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Clinical diagnoses associated with FIV seropositivity: reexamining expected clinical patterns in a large matched primary care cohort

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Abstract

Background

Feline immunodeficiency virus (FIV) has historically been associated with progressive disease across multiple organ systems, but the clinical effects of naturally acquired infection remain uncertain. This retrospective matched cohort study evaluated whether FIV seropositivity was associated with diagnoses across 12 systems-based categories in a large North American primary care population.

Results

De-identified electronic medical records from more than 1,000 Banfield Pet Hospital clinics collected from January 2013 through December 2023 included 30,034 FIV+ cats aged at least 6 months and 60,184 FIV- controls selected at approximately two controls per FIV + cat and matched by sex and birth year. Per-cat prevalence and unadjusted and adjusted ORs with 95% CIs were calculated using logistic regression. After adjustment for sex and sterilization status, cardiovascular, neurologic, and overall weight/nutrition diagnoses were not associated with FIV seropositivity. Renal/urinary diagnoses showed a small inverse association (adjusted OR, 0.94; 95% CI, 0.89-1.00). Six categories showed weak positive associations (adjusted ORs, 1.12–1.45). Dermatological diagnoses showed a moderate positive association (adjusted OR, 1.68; 95% CI, 1.63–1.73), with abscesses (9.5% vs 4.0%) and dermatitis (14.7% vs 10.0%) contributing prominently. Hematological diagnoses showed a strong positive association (adjusted OR, 6.54; 95% CI, 6.07–7.04), driven mainly by anemia and potentially influenced by surveillance bias and FIV-specific diagnostic coding.

Conclusions

FIV seropositivity was not broadly associated with disease across multiple organ systems in this large primary care population. These findings indicate that historical descriptions substantially overstate the usual clinical impact of naturally acquired FIV. A positive test should prompt hematological evaluation for anemia but, by itself, does not justify euthanasia or exclusion from adoption or return-to-field pathways.

Background

Feline immunodeficiency virus (FIV) was first identified in 1986 after an outbreak of illness in 43 intensively housed cats [1]. This discovery came only a few years after human immunodeficiency virus (HIV) was identified as the cause of acquired immunodeficiency syndrome (AIDS), and HIV research strongly influenced early FIV investigation. Publications at the time emphasized shared biologic features such as $CD4^+$ T-lymphocyte tropism and progressive $CD4^+$ depletion, supporting the use of FIV infection as an animal model for aspects of HIV pathogenesis [2]. Investigators also searched for HIV-analogous

clinical syndromes in FIV+ cats and proposed a parallel, four-stage framework: acute infection, asymptomatic infection, AIDS-related complex (ARC), and feline AIDS [3].

Within this framework, the acute phase lasted approximately 2 weeks and included generalized lymphadenopathy, fever, diarrhea, gingivitis, conjunctivitis, uveitis, icterus, and sepsis [4]. Cats then developed persistent generalized lymphadenopathy for up to 9 months before a prolonged asymptomatic phase lasting 1 to 5 years [3, 5]. During the ARC stage, cats were described as developing chronic secondary respiratory tract infections, conjunctivitis, urinary tract infections, bacterial dermatitis, and chronic abscesses [4]. These conditions were attributed to common feline pathogens, including feline leukemia virus (FeLV), feline herpesvirus (FHV-1), feline calicivirus (FCV), feline coronavirus (FeCoV), *Pseudomonas spp.*, *Staphylococcus spp.*, and *Streptococcus canis* [4, 6].

Other commonly reported conditions included weight loss, generalized lymphadenopathy, fever of unknown origin, chronic oral inflammation (i.e., gingivitis and stomatitis), dermatitis with alopecia and pruritus, gastrointestinal disease with chronic diarrhea, and renal disease. Neurologic signs such as altered behavior, seizures, intention tremors, nystagmus, ataxia, dementia, stereotypic motor behavior, and compulsive roaming were estimated to occur in approximately 5% of otherwise asymptomatic FIV+ cats and a similar proportion of clinically ill cats [6].

Because tumors were observed in FIV+ cats without evidence of infection by tumorigenic viruses such as FeLV, FIV was linked to a broad range of neoplasms, including lymphoma, fibrosarcoma, mast cell tumors, squamous cell carcinoma, myeloproliferative diseases, and rare brain tumors [6]. Up to 10% of clinically ill FIV+ cats were reported to progress to the terminal immunodeficiency stage designated “feline AIDS.” This stage was characterized by severe and often multiple secondary infections that were resistant to treatment, severe anemia and leukopenia, and marked wasting resembling human AIDS [4, 6].

