstrated in the Graphic 16, every time the rolling average of 3-month moved down and crossed the 7 months rolling average, the number of infected cases of URTD decreased. In opposition, when the rolling average of 7-month moved up and crossed the 3 months rolling average, the numbers of URTD infected cats increased.

A trend of rising cases started in the first semester of 2017 and had its peak mid 2018, from where it started to decrease again. Another visible trend was that most cases occurred at the end of Fall, and at the beginning of Winter.

Graphic 16- Temporal Distribution of URTD hospitalized cats



Concerning the statistical analysis both simple and multiple regressions were assessed to investigate possible risk factors for URTD.

Results in the Table 10 showed that, for the simple logistic model, purebred cats, intact cats, living with one or more animals, without concomitant disorders/diseases and with less than 2 years were more statistically significant of being hospitalized with URTD (p-value ≤ 0.20).

When all the significant variables in the simple model were added in the multiple regression model, as depictured in Table 10, it showed that purebred cats, cats without concomitant disorders/diseases and cats with less than 2 years cease to be significant (p-value > 0.05).

However, the odds ratio for being hospitalized with URTD for intact cats was 3.03 times higher with a 95% CI of 1.60 to 5.82 than for neutered cats. Also, the odds ratio of being hospitalized with URTD while living with more than 1 animal was 2.46 times higher with a 95% CI of 1.35 to 4.62 than cats that live with no other animal. Both were statistically significant (p-value < 0.05) and are showed in Table 10.

Table 10- Simple and Multiple regression models for URTD

Variables	Categories	Simple Logistic Regression			Multiple Logistic Regression		
		OR[1]	95% CI[1]	p-value	OR[1]	95% CI[1]	p-value
Breed n=264	Domestic	—	—		—	—	
	Purebred	2.37	0.96, 5.92	0.059	1.81	0.69, 4.79	0.2
Gender n=264	Female	—	—				
	Male	0.93	0.56, 1.56	0.8			
Neuter n=264	Yes	—	—		—	—	
	No	3.29	1.92, 5.67	<0.001	3.03	1.60, 5.82	<0.001
Number of Animals n=264	Alone	—	—		—	—	
	≥1 Animal	2.13	1.22, 3.81	0.009	2.46	1.35, 4.62	0.004
Lifestyle n=259	Indoor	—	—				
	Outdoor	1.08	0.64, 1.83	0.8			
Vaccination Status n=264	Up To Date	—	—				
	Not Up To Date	0.97	0.49, 2.05	>0.9			
Concomitant Disorders/ Diseases n=264	Yes	—	—		—	—	
	No	1.55	0.87, 2.76	0.13	1.18	0.61, 2.25	0.6
Age Groups (Years) n= 262	≥ 10	—	—		—	—	
	< 2	2.28	1.15, 4.57	0.019	1.24	0.54, 2.85	0.6
	≥ 2 & < 10	1.36	0.73, 2.57	0.3			
	[1]OR = Odds Ratio, CI = Confidence Interval						

3.2.4. Panleukopenia

The BICU facility hospitalized 64 cats with panleukopenia in the last 7 years. As previously stated, only cats without clinical signs of panleukopenia and without leukopenia were included to be controls for the population of panleukopenia infected cats. Table 11 shows a summary of a descriptive analysis of panleukopenia cases and their controls.

Table 11- Descriptive analysis of Panleukopenia

Variables	Categories	Case, n = 64 Cats (%)	Control, n = 128 Cats (%)
Breed	Purebred	4 (6.2%)	9 (7.0%)
	Domestic	60 (94%)	119 (93%)
Gender	Female	29 (45%)	56 (44%)
	Male	35 (55%)	72 (56%)
Neuter	No	37 (58%)	42 (33%)
	Yes	27 (42%)	86 (67%)
Number of Animals	Alone	17 (27%)	55 (43%)
	≥1 Animal	47 (73%)	73 (57%)
Lifestyle	Indoor	38 (61%)	79 (62%)
	Outdoor	24 (39%)	49 (38%)
	Unknown	2	0
Vaccination Status	Not Up To Date	59 (97%)	71 (55%)
	Up To Date	2 (3.3%)	57 (45%)
	Unknown	3	0
Concomitant Disorders	No	43 (67%)	32 (25%)
	Yes	21 (33%)	96 (75%)
Age Groups (Years)	< 2	48 (75%)	30 (23%)
	≥ 2 & < 10	15 (23%)	57 (45%)
	≥ 10	1 (1.6%)	41 (32%)
Survival at Discharge	% [$CI_{95\%}$]	73.4 [61.5-82.7]	-
Length of hospitalization (Days)	Median [Min, Max]	6.00 [1.00-15.00]	-
Number of hospitalizations	Median [Min, Max]	1.00 [1.00-4.00]	-

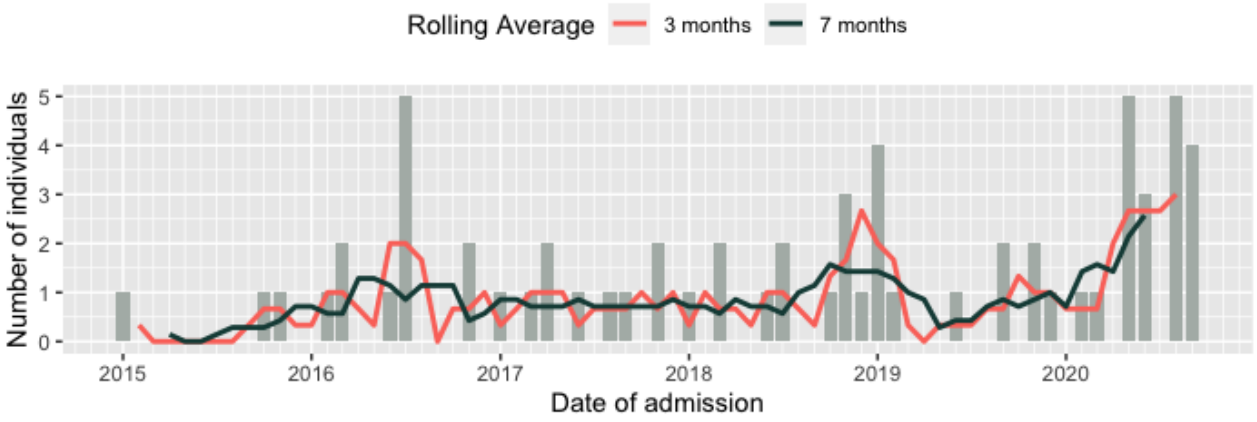
The distribution of panleukopenia cases throughout the years is shown in Graphic 17. It could be seen in the Graphic 17 that the distribution of panleukopenia cases were pretty irregular throughout the years. It was also shown that the number of hospitalized cats with panleukopenia varied between 0 and 5 cats per month.

Every time the rolling average of 3-month moved down and crossed the 7 months rolling average, as shown in the Graphic 17, the number of infected cases of panleukopenia

decreased. In contrast, when the rolling average of 7-month surpassed and crossed the 3 months rolling average, the numbers of panleukopenia infected cats increased.

While looking at Graphic 17, the major observation presented was that 2020 showed a rise of panleukopenia cases compared with the last years.

Graphic 17- Temporal Distribution of Panleukopenia hospitalized cats



Regarding the statistical analysis to identify risk factors for being hospitalized with panleukopenia both simple and multiple regression models were assessed.

When using the simple model, depicture in Table 12, it showed that intact cats, living with one or more animals, cats without up to date vaccines, cats without concomitant disorders/diseases and cats between the ages of < 2 and ≥ 2 & < 10 years, were all significant in the simple model (p-value ≤ 0.20) for being admitted at the BICU with panleukopenia.

When all the significant variables from the simple model were added in the multiple regression model, intact cats and cats living with one or more animals were not significant (p-value > 0.5).

Nonetheless, Table 12 showed that there was a significant association with absence of vaccination (OR=50.5; $CI_{95\%}$=11.83-373.09), not having concomitant disorders (OR=7.31; $CI_{95\%}$=2.77-21.01), ages between < 2 (OR=85.0; $CI_{95\%}$=13.11-1751.11) and ≥ 2 & < 10 (OR=10.7; $CI_{95\%}$=1.73-211.34) and being hospitalized with panleukopenia. All variables mentioned above were statistically relevant (p-value < 0.05).

Table 12- Simple and Multiple regression models for Panleukopenia

Variables	Categories	Simple Logistic Regression			Multiple Logistic Regression		
		OR[1]	95% CI[1]	p-value	OR[1]	95% CI[1]	p-value
Breed n=192	Purebred	—	—				
	Domestic	1.13	0.35, 4.32	0.8			
Gender n=192	Female	—	—				
	Male	0.94	0.51, 1.72	0.8			
Neuter n=192	Yes	—	—		—	—	
	No	2.81	1.52, 5.25	0.001	0.54	0.17, 1.57	0.3
Number of Animals n=192	Alone	—	—		—	—	
	≥1 Animal	2.08	1.10, 4.09	0.028	2.17	0.81, 6.10	0.13
Lifestyle n=190	Indoor	—	—				
	Outdoor	1.02	0.54, 1.89	>0.9			
Vaccination Status n=189	Up To Date	—	—		—	—	
	Not Up To Date	23.7	6.97, 148	<0.001	50.5	11.83, 373.09	<0.001
Concomitant Disorders/ Diseases n=192	Yes	—	—		—	—	
	No	6.14	3.22, 12.1	<0.001	7.31	2.77, 21.01	<0.001
Age Groups (Years) n=192	≥ 10	—	—		—	—	
	< 2	65.6	13.16, 1193.72	<0.001	85.0	13.11, 1751.11	<0.001
	≥ 2 & < 10	10.8	2.06, 198.96	0.024	10.7	1.73, 211.34	0.034
	[1]OR = Odds Ratio, CI = Confidence Interval						

4. Discussion

As previously shown in the results, various behaviors and risk factors were identified for contracting an infectious disease and being hospitalized in the BICU facility. One major problem observed throughout this study was the somewhat lack of information in some variables. This lack of information can be attributed to the owners of the patients. Firstly, they do not remember specific details, and secondly, they do not give some of the information important for an animal's history. Another liability are the veterinarians, since they can forget important aspects of the patient's anamnesis.

4.1. General characterization of the infected population

Over the seven years of this facility, 788 cats were admitted with a confirmed or suspected infectious disease. The majority of these cats had indeed an infectious disease (n=405, 51.4%), which showed that the veterinarians working in the VTH were alert to specific signs of infectious diseases and executed a good anamnesis of the patients admitted. However, 320 hospitalized cats (40.6%) remained suspect of an infectious disease. This can be explained for three reasons. Firstly, because of the owners' shortage of money, they find a definitive diagnosis too expensive. Secondly, the lack of a definitive diagnosis method; until recently, it was hard to diagnose a cat with FIP (Sykes 2013a), and although there has been some improvement, there is still a long road ahead. Thirdly, cats that tested negative, but the clinical presentation still remained highly suspicious of an infectious disease were still considered to be suspects of an infectious disease (e.g., false negatives are common in infectious URTD testing, not only because cats with chronic infections can shed at low levels, but also it can be a result of viral RNA degradation during transportation to the laboratory (Sykes 2013d)). Finally, only 63 cats (8.0%) were non-infectious. The numbers of non-infectious cats admitted are largely explained because of cats without FIV/FeLV testing and vaccination. When the cats are tested and receive a negative test, they went back to the general hospital's facility.

Almost all hospitalized cats (n=370, 91.4%) were domestic, and only 35 cats were purebred. This goes accordingly with The People's Dispensary for Sick Animals (PDSA 2020), which stated that cat owners are more likely to get their pets on a rescue center or rehoming center. This means less cats from certified breeders, so fewer purebred cats. Although this report is from the UK's population, it can be assumed that Portugal has some similarities.

Certain infectious diseases have a predisposition for purebred cats, such as coronavirus infection (Sykes 2013a). However, in this case, by having a larger number of domestic cats in this population, it was normal to see that they would contract more infectious diseases than purebred cats.

Regarding gender, the population of male cats was slightly larger (n=230, 56.8%) than female cats (n=175, 43.2%). This result is not surprising, because male cats have more behavioral risks, for example, fighting between male cats can lead to an infectious disease such as FIV (Sellon and Hartmann 2012).

Considering the neuter status, a large percentage of cats were neutered (n=226, 55.8%). From the neuter pool, 141 cats were male (34.8%), and 85 were female (21%). Which means there were more intact female cats (n=90, 22.2%) than intact male cats (n=89, 22.0%).

As Evermann et al. stated (2012), the epidemiology of infectious diseases depends on the host, the environment and the microorganism itself. While there are many host factors, age and immune status are considered to be the most critical (Evermann et al. 2012).