Subsequent evidence regarding the effects of naturally acquired FIV infection on morbidity and mortality has been inconsistent [7–10]. More recent field studies and practice guidelines suggest that the clinical effects of infection are variable and often limited, with many FIV+ cats living for years without progressive disease attributable to the virus [11, 12]. This uncertainty surrounding the prognosis of FIV+ cats has important clinical and animal-welfare consequences because misconceptions may hinder adoption, create inaccurate expectations about their care needs, and contribute to unwarranted euthanasia.

The objective of this study was to determine associations between FIV seropositivity and diagnoses across 12 systems-based disease categories and to assess whether the pattern and magnitude of those associations were consistent with the broad multisystem syndrome historically attributed to FIV infection.

Methods

A retrospective cohort study was conducted using de-identified electronic medical records from a large veterinary practice network (Banfield Pet Hospital) spanning more than 1,000 clinics in the United States, Puerto Rico, and Mexico. Records were standardized and centrally stored with formatted diagnosis fields suitable for research. All feline records from January 2013 through December 2023 were screened. Cats were classified as FIV + if they had a positive antibody test result and were ≥ 6 months old at the time of testing to reduce misclassification from maternal antibodies. Testing was performed using the IDEXX SNAP FIV/FeLV point-of-care antibody assay, which has reported sensitivity of 97.9% and specificity of 99.0% for detection of FIV antibodies [13]. While vaccine-induced seropositivity was possible, it was expected to be uncommon since the vaccine was not routinely used and was discontinued in the United States and Canada in 2015 [12].

FIV- controls were randomly sampled at approximately two controls per FIV + cat and matched by sex and birth year. Duplicate pet records were removed before analysis. The final analytic cohort included 30,034 FIV+ cats and 60,184 FIV- controls. Diagnoses potentially associated with FIV were selected by two authors (BLM, MTR) based on conditions described in the previous literature and their clinical expertise and grouped into 12 system-based categories for analysis: Neoplastic, Dermatological, Oral/Dental, Renal/Urinary, Respiratory, Hematological, Cardiovascular, Neurologic, Ophthalmic, Weight/Nutrition, Infectious/Immune, and Other (Table 1). Cats could contribute diagnoses to more than one category; however, for category-level outcomes, each cat contributed at most one event per category (the first qualifying diagnosis recorded on or after the index FIV test). This prevented inflation of counts from repeated visits for the same condition.

Table 1
Diagnoses evaluated as potentially associated with FIV seropositivity and grouped into 12 categories.

Category	Diagnoses
Neoplastic	Neoplasia, Dermal; Neoplasia, Mammary; Skin Tumors; Neoplasm of Mouth; Neoplasm of Abdomen; Lymphoma; Oral Tumor; Neoplasia, Ear; Mammary Tumor; Neoplasia, Ear Canal; Squamous Cell Carcin/Oral; Lymphosarcoma; Squamous Cell Carcin/Cutaneous
Dermatological	Dermatitis; Dermatitis, Flea Allergy; Dermatitis, Miliary; Acne; Dermatitis, Moist; Seborrhea Sicca; Seborrhea; Dermatitis, Pyotraumatic; Seborrhea Oleosa; Otitis Externa, Medical; Otitis Interna, Medical; Cellulitis, Conservative; Cellulitis, Extensive; Otitis Media; Eosinophilic Ulcer; Pyoderma; Pyoderma, Generalized; Wound Dehiscence; Alopecia, Feline Symmetric; Otitis Media, Medical; Pruritus; Eosinophilic Granuloma; Eosinophilic Granuloma Complex; Abscess, Extensive; Abscess
Oral/Dental	Gingivitis; Tooth, Cervical / Neck Lesions; Gingivostomatitis; Tooth Abscess; Oral/Lingual Ulceration; Tooth Abscess (Carnassial); Oral Eosinophilic Granuloma; Periodontal Disease Stage 3; Gingival Recession; Periodontal Disease Stage 4; Stomatitis; Gingival Hyperplasia; Neck Lesion; Feline Plasmacytic Lymphocytic Stomatitis
Renal/Urinary	Renal Failure, Chronic; Azotemia, Renal; Urinary Tract Infection; Renal Failure, Acute; Azotemia; Urinary Tract Disease, Feline; Anemia of Chronic Renal Failure; Pyelonephritis; Nephritis; Azotemia, Post-renal; Uremia; Azotemia, Pre-renal; Glomerulonephritis; Hematuria; Feline Urologic Syndrome
Respiratory	Respiratory Disease, Feline Upper; Coughing; Rhinitis, Chronic; Rhinitis; Pneumonia; Asthma, Feline; Bronchitis; Asthma; Bronchitis, Allergic; Bronchitis, Chronic; Pharyngitis; Rhinotracheitis; Laryngitis; Sinusitis; Pleuritis; Dyspnea; Pleural Effusion; Pulmonary Edema
Hematological	Anemia, FIV; Feline Infectious Anemia; Leukocytosis; Anemia, Hemolytic Autoimmune; Anemia, Chronic Infection; Anemia, Conservative; Leukopenia; Anemia, Extensive; Anemia, Congenital Hemolytic; Anemia; Thrombocytopenia; Neutropenia, Cyclic; Leukemia, Chronic Lymphocytic
Cardiovascular	Cardiomyopathy, Feline Hypertrophic; Hypertension; Aortic Saddle Thrombus; Heart Failure, Congestive; Cardiomyopathy, Hypertrophic; Heart Failure, Left Sided; Cardiomyopathy, Feline Dilated; Cardiomyopathy, Feline Restrictive; Heart Failure, Right Sided
Neurologic	Seizures; Seizures, Idiopathic; Nystagmus, Acquired; Encephalitis; Meningitis; Seizure, Active; Vestibular Syndrome; Disease of Brain, Undetermined; Brain Disorder; Cranial Nerve Disorder
Ophthalmic	Conjunctivitis; Conjunctivitis, Viral; Corneal Ulcer, Medical; Glaucoma, Medical; Uveitis, Anterior; Corneal Ulcer, Surgical; Corneal Edema; Conjunctivitis, Allergic; Iritis; Conjunctivitis, Bacterial; Uveitis, Posterior; Hyphema; Anisocoria; Chemosis; Blepharitis; Phthisis Bulbi; Keratitis; Descemetocele; Chorioretinitis
Weight/Nutrition	Underweight; Anorexia; Emaciation; Overweight; Obesity
Infectious/Immune	Herpesvirus, Feline; Feline Infectious Peritonitis; Chlamydia; Calicivirus; Systemic Mycosis; Ringworm; Feline Leukemia Virus Infection; Feline Hemobartonellosis; Infection, Viral; Cryptococcosis; Giardia; Notoedric Mange; Lungworms; Roundworms; Ear Mites; Septicemia; Pyometra; Pyothorax;

Category	Diagnoses
	Tapeworm; Inflammatory Bowel Disease; Enteritis; Cytauxzoon felis; Feline Panleukopenia
Other	Hyperthyroidism; Diabetes Mellitus; Lymphadenopathy, localized; Vomiting, Extensive; Lymphadenopathy, Generalized; Fever of Unknown Origin; Dehydration; Pale Gums; Lymphadenopathy; Lymphadenitis; Lethargy; Lymph Node Hyperplasia; Chronic enteropathy

An exploratory data analysis was performed of total visits for cats each month during the study period to visualize anomalies in visitation rates. Prevalence for each category was computed as the proportion of cats with ≥ 1 qualifying diagnosis recorded on or after the index FIV test. Because this metric was calculated per cat rather than per visit, repeated visits for the same condition did not increase prevalence counts.

To assess whether diagnoses occurred more frequently in FIV+ cats than in FIV- cats, a simple logistic regression model was fitted for each of the 12 diagnostic categories listed in Table 1, producing odds ratios (ORs) and 95% confidence intervals (CIs). Strength of positive association was categorized according to published guidance as weak positive (OR, 1.00–1.49), moderate positive (OR, 1.50–2.99), or strong positive (OR, ≥ 3.00) [14]. To examine whether sex and sterilization status affected these relationships, an additional logistic regression model was fitted for each diagnostic category to generate adjusted ORs and 95% CIs. Two-sided P values were reported, with $P < 0.05$ considered statistically significant.

This study used de-identified electronic medical data from client-owned animals. No interventions were performed, and no personally identifiable information was accessed. Institutional review board oversight was not required for this analysis of de-identified veterinary records. All analyses were performed in R.