The median age of infected, hospitalized cats was 4 years old, ranging from 1 month to 19 years. In addition, the distribution in age groups revealed that cats between 2 and 9 years were the most common to be hospitalized (n=202, 50.4%). Followed then by cats with less than 2 years (n=121, 30.2%) and finally 10-year-old cats or older (n=78, 19.4%). These results can be clarified through the most frequently diagnosed infectious diseases in the BICU. Retrovirus infection was the most frequent disease diagnosed in cats and is usually found between 2 and 9 years (Sykes 2013b). The reason that cats with less than 2 years were so represented is because of diseases such as URTD or panleukopenia which affect largely younger cats (Greene 2012; Sykes 2014).

Age is deeply connected with the development and the decline of the immune system. Younger animals do not have a proper functional immune system, and older animals have a decline in their immune system that may make them more prone to an infectious disease (Schultz et al. 2010).

As mentioned earlier, the epidemiology of infectious diseases also depends on the environment of the host (Evermann et al. 2012). Consequently, the lifestyle of a cat is extremely important to know because it can be a possible risk factor for an infectious disease.

Concerning the lifestyle of the hospitalized cats, 194 lived indoors (47.9%), and 172 cats had access or lived in the outdoors (42.5%). Comparing with the previous study in the BICU, created by Machado (2016) there was an increase in indoor cats from 34.5% to 47.9% and a decrease in outdoor cats from 44.2% to 34.5%. Nowadays, indoor cats seem to be a tendency accordingly to the PDSA (2020). However, the main reason cats are living only indoors is because their owners think it is unsafe for cats to be outside (PDSA 2020). Nevertheless, cats living strictly indoor also have risks (e.g., living in a multicat house indoors may be a source of stress and can lead to other diseases).

It is relevant to address that 39 cats (9.6%) had an unknown lifestyle. This lack of information in the animal's history is a limiting factor.

Regarding the number of animals living together, most cats lived with one or more animals (n=267, 65.9%) and only 138 cats (34.1%) lived without other animals. Living with multiple animals can be a source of feline stress. Stress can suppress the functionality of the immune system, leaving cats more susceptible to infectious diseases or reactivation of the disease (e.g., feline herpesvirus) (Clark 2016).

Furthermore, living in a densely populated home can lead to high viral excretion from other animals, exposing the non-infected cats to infectious diseases (Evermann et al. 2012).

A vaccination protocol can protect the cat from multiple infectious diseases (Day et al. 2016). Consequently, it was not surprising seeing that from the 405 infected cats admitted at the BICU, 239 cats (59.0%) did not have their vaccinations up to date, accordingly with the most recent guidelines (Day et al. 2016). Only 78 cats (19.3%) had their vaccines up to date.

Similarly to the lifestyle variable, there was a lack of information in this variable: 88 cats (21.7%) did not have any data about their vaccination status, which is troubling when dealing with patients with an infectious disease.

A large majority of hospitalized cats were admitted by first opinion appointments (n=285, 70.4%). Only 81 cats (20.0%) were referrals.

As for concomitant disorders and diseases, 272 cats (67.2%) had a concomitant disorder/disease while having an infectious disease that made them stay hospitalized. This number was not surprising because of two major reasons. Firstly, when a cat contracts an infectious disease, its immune system is suppressed, which can lead to co-infections and increase the severity of the disease (e.g., the outcome of FeLV infection is extremely variable and depends on innumerous factors such as co-infectious (Sykes and Hartmann 2013)). Secondly, while having a disease, a cat's immune system can be suppressed, being more susceptible to an infectious disease.

Over the 7 years of the BICU, the most frequent disorders/diseases found in the infected, hospitalized cats were neoplasia (e.g., lymphoma), exterior/interior parasites (e.g., fleas), urinary disorders (e.g., chronic renal disease, feline idiopathic cystitis) and anemia.

Cats may have multiple infectious diseases at the same time (Sykes and Hartmann 2013; Barrs 2019). For example, a cat can have both FIV and FeLV, or FeLV can lead do opportunistic infections such as upper respiratory tract infections, feline infectious peritonitis and dermatophytosis (Sykes 2013b; Sykes and Hartmann 2013).

However, only 38 cats (9.4%) had a concurrent infectious disease. While the majority of hospitalized cats only had one infectious disease (n=367, 90.6%). The most common concomitant infectious disease found was URTD.

Considering the hospitalization period, the median was 3 days, ranging from 1 to 21 days. Looking at the distribution of the hospitalization length, a large number of cats was hospitalized for only 1 day (n=103, 25.4%). The reason for this occurrence was that a number of cats were waiting for the results of FIV/FeLV or they were waiting for an exam. Once the results came back, the cats could return home if they were healthy.

The median number of hospitalizations per infected cat was 1 day. Ranging from one hospitalization through 7, the large majority of cats were only hospitalized once (n=349, 86.2%), which exhibits the efficacy of the intervention at the BICU.

As for the outcome of the patients, 282 (69.6%, $CI_{95\%}$=64.9-73.9) hospitalized cats were discharged. This means that most cats were healed or were good enough to come home, which represents yet again the treatment efficacy in the BICU. Only 85 cats were euthanized (21.0%, $CI_{95\%}$=17.3-25.1). The number of euthanized cats not only represented critical cases but also demonstrated insufficient funds of the owners. Another possible explanation is that the owner thinks the animal will not have a good quality of life, because they would be living with a chronic infectious disease, such as FIV or FeLV (Sellon and Hartmann 2012; Sykes 2013b; Sykes and Hartmann 2013). Or even because the prognosis of certain infectious diseases are so poor, for example, FIP (Kennedy 2020).

Although the most common follow-up for the hospitalized cat was unknown (n=70, 24.8%), it is significant to recall that a number of cats were referenced to the VHT. Therefore, it is normal that the animal went back to the original clinic/hospital when it is treated. 66 cats (24.6%) had a chronic follow-up because a lot of them were prior diagnosed with chronic infectious diseases. Nevertheless, 56 cats (19.8%) were better or healthy, which were great results for an infectious disease prognosis.

Retrovirus infection was the most diagnosed infectious disease found in this study (n=214, 48.3%). This result was not surprising because both FIV and FeLV are among the most common infectious diseases found in cats (Little et al. 2020). Nonetheless, URTD came at second place with 88 cats (19.9%), which again it was not surprising because multiple pathogens can contribute to the widespread of this disease (Sykes 2014). With less occurrence, but still extremely relevant was panleukopenia (n=64, 14.4%).

Between October 2013 and January 2016, the time period of Machado's (2016) study, there was only 3 cases of MDR, and in September 2020, there were more 19 cases. MDR percentage went from 2.7 to 5%, which goes accordingly to the emergence of antibacterial

resistance (Morris and Cerceo 2020). Additionally, the coronavirus cases went from 10 (8.8%) to 44 (9.9%), which is worrying because some of those are FIP cases, and there is still no legal treatment (Kennedy 2020).

Regarding the type of tests performed to reach an etiological diagnosis they corresponded to what the literature suggested. Using cultures for bacterial and fungal agents. Performing PCR for viral detection and ELISA for retrovirus. The low numbers of pyrosequencing PCR to identify the two mutations (M1058L and S1060A) of FIP (n=7, 16%), can be clarified into 2 reasons. Firstly, because this method is recently new. Secondly, some owners did not agreed to pay for such an expensive method.

4.2. FIV

Regarding the variable breed, in this study, domestic cats were approximately 5 times more likely to be hospitalized with FIV than purebred cats (OR=4.70; $CI_{95\%}$=1.30-30.2; p-value<0.05). This result goes accordingly with what Sykes (2013b) stated: that domestic cats can be a risk factor. A possible explanation for this is that domestic cats are more easily found in the streets or shelters, which can lead to more interaction between infected cats.

Agreeing with multiple studies (Gleich et al. 2009; Bande et al. 2012; Sykes 2013b; Biezus et al. 2019; Little et al. 2020), this study found that male cats were at a higher risk of contracting FIV and being hospitalized (p-value <0.05). FIV is shed in the saliva and one of the most common ways of transmission is through bite wounds (Sykes 2013b; Little et al. 2020). Therefore, this association is easily explained because male cats have a higher likelihood of encountering infected cats and being prone to aggression and territorial fights.

The association between intact cats and FIV positivity, mainly intact male cats, has been demonstrated in multiple studies (Goldkamp et al. 2008; Little et al. 2009). The reason why this happens is because intact cats are more prone to fights. Neutered cats are more likely to be kept indoors and have a lower risk of infection (Little et al. 2009; Bande et al. 2012). However, in this study, no association between being intact and being hospitalized with FIV was found (p-value >0.9). Although less common, there are other studies who agree that it is the gender of the cat rather the effect of the neuter status that influences the FIV status (Murray et al. 2009; Biezus et al. 2019).

Considering the number of animals living together, cohabitation with other animals was not relevant to being admitted at the BICU with FIV (p-value= 0.8). Other studies have stated the same (Gleich et al. 2009; Bande et al. 2012; Biezus et al. 2019; Little et al. 2020). A study where 130 uninfected cats were living with 8 FIV infected cats showed that there was no recognized transmission in several years (Litster 2014).

The odds ratio of cats with access or living outdoors were approximately 3 times higher than cats living indoors for being hospitalized with FIV (OR=2.80; $CI_{95\%}$=1.66-4.80; p-value<0.001). Little et al. (2020) stated that outdoor access is a risk factor for FIV. Outdoor access is a possible risk factor because free-roaming cats are more likely to encounter FIV infected cats (Bande et al. 2012).

Although there is a FIV vaccine, the subtypes available do no correspond to the existing subtypes in Europe (Little et al. 2020) and it is not considered a core vaccine (Day et al. 2016). Having said that, a cat can still have their vaccines up to date and not be vaccinated with FIV. Nevertheless, an association between not having vaccines up to date and being infected with FIV can still be relevant. However, in this study no association was found (p-value >0.9).

Cats with concomitant disorders and diseases were 2.72 times more likely to be admitted at the BICU with FIV, than cats without these disorders/diseases (OR=2.72; $CI_{95\%}$=1.45-5-30; p-value<0.05). FIV is an immunosuppressive disease, so it is presumable that FIV infected cats become predisposed to secondary and opportunistic infections (Sykes 2013b; Little et al. 2020). Another study showed a similar association with sick cats being 2 times more likely to test positive for FIV, although in this case they did not distinguish the disorders, they just called them sick (Bande et al. 2012). Still, it is important to remark that the health of the cat at the time of infection and the time after infection can be unknown, so it is difficult to assume whether the cat's health is a cause or an effect of FIV infection (Murray et al. 2009).

Both Sykes (2013b) and Little et al. (2020) stated that the mean age at diagnosis is around 6 to 8 years. The FIV infected, hospitalized cats had a mean age of 7.43$\pm$ 4.56 years, which complies with the literature. Their median age was 7 years, ranging from 6 months to 19 years. Being hospitalized with FIV was 3.80 and 3.03 times higher in cats between the ages of ≥ 2 & < 10 and ≥ 10 years, respectively, compared to cats with less than 2 years (p-value < 0.05). This result was consistent with previous observations that an increase in age leads to susceptibility of contracting FIV (Bande et al. 2012; Biezus et al. 2019; Little et al. 2020). The reason for this increase in age can be explained because FIV positive cats can remain asymptomatic for many years, and only express clinical signs later in life being diagnosed at that stage (Biezus et al. 2019).

Taking into consideration the hospitalization period for FIV infected cats, the median hospitalization period was 2 days ranging from 1 to 10 days. Comparing with the total of infected hospitalized cats, FIV cats were less time hospitalized.

Considering the number of hospitalizations, the median number was 1, ranging from 1 to 5 hospitalizations. As previously mentioned, FIV leads to secondary and opportunistic infections, so it is normal that cats would relapse and needed to be admitted again.

The survival rate at discharge was 70.4% ($CI_{95\%}$=61.5-78.0) , but it is important to clarify that FIV is an infectious chronic disease, so this result means that these cats were stable enough to go home, even though they were not cured. The survival rate at discharge for all infected animals was 69.6% ($CI_{95\%}$=64.9-73.9). This comparison just shows that FIV is not a severe disease and with the proper care, cats can live for many years (Little et al. 2020).

4.3. FeLV

While a FeLV infection typically does not have a breed predisposition, in this study, domestic cats were 4.22 times more likely to get hospitalized with FeLV than purebred cats (OR=4.22; $CI_{95\%}$=1.37-18.58; p-value<0.05). According to Hartmann and Hofmann-Lehmann (2020) FeLV is commonly found in domestic cats, rather than purebred cats. The reason why this happens is because purebreds tend to be kept indoors and there is more awareness from the owners to test their animals. However, studies assessed by Bande et al. (2012) and Biezus et al. (2019) did not find any association.

Regarding gender, no association was found for being admitted at the BICU with FeLV (p-value=0.9). Correspondingly to older studies, FeLV infection was found to be approximately equal between genders (Hartmann and Hofmann-Lehmann 2020). In the present study, the same occurred by having 53% males versus 47% females FeLV positive. The explanation for this is that FeLV transmission frequently occurs between infected queens and kittens, and among cats living in close contact, so the infection would happen regardless of gender (Gleich et al. 2009; Hartmann and Hofmann-Lehmann 2020). However, in more recent studies, male cats appear to be more at risk of contracting the disease (Gleich et al. 2009; Bande et al. 2012; Biezus et al. 2019; Hartmann and Hofmann-Lehmann 2020).

Previously underrated, aggressive behavior in male cats seems to be more important than expected, which also funds that intact cats are more likely to get infected (Gleich et al. 2009; Hartmann and Hofmann-Lehmann 2020). According to the previously mentioned statement, this study found that intact cats were 1.90 times more prone to get hospitalized with FeLV than neutered cats (OR=1.90; $CI_{95\%}$=1.05-3.46; p-value<0.05). However, there is no consensus about the neuter status, and researchers such as Levy et al. (2006) and Muchaamba et al. (2014) indicated that intact cats, especially males, are more at risk of infection. Others such as Bande et al. (2012) and Biezus et al. (2019) did not find any association. This could be because of the differences between the studied populations; while some studies are about owned cats, others are made at shelters or with stray cats, which leads to different results.

Surprisingly, in the simple model, cats who lived without other animals were more likely to get hospitalized with FeLV than cats living with multiple animals (OR=1.37; $CI_{95\%}$=0.87-2.13; p-value ≤0.2). However, when added all the significant variables to the multiple model the

number of cohabitants ceased to be meaningful (p-value=0.4). Possible explanations could be that most of the controls for FeLV were also living with multiple animals (n=148, 62%), which could disturb the results. Another conceivable reason is that this variable did not specify which animal the cat lives with, so if the number of cohabitants were redesigned to just consider cats living with other cats maybe the results would have been different. Other possible reason stated by Gleich et al. (2009) was that the increasing awareness of this disease makes the owners more susceptible to testing and being more careful when adding a new cat to a household of multiple animals. The result from the present study was unexpected because the literature and studies have stated that FeLV is a "social" disease, meaning that cats need to be in close contact with each other for transmission to happen, so living alone does not correspond to the previous standards (Gleich et al. 2009; Hartmann and Hofmann-Lehmann 2020).

Outdoor access or living was not statistically significant in this study (p-value=0.24). As Hartmann and Hofmann-Lehmann (2020) stated, cats who have access to the outdoors have a higher prevalence of FeLV infection. However, multiple studies such as Gleich et al. (2009), Bande et al. (2012) and Biezus et al. (2019) had the same result as the present one. This outcome could be for three reasons. Firstly, there was no information about the lifestyle of 17 FeLV infected cats, so this could have altered the results. Secondly, living indoors does not mean that there is no risk, because multiple cats can live together and have the same effect for transmitting the disease. Thirdly, it cannot be assumed where the cats lived before the owner received them.

Although this study had a lot more FeLV infected cats without up to date vaccines (n=57, 68%), another unexpected finding occurred. In the simple model, vaccinated cats were 1.87 times more likely to get hospitalized with FeLV than cats who had not their vaccination up to date (OR=1.87; $CI_{95\%}$=1.07-3.26; p-value <0.05). However, in the multiple model no association was found (p-value=0.07). This result cannot be interpreted literally, because according to the VGG, FeLV vaccines are not considered core (Day et al. 2016). Thus, this variable did not distinguish cats vaccinated for FeLV from those that are not vaccinated for FeLV. Therefore, the possible risk factor that non-FeLV vaccinated cats were more likely to be infected, which is stated by Hartmann and Hofmann-Lehmann (2020), cannot be concluded in the present study.

Cats with concomitant disorders and diseases were 2.44 times more likely to be hospitalized with FeLV than cats without concomitant disorders/diseases (OR=2.44; $CI_{95\%}$=1.33-4.60; p-value<0.05). This association is plausible because like FIV, FeLV is an immunosuppressive disease, so these cats are predisposed to opportunistic and secondary infectious (Bande et al. 2012; Sykes and Hartmann 2013; Hartmann and Hofmann-Lehmann

2020). Similar to FIV, it is difficult to assume whether the cat's health is a cause or effect of FeLV infection.

FeLV is considered to be age dependent, which means that as cats mature they become more resistant to the infection. Thus, it is more likely to encounter younger cats progressively infected with FeLV (Hartmann and Hofmann-Lehmann 2020). However, in more recent studies adult cats were more likely to be infected with FeLV (Hartmann and Hofmann-Lehmann 2020). A possible explanation that Hartmann and Hofmann-Lehmann (2020) stated is that because of an increase in awareness the owners test their cats more frequently, therefore the cat is provided with medical care earlier leading to a longer life. The literature stated that the median age of infection is around 3 years (Sykes and Hartmann 2013). Similarly the median age of FeLV positive cats at the BICU was 4 years, ranging from 4 months to 17 years. Comparing FIV and FeLV ages, it was shown that FeLV infection affected relatively younger animals than FIV infection did, this was also stated in the literature (Sykes and Hartmann 2013). In the multiple model, cats between ≥ 2 & < 10 years were 2.01 times more prone to get hospitalized with FeLV than less than 2-years-old cats (OR=2.01; $CI_{95\%}$=1.04-3.99; p-value <0.05). In addition to agreeing with literature previously exposed, this result also agreed with different studies made by Bande et al. (2012) and Chhetri et al. (2015) in which both stated that FeLV infection was increased in younger cats, compared to FIV infection.

Considering the hospitalization period for FeLV infected cats, their median hospitalization period was 2 days, ranging from 1 to 10 days. Like FIV, FeLV hospitalization period compared with the total of infected cats was less time.

Regarding the number of hospitalizations, the median number was 1, ranging from 1 to 4 hospitalizations. As similarly stated in the FIV discussion, FeLV leads to secondary infections, so it is normal that cats may need more than one hospitalization in their lifetime.

The survival rate at discharge was 57.9% ($CI_{95\%}$=49.0-66.5). Yet again, it is important to refer that FeLV is a chronic infectious disease, so this does not mean the cat was cured. Comparing this result with both the survival rate for all infected cats (69,6%, $CI_{95\%}$=64.9-73.9) and the FIV positive (70.4%, $CI_{95\%}$=61.5-78.0) shows how FeLV can be serious and often a fatal disease.

4.4. URTD

Results from the simple model found that purebred cats were 2.37 times at higher risk of getting admitted at the BICU with URTD, rather than domestic cats (OR=2.37; $CI_{95\%}$=0.96-5.92; p-value ≤ 0.20). However, when all the other significant variables were added in the multiple model breed was not a significant factor (p-value=0.2). There is no real consensus about breed predisposition. Some researches such as Edwards et al. (2008) and Fernandez et al. (2017) reported that purebred cats were at a higher risk of infection. One possible reason

is because of a lack of prior exposure to these pathogens (Edwards et al. 2008). While others studies did not find any association between breed and contracting URTD (Berger et al. 2015). It is important to note that some of these studies were developed in shelters, so their results cannot be strictly compared with the present one.

Regarding gender, no association was found (p-value=0.8). There is no reference about gender predisposition in the literature (Gaskell et al. 2012; Sykes 2013d). Yet, Fernandez et al. (2017) found that male cats had a higher risk of infection. They explained the possibility that male cats would more likely go outside and be exposed to infection. However, when looking at their results, indoor cats did not have a protective factor of infection, so their hypothesis was discarded (Fernandez et al. 2017).

Concerning the neutered status, this study found that intact cats were at a higher risk of getting hospitalized with URTD than neutered cats (OR=3.03; $CI_{95\%}$=1.60-5.82; p-value<0.001). Yet again, Gaskell et al. (2012) and Sykes (2013d) did not reference any predisposition. A possible reason for this is that neutered cats stay indoors more often and have more health care and vigilance from their owners than intact cats.

Unsurprisingly, cats that did live with multiple animals were 2.46 times more likely to get hospitalized with URTD than cats who lived with no other animal (OR=2.46; $CI_{95\%}$=1.35-4.62; p-value <0.05). Both Gaskell and Knowles (2012) and Sykes (2013b) have stated that URTD infection is widely spread in multicat households and shelters. This happens because the transmission of the disease is spread by close contact and indirect contact with materials such as feeding bowls and cleaning utensils. Both Binns et al. (2000) and Fernandez et al. (2017) also reported that intensive housing can predispose to respiratory disease.

Considering the variable lifestyle, no association was found (p-value=0.8). This is normal to happen, because both situations have their own risk. Indoor cats can live in a highly populated house, which is a risk for this complex of diseases. While outdoor cats can also live with multiple animals, such as colonies, they could also live alone but can encounter an infected cat; Fernandez et al. (2017) also found the same result.

An unexpected finding was that cats without up to date vaccines did not have an increase in risk for URTD (p-value >0.9). This result is surprising because FHV-1 and FCV vaccines are considered core (Day et al. 2016). However, both *Chlamydia felis* and *Bordetella bronchiseptica* vaccines are considered noncore (Day et al. 2016). Another possible reason is that there was no information about the vaccination status of 18 cats, which could have influenced the results. An additional reason is that both FHV-1 and FCV vaccines do not prevent infection and their carrier state (Sykes 2013d). Furthermore, FCV attenuated vaccine can lead to an increase in shedding, when the cat is already infected (Sykes 2013d).

Even though most hospitalized cats had concomitant disorders and diseases (69%), the simple model found an association between cats without concomitant disorders/diseases

and getting hospitalized with URTD (p-value ≤ 0.20). Nevertheless, when this variable was added with the others in the multiple model, the association was no longer found (p-value=0.6). Knowing that URTD severity can be increased with concomitant immunosuppressive diseases, opportunistic bacteria, and other respiratory pathogens (Gaskell et al. 2012; Sykes 2013d), this last result goes against of what is stated. A conceivable reason for this is that in the control group the majority of cats (78%) also had concomitant disorders and diseases.

Interpreting the variable age in the simple model, less than 2-years-old cats were 2.28 times at a higher risk of getting admitted at the BICU with URTD, rather than 10-year-old cats or older (OR=2.28; $CI_{95\%}$=1.15-4.57; p-value<0.05). This result goes accordingly with multiple statements saying that cats with a younger age are positively associated with URTD (Binns et al. 2000; Bannasch and Foley 2005; Zicola et al. 2009; Gaskell et al. 2012). Anyhow, when adjusted for the other variables in the multiple model, this association was not found (p-value=0.6). Although a bit surprising, this result also happened in Fernandez et al. (2017) study. The median age of URTD infected cats in the BICU was 4.5 years, ranging from 1 month to 19 years. Gaskell et al. (2012) stated that cats can have a reactive episode or undergo cycles of infection through their lifetime. Therefore, it explains why the median age in the present study was not smaller and why in the multiple model younger cats were not at a higher risk compared with other age stages.

The median hospitalization length for URTD infected cats was 3 days, ranging from 1 to 14 days. Comparing with the total of infected cats in the BICU the median was the same, which shows they stayed hospitalized a standard time.

Regarding the number of hospitalizations, the median number was 1, ranging from 1 to 3 hospitalizations. It is plausible that cats could be hospitalized again. Firstly, because they can have a reactive episode; and secondly, they could catch another infectious disease.

The survival rate at discharge was 76.1% ($CI_{95\%}$=66.3-83.8). Usually, morbidity is more relevant than mortality in URTD (Sykes 2013d). However, this percentage shows that mortality can and also happens, so a good prevention is always the answer.

All the peaks in both rolling averages showed that most URTD cases happened in the Winter or at the end of Spring/beginning of Summer months. For the Winter months, possible reasons are that both FCV and FHV-1 stability increases at low temperatures, so indirect transmission is more prone to occur (Wong et al. 2013). Another one is that cats who live outside might be more stressed in the Winter, therefore being more susceptible to infection or reactivation (Wong et al. 2013). For the mixture of Spring and Summer months, it could be explained by the fact that these months are associated with the parturition period of the queens and when the kittens lose their maternally derived antibodies (Zicola et al. 2009; Gaskell et al. 2012).

4.5. Panleukopenia

No association was found between domestic cats and getting admitted at the BICU with Panleukopenia (p-value=0.8). There is no reference about breed predisposition for the disease (Greene 2012; Sykes 2013c). Mende et al. (2014) tried to identify factors associated with lack of antibodies to determine groups that could be at more risk of getting the disease, and they also did not find any association with breed. Although Mende's study was different from the present one, some comparisons can be established.

Likewise, no association between gender and panleukopenia hospitalized cats was found (p-value=0.8). Both Greene (2012) and Sykes (2013c) did not reference any gender predisposition. Barrs (2019) documented that in older studies, male cats were more commonly affected; however, the reason for this was that male cats were preferred as pets because in that time neutering was not a practiced routine.

Regarding the neuter status, in the simple regression analysis, intact cats were more likely to get hospitalized with panleukopenia, rather than neutered cats (OR=2.81; $CI_{95\%}$=1.52-5.25; p-value<0.01). However, when all the variables were added in the multiple model this association was no longer found (p-value=0.3). A possible reason that in the simple model an association was found could be that neutered cats tend to have more health care and vigilance from their owners. No reference is given about neuter or intact predisposition in the literature (Greene 2012; Sykes 2013c; Barrs 2019), agreeing with this multiple model.

An association was found between cats living with more animals and getting hospitalized with panleukopenia, rather than cats living with no other animals in the simple model analysis (OR=2.08; $CI_{95\%}$=1.10-4.09; p-value<0.05). This association was lost when adjusted for the other variables in the multiple model (p-value=0.13). Panleukopenia is a highly contagious disease, so it is normal that cats living in multicat households, shelters, breeding catteries are at a higher risk of catching the disease (Greene 2012; Sykes 2013c). Nonetheless, the disease has the ability to survive long periods in the environment, so fomites can play an important part in its transmission (Greene 2012; Sykes 2013c). Therefore, cats living without other animals can get infected, because fomite transmission is so effective.

Considering the variable lifestyle, outdoor living had no association with panleukopenia infection (p-value >0.9). This finding was not surprising because both outdoor and indoor living have risks. Although panleukopenia is generally found in favorably dense populations, like previously stated, outdoor exposure can leave cats to encounter infected cats or fomites (Greene 2012; Sykes 2013c).

Without any surprise, cats without up to date vaccines were 50.5 times more likely to get hospitalized with panleukopenia, compared with cats with their vaccines up to date (OR=50.5; $CI_{95\%}$=11.83-373.09; p-value<0.001). It is well known that the panleukopenia vaccine is considered core and can prevent the disease, when well administered (Day et al.

2016). Therefore, it is reasonable to predict that unvaccinated and incompletely vaccinated cats for the disease have higher odds of getting infected (Greene 2012; Sykes 2013c; Barrs 2019).

Panleukopenia is characterized by severe enteritis and immunosuppression, so co-infections with other viral pathogens (e.g., feline enteric coronavirus, FeLV) are likely to occur (Kruse et al. 2010; Greene 2012; Sykes 2013c). However, in this study, cats without concomitant disorders/diseases were 7.31 times more likely to get admitted at the BICU with panleukopenia, rather than cats with concomitant disorders/diseases (OR=7.31; $CI_{95\%}$=2.77-21.01; p-value<0.001). Before the interpretation of this result, it is important to reference that the variable concomitant disorders and diseases in the BICU stands for disorders/diseases that are not needed to be hospitalized in an isolation unit, as earlier mentioned. So, diseases that are likely to occur when the cat is infected with panleukopenia are unlikely present in this variable. With that, it was normal to see this result, because panleukopenia usually affects younger cats and they are less likely to have other diseases such as chronic renal disease or neoplasia, which are more common in older animals.

Concerning the variable age, less than 2-years-old cats and cats between the ages of ≥ 2 & < 10 years were 85 and 10.7 times more likely to get admitted at the BICU with panleukopenia rather than 10-year-old cats or older, respectively (OR=85.0; $CI_{95\%}$=13.11-1751.11; p-value<0.001) (OR=10.7; $CI_{95\%}$=1.73-211.34; p-value<0.05). These associations were plausible because it is recognized that younger cats are at more risk of infection. The median age of hospitalized cats with panleukopenia was 6 months, ranging from 1 month to 14 years. Sykes (2013c) stated that the median age of panleukopenia infected cats was 4 months. The reason why age is important for disease susceptibility is because younger animals are more likely to be unvaccinated and/or have an incomplete vaccination. Another reason is that cats normally develop immunity to panleukopenia from exposure to the virus, so older cats, even if they are unvaccinated have probably contacted with the disease and have developed immunity against it (Barrs 2019).

Considering the hospitalization length for panleukopenia infected cats, the median hospitalization length was 6 days, ranging from 1 to 15 days. Comparing with the total of infected cats in the BICU, the median was longer. Sykes (2013c) stated that cats that survive longer than the 5-day hospitalization period usually recover.

Regarding the number of hospitalizations, the median number was 1, ranging from 1 to 4 hospitalizations. This is because these cats were admitted with other infectious diseases.

The survival rate at discharge was 73.4% (CI_{95}=61.5-82.7). In 2016, a study made at the BICU reported a survival rate at discharge from 43.8% ($CI_{95\%}$=23.1-66.8) (Machado 2016). Therefore, the present result represented how specialized equipment and nursing care can improve the survival rate of panleukopenia infected cats.

A rising number of new cases of panleukopenia was seen in 2020 in the temporal distribution of cases throughout the years, specially from May to September. A possible reason for this is that cats were acquired in the middle of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) lockdown, and the owners being in lockdown were less likely to take their animals to the veterinary, hence more unvaccinated cats. When the lockdown restriction was lifted, around May, the owners could leave their houses and possibly bring back infectious particles of the virus, making the cats infected. Another conceivable reason is that other hospitals and clinics are getting more used to reference their patients to the BICU.

4.6. Final remarks

Overall, several risk factors were found in this study, the following figure 5, shows a summary of all the risk factor found for the multiple infectious diseases explored.

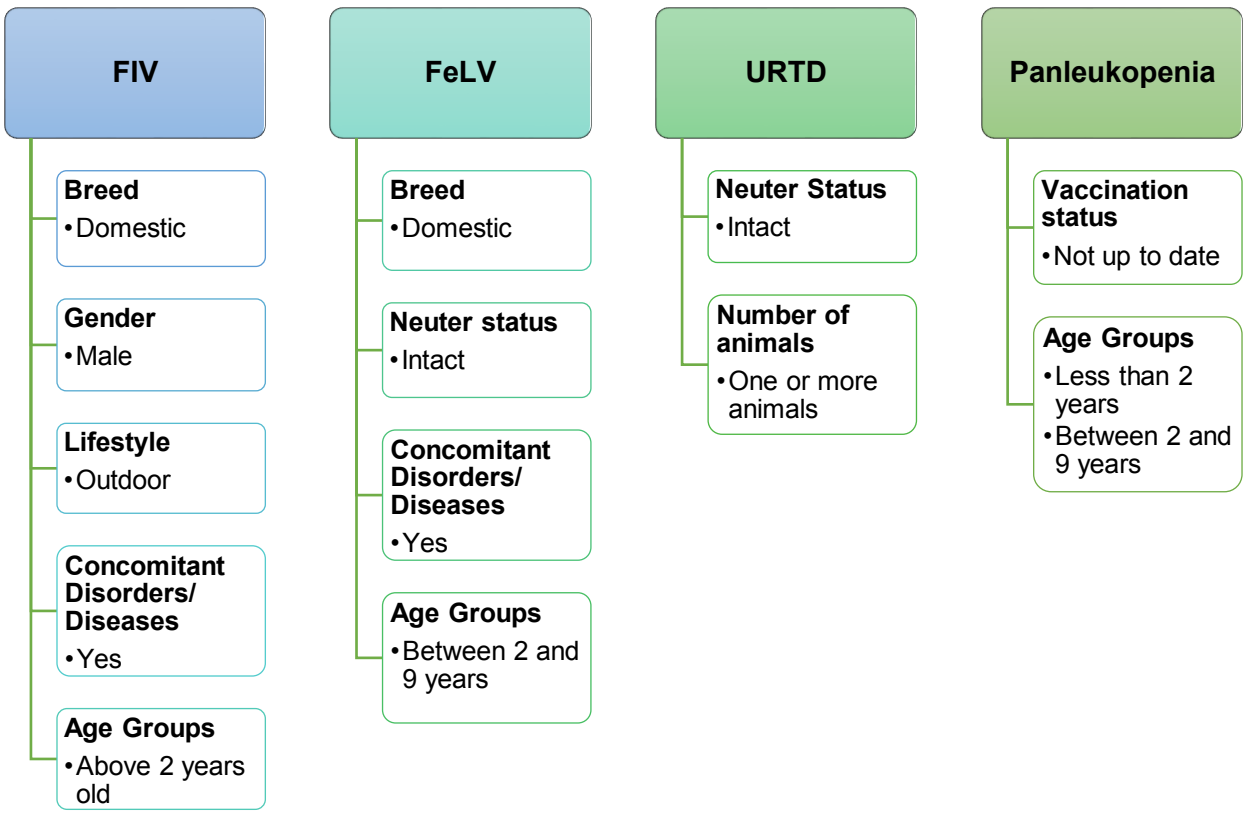


Figure 5- Which factor does the veterinarian and the owner have to be more careful for each disease

5. Conclusion

The present study was assessed in order to analyze the infectious patients and to evidence possible risk factors for the most frequent infectious diseases documented in the BICU since its opening.

None of these objectives would be possible without the detailed history recorded from the veterinarians working at the VTH and at the BICU. This shows how important a systematic collection of clinical data is and how the lack of information could restrain an epidemiological study like this.

Multiple risk factors were identified for several diseases, some of them expected as the literature stated, for example vaccination status and age stage for panleukopenia patients. There were also unexpected results; some were anticipated to be a risk factor and turned out to have no association (e.g., number of animals for FeLV) and others were surprisingly risk factors (e.g., intact cats for URTD).

These results just proved how important preventive measures for infectious diseases are, and that the owner should be more educated towards the possible risks for these diseases. The third annex shows a proposed poster to alert both veterinarians and owners of possible risk factors when they buy or adopt a cat.

In the author's knowledge the present study is the first to assess risk factors for infectious diseases and being hospitalized in an isolation unit. Throughout this study some difficulties and limitations were found. Firstly, the data used depends on the accuracy of the information shared by the owner and the precision of the veterinarian who registered the history (e.g., lack of information about the cat's lifestyle or vaccination status). Therefore, a certain interviewer bias could have happened. Secondly, all the patients chosen to be controls were patients at the BICU, so a Berkson's bias could happen. This type of bias happens when controls are selected among the hospital's patients. Thirdly, multiple animals could not be used because a definitive diagnosis was needed, and this is dependent on the clinical status of the animal and the economic situation of the owner. Lastly, articles used for the discussion generally reported the animals without being hospitalized. Therefore, the comparisons made must be interpreted carefully because the population used is different from other studies, so the results and conclusions can always differ.

For future studies, some improvements can be made to the data frame of patients admitted at the BICU, such as a redesigned follow-up column, where a specific time frame is established. A column with zip-codes so possible clusters of diseases could be identified. Additionally, a column of the date of death/euthanasia should be added, for a better survival analysis.

Unlike other countries (e.g., Australia), Portugal does not have a national data set where all companion animals' diseases are recorded by veterinarians and nurses. A

surveillance system like that could help in making epidemiological studies nationwide and also monitor disease occurrences or outbreaks.

Lastly, it is important to clearly show the improvement in the survival rates at discharge in the BICU over these 7 years. For example, survival rate at discharge for panleukopenia patients in 2016 was 43.8% ($CI_{95\%}$=23.1-66.8) and in 2020 it is at its highest with 73.4% ($CI_{95\%}$=61.5-82.7). This shows the hard work and dedication put throughout the years from all the people working in the VTH and in the BICU.

In conclusion, this study shows how important and relevant infectious diseases are. How critical it is not to neglect these diseases from both the perspective of the veterinarian and the owner, because these types of diseases are not only a concern for the animal, but for the public health.

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V- Annexes

Annex 1. Abstract submitted and accepted to the International Society of Feline Medicine Congress 2021

RISK FACTORS AND SURVIVAL RATES FOR PORTUGUESE CATS NATURALLY INFECTED WITH FELINE PANLEUKOPENIA

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Feline panleukopenia virus (FPV) is responsible for serious systemic infection and is a major health and welfare concern among cat populations due to high morbidity and mortality.

The main objectives of this study were to characterize feline panleukopenia cases, identify risk factors associated with infection and analyze the survival rates of patients hospitalized at the Biological Isolation and Containment Unit in the Teaching Hospital of the University of Lisbon, Portugal, during a 7-year period (2013-2020).

A case-control study was conducted using data from 64 panleukopenia virus-infected cats and matched controls. First, a simple regression analysis investigated eight potential risk factors: age, breed, sex, neuter, number of cohabitants, lifestyle, vaccination status, and the presence of concomitant disorders. Variables with a *P* value ≤0.20 were then included in a multiple regression model: neuter status, vaccination status, number of cohabitants, presence of concomitant disorders, and age (≤1 year-old vs ≥2 years old).

Absence of correct vaccination (OR=47.1; $CI_{95\%}$=10.99-346.86), age ≤1 year-old (OR=13.2; $CI_{95\%}$=4.87-40.63) and absence of concomitant disorders (OR=7.3; $CI_{95\%}$=2.88-19.83) were identified as risk factors (with *P* values <0.05).

The median hospitalization stay was 6.0 days (1-15 days), with a discharge rate of 73.4%. This proportion was 43.8% in 2016, demonstrating that specialized equipment and nursing care can lead to an excellent improvement.

These results demonstrate that with specialized animal care, good survival rates can be achieved, even in critically ill young, non-vaccinated kittens; however, prolonged hospital stays are necessary.

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Annex 2. Abstracts submitted and accepted to the European College of Veterinary Internal Medicine Companion Animals Congress 2021

Canine parvovirosis *versus* canine distemper: risk factors, hospitalization course, and outcome

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Parvovirosis and canine distemper are major causes of morbidity and mortality among dog populations, caused respectively by canine parvovirus (CPV-2) and canine distemper virus (CDV).

The aim of this study was to identify host-related risk factors leading to the hospitalization of infected dogs at the Teaching Hospital, and to compare the course of hospitalization and outcome between diseases.

Data from 130 dogs with confirmed parvovirosis and 26 dogs with confirmed distemper were retrieved from the hospital information system over a 7-year period (2013-2020). The influence of age, gender, neuter status, vaccination, breed, and presence of concomitant disorders was investigated through a logistic regression model. A descriptive analysis assessed the length of stay, outcome, readmissions and survival rate. A two-step approach was used to evaluate the hospitalization length and range, considering first all patients and then only discharged patients.

Concerning parvovirosis, age ≤1 year old ($p<0.001$; OR=71.8; $CI_{95\%}$=27.7-227.6) and absence of vaccination ($p<0.001$; OR=73.8; $CI_{95\%}$=12.9-1410.9) were risk factors for hospitalization. The overall median hospitalization stay was 4.5 days (1.0-18.0) and 5.0 days for discharged dogs, within the same range. The discharge rate (83.8%) and the survival rate (82.3%) were very close, when considering readmissions.

Regarding canine distemper, age ≤1 year old ($p=0.0013$; OR=43.8 $CI_{95\%}$=6.4-930.9) and absence of vaccination ($p=0.032$; OR=14.9, $CI_{95\%}$=1.8-352.3) were risk factors and being neutered was a protection factor ($p=0.036$; OR=0.04, $CI_{95\%}$=0.001-0.51). The overall median hospitalization stay was 3.5 days (1.0-20.0) and 4.0 days for discharged dogs within the same range. The discharge rate was 50.0%, decreasing to 34.6% survival rate, when considering readmissions.

This study found similar patterns of host-related risk factors between both diseases, as young unvaccinated dogs were high-risk animals, even though the courses of disease were different. In parvovirosis, longer hospitalization was need but full recovery was achieved in most cases with high survival rates. In opposition, distemper patients recovered faster from clinical episodes, but lower survival rates were observed. After an initial hospitalization, distemper patients tend to be readmitted with recurrent clinical episodes leading in many cases to euthanasia months after their first hospitalization.

Annex 3. Poster proposal for the owners' awareness of infectious diseases

DO YOU KNOW IF YOUR CAT IS AT RISK OF GETTING HOSPITALIZED WITH AN INFECTIOUS DISEASE?

GENDER

Male cats were at a **higher risk** of getting hospitalized with **FIV**

BREED

Domestic cats were **more likely** to get hospitalized with **FIV and FeLV**

NEUTER STATUS

Intact cats were **more likely** to get hospitalized with **FIV and URTD**

COHABITANTS

Cats **living with multiple animals** were **more likely** to get hospitalized with **URTD**

LIFESTYLE

Cats with **access to the oudoors or living outdoo**r were **more likely** to get hospitalized with **FIV**

VACCINATION

Unvaccinated or incompletly vaccinated cats were **more likely** to get hospitalized with **Panleukopenia**

CONCOMITANT DISORDERS

Cats with **concomitant disorders** were **more likely** to get hospitalized with **FIV and FeLV**

AGE GROUPS

<2 years cats were at **more risk** of getting hospitalized with **Panleukopenia**

≥2 & <10 years cats were at more risk of getting hospitalized with **FIV, FeLV and Panleukopenia**

≥10 years cats were at **more risk** of getting hospitalized with **FIV**

!FOR MORE INFORMATION!

You should look up the flyers that your veterinarian gave to you about infectious diseases!

Annex 5. R code for the statistical analysis

The R code created to establish the risk factors for being hospitalized for the multiple infectious diseases is shown below.

The code started with creating the simple regression model for each explored variable within each explored infectious disease, with their odds ratio and confidence intervals being calculated. The next step was adding all significant variables with a p-value ≤0.20 in the multiple regression model. Then their odds ratios and confidence intervals were also calculated.

```
#Breed
breed_model <- glm( fiv_positive ~ breed, data= bd_FIV, family="binomial"
(link=logit))
summary( breed_model)

##
## Call:
## glm(formula = fiv_positive ~ breed, family = binomial(link = logit),
##     data = bd_FIV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9371  -0.9371  -0.9371   1.4385   2.2815
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept)  -2.5257     0.7348  -3.437 0.000588 ***
## breedDSH      1.9301     0.7441   2.594 0.009493 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 439.19  on 344  degrees of freedom
## Residual deviance: 428.10  on 343  degrees of freedom
## AIC: 432.1
##
## Number of Fisher Scoring iterations: 5

#Odds ratio
exp(coef(breed_model))

## (Intercept)    breedDSH
##    0.080000    6.890244

#Confidence Intervals
exp(confint(breed_model))

## Waiting for profiling to be done...

##                   2.5 %     97.5 %
## (Intercept) 0.01287187  0.2683006
## breedDSH    2.00315775 43.3124340

#Gender
gender_model <- glm( fiv_positive ~ gender, data= bd_FIV, family="binomial
```

```
" (link=logit))
summary( gender_model)

##
## Call:
## glm(formula = fiv_positive ~ gender, family = binomial(link = logit),
##     data = bd_FIV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9898  -0.9898  -0.7679   1.3774   1.6524
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept)  -1.0704     0.1931  -5.542 2.98e-08 ***
## genderM       0.6116     0.2407   2.540   0.0111 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 439.19  on 344  degrees of freedom
## Residual deviance: 432.55  on 343  degrees of freedom
## AIC: 436.55
##
## Number of Fisher Scoring iterations: 4

#Odds ratio
exp(coef(gender_model))

## (Intercept)     genderM
##   0.3428571   1.8433333

#Confidence Intervals
exp(confint(gender_model))

## Waiting for profiling to be done...

##                 2.5 %   97.5 %
## (Intercept) 0.2317854 0.495386
## genderM     1.1563650 2.976926

#Neuter status
neuter_model <- glm( fiv_positive ~ neuter, data= bd_FIV, family="binomial
" (link=logit))
summary( neuter_model)

##
## Call:
## glm(formula = fiv_positive ~ neuter, family = binomial(link = logit),
##     data = bd_FIV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9054  -0.8981  -0.8981   1.4764   1.4852
##
```

```
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept) -0.69962    0.13942  -5.018 5.22e-07 ***
## neuterN      0.01972    0.24308   0.081    0.935
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 439.19  on 344  degrees of freedom
## Residual deviance: 439.19  on 343  degrees of freedom
## AIC: 443.19
##
## Number of Fisher Scoring iterations: 4

#Odds ratio
exp(coef(neuter_model))

## (Intercept)     neuterN
##   0.4967742   1.0199134

#Confidence Intervals
exp(confint(neuter_model))

## Waiting for profiling to be done...

##                 2.5 %    97.5 %
## (Intercept) 0.3762415 0.6504362
## neuterN     0.6300880 1.6369565

#Number of animals
n_animals_model <- glm( fiv_positive ~ n_animals, data= bd_FIV, family="bi
nomial" (link=logit))
summary( n_animals_model)

##
## Call:
## glm(formula = fiv_positive ~ n_animals, family = binomial(link = logit)
,
##     data = bd_FIV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9174  -0.8901  -0.8901   1.4619   1.4950
##
## Coefficients:
##                              Estimate Std. Error z value Pr(>|z|)
## (Intercept)                  -0.64768    0.18398  -3.520 0.000431 ***
## n_animalsMORE THAN 1 ANIMAL -0.07363    0.23469  -0.314 0.753715
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 439.19  on 344  degrees of freedom
```

```
## Residual deviance: 439.10  on 343  degrees of freedom
## AIC: 443.1
##
## Number of Fisher Scoring iterations: 4

#Odds ratio
exp(coef(n_animals_model))

##                 (Intercept) n_animalsMORE THAN 1 ANIMAL
##                   0.5232558                   0.9290123

#Confidence Intervals
exp(confint(n_animals_model))

## Waiting for profiling to be done...

##                                 2.5 %    97.5 %
## (Intercept)                 0.3619988 0.7461087
## n_animalsMORE THAN 1 ANIMAL 0.5874374 1.4762206

#Lifestyle----
lifestyle_model <- glm( fiv_positive ~ lifestyle, data= bd_FIV, family="bi
nomial" (link=logit))
summary( lifestyle_model)

##
## Call:
## glm(formula = fiv_positive ~ lifestyle, family = binomial(link = logit)
,
##     data = bd_FIV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.0374  -1.0374  -0.6768   1.3242   1.7812
##
## Coefficients:
##                   Estimate Std. Error z value Pr(>|z|)
## (Intercept)       -1.3573     0.1895  -7.161 8.00e-13 ***
## lifestyleOUTDOOR   1.0187     0.2480   4.108 3.99e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 409.60  on 331  degrees of freedom
## Residual deviance: 391.98  on 330  degrees of freedom
##   (13 observations deleted due to missingness)
## AIC: 395.98
##
## Number of Fisher Scoring iterations: 4

#Vaccination status----

vaccination_model <- glm( fiv_positive ~ vaccinestatus, data=bd_FIV, famil
y="binomial" (link = logit))
summary( vaccination_model)
```

```
##
## Call:
## glm(formula = fiv_positive ~ vaccinestatus, family = binomial(link = lo
git),
##     data = bd_FIV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.7655  -0.7531  -0.7531  -0.7531   1.6725
##
## Coefficients:
##                              Estimate Std. Error z value Pr(>|z|)
## (Intercept)                  -1.07756    0.28944  -3.723 0.000197 ***
## vaccinestatusNOT UP TO DATE -0.03758    0.32543  -0.115 0.908061
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 343.05  on 305  degrees of freedom
## Residual deviance: 343.03  on 304  degrees of freedom
##   (39 observations deleted due to missingness)
## AIC: 347.03
##
## Number of Fisher Scoring iterations: 4

#Odds ratio
exp(coef(vaccination_model))

##                 (Intercept) vaccinestatusNOT UP TO DATE
##                   0.3404255                   0.9631148

#Confidence Intervals
exp(confint(vaccination_model))

## Waiting for profiling to be done...

##                                 2.5 %    97.5 %
## (Intercept)                 0.1871985 0.5869877
## vaccinestatusNOT UP TO DATE 0.5172097 1.8653998

#Age Group

agegroup_model <- glm( fiv_positive ~ agegroup, data=bd_FIV, family="binom
ial" (link = logit))
summary( agegroup_model)

##
## Call:
## glm(formula = fiv_positive ~ agegroup, family = binomial(link = logit),
##     data = bd_FIV)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -1.017  -1.017  -0.513   1.347   2.046
```

```
##
## Coefficients:
##                   Estimate Std. Error z value Pr(>|z|)
## (Intercept)        -1.9617     0.3560  -5.510 3.58e-08 ***
## agegroup≥ 10        1.3863     0.4125   3.361 0.000777 ***
## agegroup≥ 2 & < 10   1.5708     0.3886   4.042 5.30e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 436.99  on 343  degrees of freedom
## Residual deviance: 415.85  on 341  degrees of freedom
##   (1 observation deleted due to missingness)
## AIC: 421.85
##
## Number of Fisher Scoring iterations: 4

#Odds Ratio
exp(coef(agegroup_model))

##       (Intercept)      agegroup≥ 10 agegroup≥ 2 & < 10
##          0.140625          4.000000          4.810458

#Confidence Intervals
exp(confint(agegroup_model))

## Waiting for profiling to be done...

##                        2.5 %     97.5 %
## (Intercept)       0.06523447  0.2678373
## agegroup≥ 10      1.84843463  9.4600477
## agegroup≥ 2 & < 10 2.34609922 10.9379623

#Concomitants----
concomitant <- glm( fiv_positive ~ yn_nconcomitants, data=bd_FIV, family =
"binomial" (link=logit))
summary(concomitant)

##
## Call:
## glm(formula = fiv_positive ~ yn_nconcomitants, family = binomial(link =
logit),
##     data = bd_FIV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.0012  -1.0012  -0.6536   1.3645   1.8158
##
## Coefficients:
##                   Estimate Std. Error z value Pr(>|z|)
## (Intercept)        -1.4351     0.2488  -5.768 8.03e-09 ***
## yn_nconcomitantsY   1.0054     0.2816   3.571 0.000356 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 439.19  on 344  degrees of freedom
## Residual deviance: 425.05  on 343  degrees of freedom
## AIC: 429.05
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(concomitant))
```

```
##       (Intercept) yn_nconcomitantsY
##         0.2380952         2.7328767
```

```
exp(confint(concomitant))
```

```
## Waiting for profiling to be done...
```

```
##                        2.5 %   97.5 %
## (Intercept)       0.1422734 0.379372
## yn_nconcomitantsY 1.5997363 4.846719
```

```
#Multiple model ----

fiv_model <- glm( fiv_positive ~ breed + gender + lifestyle + yn_nconcomit
ants+ agegroup,
                  data= bd_FIV, family = "binomial" (link = logit))

summary(fiv_model)
```

```
##
## Call:
## glm(formula = fiv_positive ~ breed + gender + lifestyle + yn_nconcomita
nts +
##     agegroup, family = binomial(link = logit), data = bd_FIV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.3990  -0.8856  -0.5426   0.9709   2.2461
##
## Coefficients:
##                   Estimate Std. Error z value Pr(>|z|)
## (Intercept)        -5.0098     0.8942  -5.603 2.11e-08 ***
## breedDSH            1.5418     0.7621   2.023 0.043060 *
## genderM             0.6045     0.2745   2.203 0.027621 *
## lifestyleOUTDOOR    1.0219     0.2711   3.770 0.000164 ***
## yn_nconcomitantsY   1.0291     0.3278   3.140 0.001692 **
## agegroup≥ 10        1.1007     0.4635   2.375 0.017558 *
## agegroup≥ 2 & < 10  1.3198     0.4302   3.068 0.002154 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 407.23  on 330  degrees of freedom
```

```
## Residual deviance: 350.34  on 324  degrees of freedom
##   (14 observations deleted due to missingness)
## AIC: 364.34
##
## Number of Fisher Scoring iterations: 5
```

```
exp(coef(fiv_model))
```

```
##       (Intercept)          breedDSH           genderM  lifestyleOUTDOOR
##       0.006672313       4.673153022       1.830368356       2.778481794
## yn_nconcomitantsY      agegroup≥ 10 agegroup≥ 2 & < 10
##       2.798474053       3.006128433       3.742497702
```

```
exp(confint(fiv_model))
```

```
## Waiting for profiling to be done...
```

```
##                            2.5 %      97.5 %
## (Intercept)       0.0008564838  0.03200839
## breedDSH          1.2926415358 30.02692857
## genderM           1.0753021065  3.16194510
## lifestyleOUTDOOR  1.6445942285  4.77079316
## yn_nconcomitantsY 1.4977957580  5.44487377
## agegroup≥ 10      1.2552156739  7.86172773
## agegroup≥ 2 & < 10 1.6814420783  9.25354460
```

```
#Breed ----
breed_felv_model <- glm( felv_positive ~ breed, data= bd_FELV, family="bin
omial" (link=logit))
summary(breed_felv_model)
```

```
##
## Call:
## glm(formula = felv_positive ~ breed, family = binomial(link = logit),
##     data = bd_FELV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9361  -0.9361  -0.9361   1.4397   2.1460
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept)  -2.1972     0.6085  -3.611 0.000305 ***
## breedDSH      1.5990     0.6194   2.581 0.009840 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 454.47  on 356  degrees of freedom
## Residual deviance: 444.82  on 355  degrees of freedom
## AIC: 448.82
```

```
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(breed_felv_model))
```

```
## (Intercept)    breedDSH
##   0.1111111   4.9478672
```

```
exp(confint(breed_felv_model))
```

```
## Waiting for profiling to be done...
```

```
##                  2.5 %     97.5 %
## (Intercept) 0.02653338  0.3144361
## breedDSH    1.70101197 21.0292426
```

```
#Gender ----
```

```
gender_felv_model <- glm(felv_positive ~ gender, data=bd_FELV, family = "b
inomial" (link=logit))
summary(gender_felv_model)
```

```
##
## Call:
## glm(formula = felv_positive ~ gender, family = binomial(link = logit),
##     data = bd_FELV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9072  -0.9072  -0.8947   1.4742   1.4894
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept) -0.67513    0.16416  -4.113 3.91e-05 ***
## genderM     -0.03377    0.22502  -0.150    0.881
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 454.47  on 356  degrees of freedom
## Residual deviance: 454.45  on 355  degrees of freedom
## AIC: 458.45
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(gender_felv_model))
```

```
## (Intercept)     genderM
##   0.5090909   0.9667969
```

```
exp(confint(gender_felv_model))
```

```
## Waiting for profiling to be done...
```

```
##                 2.5 %    97.5 %
## (Intercept) 0.3666931 0.6988652
## genderM     0.6219966 1.5044776

#Neuter----
neuter_felv_model <- glm ( felv_positive ~ neuter, data=bd_FELV, family="b
inomial" (link=logit))
summary(neuter_felv_model)

##
## Call:
## glm(formula = felv_positive ~ neuter, family = binomial(link = logit),
##     data = bd_FELV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9931  -0.8461  -0.8461   1.3736   1.5499
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept)  -0.8431     0.1450  -5.813 6.14e-09 ***
## neuterN       0.3929     0.2305   1.704   0.0883 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 454.47  on 356  degrees of freedom
## Residual deviance: 451.58  on 355  degrees of freedom
## AIC: 455.58
##
## Number of Fisher Scoring iterations: 4

exp(coef(neuter_felv_model))

## (Intercept)     neuterN
##   0.4303797   1.4812500

exp(confint(neuter_felv_model))

## Waiting for profiling to be done...

##                 2.5 %   97.5 %
## (Intercept) 0.3219893 0.569099
## neuterN     0.9415326 2.327357

#Cohabitants----

n_animals_felv_model <- glm( felv_positive ~ n_animals, data= bd_FELV, fam
ily="binomial" (link=logit))
summary(n_animals_felv_model)

##
## Call:
## glm(formula = felv_positive ~ n_animals, family = binomial(link = logit
),
```

```
##     data = bd_FELV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9695  -0.9695  -0.8533   1.4006   1.5407
##
## Coefficients:
##                Estimate Std. Error z value Pr(>|z|)
## (Intercept)     -0.8228     0.1488  -5.530 3.21e-08 ***
## n_animalsALONE   0.3120     0.2275   1.371     0.17
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 454.47  on 356  degrees of freedom
## Residual deviance: 452.60  on 355  degrees of freedom
## AIC: 456.6
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(n_animals_felv_model))
```

```
##    (Intercept) n_animalsALONE
##      0.4391892      1.3661538
```

```
exp(confint(n_animals_felv_model))
```

```
## Waiting for profiling to be done...
```

```
##                    2.5 %    97.5 %
## (Intercept)    0.3260986 0.5849779
## n_animalsALONE 0.8737648 2.1344673
```

```
#Lifestyle----

lifestyle_felv_model <- glm( felv_positive ~ lifestyle, data=bd_FELV,
                             family = "binomial" (link=logit))
summary(lifestyle_felv_model)
```

```
##
## Call:
## glm(formula = felv_positive ~ lifestyle, family = binomial(link = logit
## ),
##     data = bd_FELV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9005  -0.9005  -0.8013   1.4823   1.6077
##
## Coefficients:
##                   Estimate Std. Error z value Pr(>|z|)
## (Intercept)       -0.9714     0.1613  -6.023 1.71e-09 ***
## lifestyleOUTDOOR   0.2782     0.2380   1.169    0.242
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 415.39  on 339  degrees of freedom
## Residual deviance: 414.02  on 338  degrees of freedom
##   (17 observations deleted due to missingness)
## AIC: 418.02
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(lifestyle_felv_model))
```

```
##      (Intercept) lifestyleOUTDOOR
##        0.3785714        1.3207547
```

```
exp(confint(lifestyle_felv_model))
```

```
## Waiting for profiling to be done...
```

```
##                       2.5 %    97.5 %
## (Intercept)      0.2737089 0.5157771
## lifestyleOUTDOOR 0.8277417 2.1070253
```

```
#Vaccination----
vaccination_felv_model <- glm( felv_positive ~ vaccinestatus, data= bd_FEL
V,
                               family = "binomial" (link=logit))
summary(vaccination_felv_model)
```

```
##
## Call:
## glm(formula = felv_positive ~ vaccinestatus, family = binomial(link = l
ogit),
##     data = bd_FELV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9448  -0.7244  -0.7244   1.4294   1.7125
##
## Coefficients:
##                          Estimate Std. Error z value Pr(>|z|)
## (Intercept)               -1.2040     0.1510  -7.972 1.56e-15 ***
## vaccinestatusUP TO DATE    0.6286     0.2840   2.213   0.0269 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 369.63  on 321  degrees of freedom
## Residual deviance: 364.87  on 320  degrees of freedom
##   (35 observations deleted due to missingness)
## AIC: 368.87
##
## Number of Fisher Scoring iterations: 4
```

```r
exp(coef(vaccination_felv_model))
```

```
##             (Intercept) vaccinestatusUP TO DATE
##                   0.300                   1.875
```

```r
exp(confint(vaccination_felv_model))
```

```
## Waiting for profiling to be done...
```

```
##                               2.5 %    97.5 %
## (Intercept)             0.2212529 0.4004068
## vaccinestatusUP TO DATE 1.0670383 3.2599337
```

```r
#Concomitants----
concomitants_felv_model <- glm( felv_positive ~ yn_nconcomitants, data= bd
_FELV,
                                family = "binomial" (link=logit))

summary(concomitants_felv_model)
```

```
##
## Call:
## glm(formula = felv_positive ~ yn_nconcomitants, family = binomial(link
= logit),
##     data = bd_FELV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9738  -0.9738  -0.7433   1.3957   1.6861
##
## Coefficients:
##                   Estimate Std. Error z value Pr(>|z|)
## (Intercept)        -1.1451     0.2170  -5.278 1.31e-07 ***
## yn_nconcomitantsY   0.6454     0.2544   2.537   0.0112 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 454.47  on 356  degrees of freedom
## Residual deviance: 447.72  on 355  degrees of freedom
## AIC: 451.72
##
## Number of Fisher Scoring iterations: 4
```

```r
exp(coef(concomitants_felv_model))
```

```
##       (Intercept) yn_nconcomitantsY
##         0.3181818         1.9066667
```

```r
exp(confint(concomitants_felv_model))
```

```
## Waiting for profiling to be done...
```

```
##                        2.5 %    97.5 %
## (Intercept)       0.2043726 0.4800849
## yn_nconcomitantsY 1.1687742 3.1775826

#Age Groups----

agegroup_felv_model <- glm( felv_positive ~ agegroup, data= bd_FELV,
                            family = "binomial" (link=logit))

summary(agegroup_felv_model)

##
## Call:
## glm(formula = felv_positive ~ agegroup, family = binomial(link = logit)
,
##     data = bd_FELV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.0833  -1.0833  -0.5997   1.2746   1.8997
##
## Coefficients:
##                     Estimate Std. Error z value Pr(>|z|)
## (Intercept)          -1.6247     0.3034  -5.354 8.59e-08 ***
## agegroup< 2           0.4962     0.3902   1.272    0.203
## agegroup≥ 2 & < 10  1.3992     0.3373   4.149 3.34e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 452.27  on 355  degrees of freedom
## Residual deviance: 427.63  on 353  degrees of freedom
##   (1 observation deleted due to missingness)
## AIC: 433.63
##
## Number of Fisher Scoring iterations: 4

exp(coef(agegroup_felv_model))

##       (Intercept)       agegroup< 2 agegroup≥ 2 & < 10
##         0.1969697         1.6425339         4.0517751

exp(confint(agegroup_felv_model))

## Waiting for profiling to be done...

##                        2.5 %    97.5 %
## (Intercept)       0.1038898 0.3447851
## agegroup< 2       0.7731508 3.6062429
## agegroup≥ 2 & < 10 2.1506307 8.1402662

#Multiple Model----

felv_model <- glm( felv_positive ~ breed  + neuter + n_animals+
                     vaccinestatus + yn_nconcomitants + agegroup,
```

```
                  data=bd_FELV, family = "binomial" (link=logit))

summary(felv_model)

##
## Call:
## glm(formula = felv_positive ~ breed + neuter + n_animals + vaccinestatu
s +
##     yn_nconcomitants + agegroup, family = binomial(link = logit),
##     data = bd_FELV)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.3927  -0.8411  -0.5649   0.8812   2.2974
##
## Coefficients:
##                           Estimate Std. Error z value Pr(>|z|)
## (Intercept)               -4.5191     0.8068  -5.601 2.13e-08 ***
## breedDSH                   1.4406     0.6432   2.240 0.025113 *
## neuterN                    0.6418     0.3027   2.120 0.033980 *
## n_animalsALONE             0.2527     0.2754   0.918 0.358870
## vaccinestatusUP TO DATE    0.5495     0.3048   1.803 0.071356 .
## yn_nconcomitantsY          0.9269     0.3125   2.966 0.003017 **
## agegroup< 2                0.7746     0.4786   1.618 0.105573
## agegroup≥ 2 & < 10         1.4534     0.4075   3.566 0.000362 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 369.63  on 321  degrees of freedom
## Residual deviance: 331.76  on 314  degrees of freedom
##   (35 observations deleted due to missingness)
## AIC: 347.76
##
## Number of Fisher Scoring iterations: 5

exp(coef(felv_model))

##             (Intercept)                 breedDSH                  neuterN
##              0.01089877              4.22304359              1.89990494
##          n_animalsALONE vaccinestatusUP TO DATE       yn_nconcomitantsY
##              1.28743314              1.73246740              2.52676721
##             agegroup< 2       agegroup≥ 2 & < 10
##              2.16970562              4.27770496

exp(confint(felv_model))

## Waiting for profiling to be done...

##                                2.5 %      97.5 %
## (Intercept)              0.001891951  0.04701463
## breedDSH                 1.374414150 18.58248314
## neuterN                  1.051590796  3.45632333
## n_animalsALONE           0.748399455  2.20853441
```

```
## vaccinestatusUP TO DATE 0.947640423  3.14142210
## yn_nconcomitantsY       1.388908950  4.74957639
## agegroup< 2             0.866212844  5.74173039
## agegroup≥ 2 & < 10      2.001240778 10.04116560
```

```
#Breed----

breed_urtd_model <- glm( urtd~ breed, data= bd_URTD, family = "binomial" (
link=logit))
summary(breed_urtd_model)

##
## Call:
## glm(formula = urtd ~ breed, family = binomial(link = logit),
##     data = bd_URTD)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -1.218  -0.873  -0.873   1.516   1.516
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept)  -0.7682     0.1379  -5.571 2.53e-08 ***
## breedBREED    0.8635     0.4582   1.885   0.0595 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 336.08  on 263  degrees of freedom
## Residual deviance: 332.57  on 262  degrees of freedom
## AIC: 336.57
##
## Number of Fisher Scoring iterations: 4

exp(coef(breed_urtd_model))

## (Intercept)  breedBREED
##   0.4638554   2.3714286

exp(confint(breed_urtd_model))

## Waiting for profiling to be done...

##                 2.5 %    97.5 %
## (Intercept) 0.3522805 0.6053295
## breedBREED  0.9605674 5.9228345

#Gender----
gender_urtd_model <- glm( urtd~ gender, data= bd_URTD, family = "binomial"
(link=logit))
summary(gender_urtd_model)

##
## Call:
```

```
## glm(formula = urtd ~ gender, family = binomial(link = logit),
##     data = bd_URTD)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9140  -0.9140  -0.8887   1.4660   1.4967
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept) -0.65678    0.19015  -3.454 0.000552 ***
## genderM     -0.06846    0.26157  -0.262 0.793546
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 336.08  on 263  degrees of freedom
## Residual deviance: 336.01  on 262  degrees of freedom
## AIC: 340.01
##
## Number of Fisher Scoring iterations: 4

exp(coef(gender_urtd_model))

## (Intercept)     genderM
##   0.5185185   0.9338346

exp(confint(gender_urtd_model))

## Waiting for profiling to be done...

##                 2.5 %   97.5 %
## (Intercept) 0.3541795 0.747996
## genderM     0.5590176 1.561531

#Neuter----
neuter_urtd_model <- glm( urtd~ neuter, data= bd_URTD, family = "binomial"
(link=logit))
summary(neuter_urtd_model)

##
## Call:
## glm(formula = urtd ~ neuter, family = binomial(link = logit),
##     data = bd_URTD)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.1963  -0.7433  -0.7433   1.1586   1.6861
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept)  -1.1451     0.1772  -6.464 1.02e-10 ***
## neuterN       1.1896     0.2754   4.319 1.57e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 336.08  on 263  degrees of freedom
## Residual deviance: 317.05  on 262  degrees of freedom
## AIC: 321.05
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(neuter_urtd_model))
```

```
## (Intercept)     neuterN
##   0.3181818   3.2857143
```

```
exp(confint(neuter_urtd_model))
```

```
## Waiting for profiling to be done...
```

```
##                 2.5 %    97.5 %
## (Intercept) 0.2222963 0.4460205
## neuterN     1.9221676 5.6692561
```

```
#Cohabitants----

n_animals_urtd_model <- glm( urtd~ n_animals, data= bd_URTD, family = "bin
omial" (link=logit))
summary(n_animals_urtd_model)
```

```
##
## Call:
## glm(formula = urtd ~ n_animals, family = binomial(link = logit),
##     data = bd_URTD)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9952  -0.9952  -0.7258   1.3713   1.7105
##
## Coefficients:
##                              Estimate Std. Error z value Pr(>|z|)
## (Intercept)                   -1.1994     0.2432  -4.932 8.16e-07 ***
## n_animalsMORE THAN 1 ANIMAL    0.7543     0.2899   2.603  0.00925 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 336.08  on 263  degrees of freedom
## Residual deviance: 328.94  on 262  degrees of freedom
## AIC: 332.94
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(n_animals_urtd_model))
```

```
##                 (Intercept) n_animalsMORE THAN 1 ANIMAL
##                   0.3013699                   2.1262136
```

```r
exp(confint(n_animals_urtd_model))
```

```
## Waiting for profiling to be done...
```

```
##                                 2.5 %    97.5 %
## (Intercept)                 0.1828609 0.4767796
## n_animalsMORE THAN 1 ANIMAL 1.2185804 3.8108985
```

```r
#Vaccination----
vaccination_urtd_model <- glm( urtd~ vaccinestatus, data= bd_URTD, family
= "binomial" (link=logit))
summary(vaccination_urtd_model)
```

```
##
## Call:
## glm(formula = urtd ~ vaccinestatus, family = binomial(link = logit),
##     data = bd_URTD)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.8257  -0.8167  -0.8167   1.5759   1.5876
##
## Coefficients:
##                             Estimate Std. Error z value Pr(>|z|)
## (Intercept)                 -0.90079    0.32890  -2.739  0.00617 **
## vaccinestatusNOT UP TO DATE -0.02598    0.36423  -0.071  0.94315
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 293.82  on 245  degrees of freedom
## Residual deviance: 293.82  on 244  degrees of freedom
##   (18 observations deleted due to missingness)
## AIC: 297.82
##
## Number of Fisher Scoring iterations: 4
```

```r
exp(coef(vaccination_urtd_model))
```

```
##                 (Intercept) vaccinestatusNOT UP TO DATE
##                    0.406250                   0.974359
```

```r
exp(confint(vaccination_urtd_model))
```

```
## Waiting for profiling to be done...
```

```
##                                 2.5 %    97.5 %
## (Intercept)                 0.2057904 0.7559494
## vaccinestatusNOT UP TO DATE 0.4858612 2.0459957
```

```r
#Lifestyle----

lifestyle_urtd_model <- glm( urtd~ lifestyle, data= bd_URTD, family = "bin
omial" (link=logit))
summary(lifestyle_urtd_model)
```

```
##
## Call:
## glm(formula = urtd ~ lifestyle, family = binomial(link = logit),
##     data = bd_URTD)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.8956  -0.8956  -0.8664   1.4883   1.5243
##
## Coefficients:
##                   Estimate Std. Error z value Pr(>|z|)
## (Intercept)      -0.78648    0.17788  -4.421  9.8e-06 ***
## lifestyleOUTDOOR  0.07991    0.26833   0.298    0.766
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 324.90  on 258  degrees of freedom
## Residual deviance: 324.81  on 257  degrees of freedom
##   (5 observations deleted due to missingness)
## AIC: 328.81
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(lifestyle_urtd_model))
```

```
##      (Intercept) lifestyleOUTDOOR
##        0.4554455        1.0831884
```

```
exp(confint(lifestyle_urtd_model))
```

```
## Waiting for profiling to be done...
```

```
##                       2.5 %    97.5 %
## (Intercept)      0.3186537 0.6411243
## lifestyleOUTDOOR 0.6384599 1.8317979
```

```
#Concomitants----
concomitants_urtd_model <- glm( urtd~ yn_nconcomitants, data= bd_URTD, fam
ily = "binomial" (link=logit))
summary(concomitants_urtd_model)
```

```
##
## Call:
## glm(formula = urtd ~ yn_nconcomitants, family = binomial(link = logit),
##     data = bd_URTD)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.0258  -0.8582  -0.8582   1.3370   1.5345
##
## Coefficients:
##                    Estimate Std. Error z value Pr(>|z|)
## (Intercept)         -0.3677     0.2504  -1.469    0.142
```

```
## yn_nconcomitantsY  -0.4414     0.2939  -1.502    0.133
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 336.08  on 263  degrees of freedom
## Residual deviance: 333.85  on 262  degrees of freedom
## AIC: 337.85
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(concomitants_urtd_model))
```

```
##       (Intercept) yn_nconcomitantsY
##         0.6923077         0.6431468
```

```
exp(confint(concomitants_urtd_model))
```

```
## Waiting for profiling to be done...
```

```
##                        2.5 %   97.5 %
## (Intercept)       0.4196788 1.125375
## yn_nconcomitantsY 0.3622646 1.150459
```

```
#Age groups
agegroup_urtd_model <- glm( urtd~ agegroup, data= bd_URTD, family = "binom
ial" (link=logit))
summary(agegroup_urtd_model)
```

```
##
## Call:
## glm(formula = urtd ~ agegroup, family = binomial(link = logit),
##     data = bd_URTD)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.0759  -0.8752  -0.7687   1.2825   1.6512
##
## Coefficients:
##                   Estimate Std. Error z value Pr(>|z|)
## (Intercept)        -1.0678     0.2471  -4.321 1.56e-05 ***
## agegroup< 2         0.8242     0.3501   2.354   0.0186 *
## agegroup≥ 2 & < 10  0.3057     0.3209   0.953   0.3408
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 331.65  on 261  degrees of freedom
## Residual deviance: 325.94  on 259  degrees of freedom
##   (2 observations deleted due to missingness)
## AIC: 331.94
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(agegroup_urtd_model))
```

```
##       (Intercept)       agegroup< 2 agegroup≥ 2 & < 10
##          0.343750          2.280098          1.357576
```

```
exp(confint(agegroup_urtd_model))
```

```
## Waiting for profiling to be done...
```

```
##                         2.5 %    97.5 %
## (Intercept)       0.2072136 0.5487526
## agegroup< 2       1.1536729 4.5713111
## agegroup≥ 2 & < 10 0.7275992 2.5710879
```

```
#Multiple Model----

urtd_model <- glm( urtd ~ breed + neuter + n_animals + yn_nconcomitants +
agegroup,
                   data= bd_URTD, family = "binomial" (link=logit))

summary(urtd_model)
```

```
##
## Call:
## glm(formula = urtd ~ breed + neuter + n_animals + yn_nconcomitants +
##     agegroup, family = binomial(link = logit), data = bd_URTD)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.6224  -0.8350  -0.5837   1.0738   2.0527
##
## Coefficients:
##                               Estimate Std. Error z value Pr(>|z|)
## (Intercept)                    -1.8128     0.4589  -3.951 7.79e-05 ***
## breedBREED                      0.5911     0.4905   1.205  0.22823
## neuterN                         1.1087     0.3278   3.382  0.00072 ***
## n_animalsMORE THAN 1 ANIMAL     0.8995     0.3126   2.878  0.00400 **
## yn_nconcomitantsY              -0.1644     0.3332  -0.493  0.62184
## agegroup< 2                     0.2176     0.4233   0.514  0.60719
## agegroup≥ 2 & < 10              0.2032     0.3384   0.600  0.54828
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 331.65  on 261  degrees of freedom
## Residual deviance: 302.69  on 255  degrees of freedom
##   (2 observations deleted due to missingness)
## AIC: 316.69
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(urtd_model))
```

```
##                 (Intercept)                   breedBREED
##                   0.1631926                    1.8058841
##                     neuterN n_animalsMORE THAN 1 ANIMAL
```

```
##                   3.0303152                     2.4582998
##           yn_nconcomitantsY                   agegroup< 2
##                   0.8484400                     1.2430787
##           agegroup≥ 2 & < 10
##                   1.2252844
```

```
exp(confint(urtd_model))
```

```
## Waiting for profiling to be done...
```

```
##                                    2.5 %   97.5 %
## (Intercept)                   0.06402293 0.389128
## breedBREED                    0.68507533 4.785069
## neuterN                       1.60121896 5.815887
## n_animalsMORE THAN 1 ANIMAL 1.35177300 4.623817
## yn_nconcomitantsY             0.44381630 1.646193
## agegroup< 2                   0.53903154 2.850275
## agegroup≥ 2 & < 10            0.63317363 2.397637
```

```
#Breed

breed_panleu_model <- glm( panleukopenia_positive~ breed, data= bd_panleu,
                           family = "binomial" (link=logit))
summary(breed_panleu_model)
```

```
##
## Call:
## glm(formula = panleukopenia_positive ~ breed, family = binomial(link =
logit),
##     data = bd_panleu)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9036  -0.9036  -0.9036   1.4785   1.5353
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept)  -0.8109     0.6009  -1.349    0.177
## breedDSH      0.1262     0.6214   0.203    0.839
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 244.42  on 191  degrees of freedom
## Residual deviance: 244.38  on 190  degrees of freedom
## AIC: 248.38
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(breed_panleu_model))
```

```
## (Intercept)    breedDSH
##   0.4444444   1.1344538
```

```
exp(confint(breed_panleu_model))
```

```
## Waiting for profiling to be done...

##                 2.5 %   97.5 %
## (Intercept) 0.1204160 1.364761
## breedDSH    0.3537269 4.324146

#Gender

gender_panleu_model <- glm( panleukopenia_positive~ gender, data= bd_panle
u,
                            family = "binomial" (link=logit))
summary(gender_panleu_model)

##
## Call:
## glm(formula = panleukopenia_positive ~ gender, family = binomial(link =
logit),
##     data = bd_panleu)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9136  -0.9136  -0.8901   1.4665   1.4950
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept) -0.65806    0.22878  -2.876  0.00402 **
## genderM     -0.06326    0.30790  -0.205  0.83721
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 244.42  on 191  degrees of freedom
## Residual deviance: 244.38  on 190  degrees of freedom
## AIC: 248.38
##
## Number of Fisher Scoring iterations: 4

exp(coef(gender_panleu_model))

## (Intercept)     genderM
##   0.5178571   0.9386973

exp(confint(gender_panleu_model))

## Waiting for profiling to be done...

##                 2.5 %    97.5 %
## (Intercept) 0.3265690 0.8037894
## genderM     0.5134541 1.7219718

#Neuter

neuter_panleu_model <- glm( panleukopenia_positive~ neuter, data= bd_panle
u,
```

```
                              family = "binomial" (link=logit))
summary(neuter_panleu_model)

##
## Call:
## glm(formula = panleukopenia_positive ~ neuter, family = binomial(link =
logit),
##     data = bd_panleu)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -1.124  -0.739  -0.739   1.232   1.692
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept)  -1.1585     0.2206  -5.252 1.51e-07 ***
## neuterN       1.0318     0.3154   3.271  0.00107 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 244.42  on 191  degrees of freedom
## Residual deviance: 233.47  on 190  degrees of freedom
## AIC: 237.47
##
## Number of Fisher Scoring iterations: 4

exp(coef(neuter_panleu_model))

## (Intercept)     neuterN
##   0.3139535   2.8059965

exp(confint(neuter_panleu_model))

## Waiting for profiling to be done...

##                 2.5 %    97.5 %
## (Intercept) 0.2000734 0.4768025
## neuterN     1.5202451 5.2514576

#Cohabitants

n_animals_panleu_model <- glm( panleukopenia_positive~ n_animals, data= bd
_panleu,
                               family = "binomial" (link=logit))
summary(n_animals_panleu_model)

##
## Call:
## glm(formula = panleukopenia_positive ~ n_animals, family = binomial(lin
k = logit),
##     data = bd_panleu)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
```

```
## -0.9970  -0.9970  -0.7339   1.3692   1.6991
##
## Coefficients:
##                              Estimate Std. Error z value Pr(>|z|)
## (Intercept)                   -1.1741     0.2775  -4.231 2.33e-05 ***
## n_animalsMORE THAN 1 ANIMAL    0.7338     0.3346   2.193   0.0283 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 244.42  on 191  degrees of freedom
## Residual deviance: 239.38  on 190  degrees of freedom
## AIC: 243.38
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(n_animals_panleu_model))
```

```
##                 (Intercept) n_animalsMORE THAN 1 ANIMAL
##                   0.3090909                   2.0829976
```

```
exp(confint(n_animals_panleu_model))
```

```
## Waiting for profiling to be done...
```

```
##                                 2.5 %    97.5 %
## (Intercept)                 0.1741397 0.5205986
## n_animalsMORE THAN 1 ANIMAL 1.0959570 4.0927304
```

```
#Lifestyle
lifestyle_panleu_model <- glm( panleukopenia_positive~ lifestyle, data= bd
_panleu,
                               family = "binomial" (link=logit))
summary(lifestyle_panleu_model)
```

```
##
## Call:
## glm(formula = panleukopenia_positive ~ lifestyle, family = binomial(lin
k = logit),
##     data = bd_panleu)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.8929  -0.8929  -0.8863   1.4916   1.4997
##
## Coefficients:
##                   Estimate Std. Error z value Pr(>|z|)
## (Intercept)       -0.7319     0.1974  -3.707  0.00021 ***
## lifestyleOUTDOOR   0.0181     0.3179   0.057  0.95461
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
```

```
##     Null deviance: 239.98  on 189  degrees of freedom
## Residual deviance: 239.98  on 188  degrees of freedom
##   (2 observations deleted due to missingness)
## AIC: 243.98
##
## Number of Fisher Scoring iterations: 4
```

```
exp(coef(lifestyle_panleu_model))
```

```
##      (Intercept) lifestyleOUTDOOR
##        0.4810127        1.0182599
```

```
exp(confint(lifestyle_panleu_model))
```

```
## Waiting for profiling to be done...
```

```
##                       2.5 %    97.5 %
## (Intercept)      0.3234071 0.7029598
## lifestyleOUTDOOR 0.5423029 1.8926283
```

```
#Vaccination
vaccination_panleu_model <- glm( panleukopenia_positive~ vaccinestatus, da
ta= bd_panleu,
                                 family = "binomial" (link=logit))
summary(vaccination_panleu_model)
```

```
##
## Call:
## glm(formula = panleukopenia_positive ~ vaccinestatus, family = binomial
(link = logit),
##     data = bd_panleu)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.0999  -1.0999  -0.2626   1.2570   2.6017
##
## Coefficients:
##                             Estimate Std. Error z value Pr(>|z|)
## (Intercept)                  -3.3499     0.7194  -4.656 3.22e-06 ***
## vaccinestatusNOT UP TO DATE   3.1648     0.7407   4.273 1.93e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 237.73  on 188  degrees of freedom
## Residual deviance: 196.58  on 187  degrees of freedom
##   (3 observations deleted due to missingness)
## AIC: 200.58
##
## Number of Fisher Scoring iterations: 6
```

```
exp(coef(vaccination_panleu_model))
```

```
##                 (Intercept) vaccinestatusNOT UP TO DATE
##                  0.03508772                 23.68309859
```

```r
exp(confint(vaccination_panleu_model))
```

```
## Waiting for profiling to be done...
```

```
##                                    2.5 %      97.5 %
## (Intercept)                 0.005748952   0.1123211
## vaccinestatusNOT UP TO DATE 6.971327050 148.3223673
```

```r
#Concomitants
concomitants_panleu_model <- glm( panleukopenia_positive~ yn_nconcomitants
, data= bd_panleu,
                                  family = "binomial" (link=logit))
summary(concomitants_panleu_model)
```

```
##
## Call:
## glm(formula = panleukopenia_positive ~ yn_nconcomitants, family = binom
ial(link = logit),
##     data = bd_panleu)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -1.305  -0.629  -0.629   1.055   1.853
##
## Coefficients:
##                   Estimate Std. Error z value Pr(>|z|)
## (Intercept)        -1.5198     0.2409  -6.309 2.81e-10 ***
## yn_nconcomitantsN   1.8153     0.3355   5.411 6.26e-08 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 244.42  on 191  degrees of freedom
## Residual deviance: 212.48  on 190  degrees of freedom
## AIC: 216.48
##
## Number of Fisher Scoring iterations: 4
```

```r
exp(coef(concomitants_panleu_model))
```

```
##       (Intercept) yn_nconcomitantsN
##          0.218750          6.142857
```

```r
exp(confint(concomitants_panleu_model))
```

```
## Waiting for profiling to be done...
```

```
##                       2.5 %     97.5 %
## (Intercept)       0.1328614  0.3433148
## yn_nconcomitantsN 3.2243668 12.0554717
```

```r
#Age Groups
agegroup_panleu_model <- glm( panleukopenia_positive~ agegroup, data= bd_p
anleu,
```

```
                              family = "binomial" (link=logit))
summary(agegroup_panleu_model)

##
## Call:
## glm(formula = panleukopenia_positive ~ agegroup, family = binomial(link
= logit),
##     data = bd_panleu)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.3824  -0.6835  -0.2195   0.9854   2.7341
##
## Coefficients:
##                    Estimate Std. Error z value Pr(>|z|)
## (Intercept)          -3.714      1.012  -3.669 0.000243 ***
## agegroup< 2           4.184      1.039   4.028 5.62e-05 ***
## agegroup≥ 2 & < 10    2.379      1.053   2.259 0.023877 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 244.42  on 191  degrees of freedom
## Residual deviance: 187.08  on 189  degrees of freedom
## AIC: 193.08
##
## Number of Fisher Scoring iterations: 6

exp(coef(agegroup_panleu_model))

##       (Intercept)       agegroup< 2 agegroup≥ 2 & < 10
##        0.02439024       65.59999997       10.78947368

exp(confint(agegroup_panleu_model))

## Waiting for profiling to be done...

##                           2.5 %       97.5 %
## (Intercept)        0.001375096    0.1118975
## agegroup< 2       13.165417584 1193.7177503
## agegroup≥ 2 & < 10 2.059478832  198.9596904

#Multiple Model

panleukopenia_model <- glm ( panleukopenia_positive ~ neuter + n_animals+
                               vaccinestatus + yn_nconcomitants+ agegroup,
                             data=bd_panleu, family="binomial" (link=logit
))

summary(panleukopenia_model)

##
## Call:
## glm(formula = panleukopenia_positive ~ neuter + n_animals + vaccinestat
us +
```

```
##     yn_nconcomitants + agegroup, family = binomial(link = logit),
##     data = bd_panleu)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -2.4427  -0.5274  -0.1663   0.4348   3.5240
##
## Coefficients:
##                              Estimate Std. Error z value Pr(>|z|)
## (Intercept)                   -8.1966     1.4557  -5.631 1.79e-08 ***
## neuterN                       -0.6202     0.5673  -1.093 0.274282
## n_animalsMORE THAN 1 ANIMAL    0.7729     0.5101   1.515 0.129749
## vaccinestatusNOT UP TO DATE    3.9227     0.8498   4.616 3.91e-06 ***
## yn_nconcomitantsN              1.9893     0.5121   3.884 0.000103 ***
## agegroup< 2                    4.4432     1.1482   3.870 0.000109 ***
## agegroup≥ 2 & < 10             2.3718     1.1156   2.126 0.033500 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 237.73  on 188  degrees of freedom
## Residual deviance: 116.95  on 182  degrees of freedom
##   (3 observations deleted due to missingness)
## AIC: 130.95
##
## Number of Fisher Scoring iterations: 6
```

```
exp(coef(panleukopenia_model))
```

```
##                 (Intercept)                     neuterN
##                2.755764e-04                5.378556e-01
## n_animalsMORE THAN 1 ANIMAL vaccinestatusNOT UP TO DATE
##                2.165965e+00                5.053474e+01
##           yn_nconcomitantsN                 agegroup< 2
##                7.310389e+00                8.504562e+01
##           agegroup≥ 2 & < 10
##                1.071621e+01
```

```
exp(confint(panleukopenia_model))
```

```
## Waiting for profiling to be done...
```

```
##                                    2.5 %       97.5 %
## (Intercept)                 8.502442e-06 3.220737e-03
## neuterN                     1.664130e-01 1.570664e+00
## n_animalsMORE THAN 1 ANIMAL 8.106855e-01 6.102788e+00
## vaccinestatusNOT UP TO DATE 1.182799e+01 3.730932e+02
## yn_nconcomitantsN           2.773749e+00 2.101432e+01
## agegroup< 2                 1.311039e+01 1.751119e+03
## agegroup≥ 2 & < 10          1.732557e+00 2.113755e+02
```