Generative artificial intelligence (ChatGPT, OpenAI) was used only during manuscript revision for editorial assistance with wording and concision. It was not used to generate or analyze data, conduct statistical analyses, or draw scientific conclusions. All AI-assisted text was reviewed and approved by the authors, who take responsibility for the final content.

Results

Data were collected from January 2013 through December 2023, and the analytic cohort included 30,034 FIV+ cats and 60,184 FIV- controls (90,218 cats total). Each month included at least 1,000 recorded feline veterinary visits, beginning in January 2013, with a steady increase to reach over 4,000 visits per month by June 2016. By March 2019, the number of visits reached over 5,000 cats each month, peaking in June 2020 at 5,803 visits before declining.

Clear seasonal and cyclical patterns were observed in visit volume (Fig. 1). Age and sex distributions were similar between the FIV + and FIV- cohorts, consistent with the matching design. Most cats in both

groups were sterilized, although sterilization was more common among FIV- than FIV+ cats. Intact males were more common among FIV+ cats than FIV- controls (3,636/30,034 [12.1%] vs 3,373/60,184 [5.6%]). Breed distribution was similar across groups, with domestic short hair (DSH) cats representing the overwhelming majority.

Prevalence was similar between the FIV + and FIV- cohorts for most diagnostic categories, with absolute differences of fewer than 4 percentage points. Notable exceptions were the dermatological category (38.1% vs 27.6%; 10.5-percentage-point difference) and the hematological category (10.2% vs 1.7%; 8.5-percentage-point difference), based on diagnoses recorded on or after the index FIV test. Category-level prevalences and association estimates are presented in Table 2. Counts and prevalences for selected diagnoses are presented in Table 3.

Table 2
Prevalence and logistic-regression associations for 12 diagnostic categories in FIV+ cats and matched FIV- controls.

Diagnostic Category	Prev. FIV+	Prev. FIV-	OR (95% CI) FIV + vs FIV−	Adjusted OR (95% CI) FIV + vs FIV−
Neoplastic	3.1%	2.4%	1.34*** (1.23, 1.45)	1.42*** (1.31, 1.55)
Dermatological	38.1%	27.6%	1.62*** (1.57, 1.67)	1.68*** (1.63, 1.73)
Oral/Dental	36.6%	32.5%	1.20*** (1.16, 1.23)	1.32*** (1.28, 1.36)
Renal/ Urinary	6.7%	7.6%	0.87*** (0.83, 0.92)	0.94* (0.89, 1.00)
Respiratory	17.6%	13.0%	1.43*** (1.36, 1.48)	1.45*** (1.40, 1.51)
Hematological	10.2%	1.7%	6.55*** (6.09, 7.06)	6.54*** (6.07, 7.04)
Cardiovascular	0.7%	0.7%	0.99 (0.83, 1.17)	1.07 (0.89, 1.27)
Neurological	0.6%	0.6%	1.04 (0.86, 1.25)	1.07 (0.88, 1.28)
Ophthalmic	11.6%	8.9%	1.33*** (1.27, 1.39)	1.34*** (1.28, 1.41)
Weight/ Nutrition	39.3%	42.1%	0.89*** (0.87, 0.92)	0.99 (0.96, 1.02)
Infectious/ Immune	23.8%	21.8%	1.12*** (1.08, 1.16)	1.12*** (1.09, 1.16)

Prevalence is the proportion of cats with at least one qualifying diagnosis recorded on or after the index FIV test; repeated visits do not increase counts. Denominators were 30,034 FIV+ cats and 60,184 FIV- controls. ORs compare the odds of at least one diagnosis in FIV+ versus FIV- cats. Adjusted ORs include sex and sterilization status. Estimates are shown with 95% CIs. Significance markers are *** $P < 0.001$, ** $P < 0.01$, and * $P < 0.05$; no marker indicates $P \geq 0.05$.

Diagnostic Category	Prev. FIV+	Prev. FIV-	OR (95% CI) FIV + vs FIV−	Adjusted OR (95% CI) FIV + vs FIV−
Other	9.5%	8.2%	1.17*** (1.11, 1.23)	1.21*** (1.15, 1.27)

Prevalence is the proportion of cats with at least one qualifying diagnosis recorded on or after the index FIV test; repeated visits do not increase counts. Denominators were 30,034 FIV+ cats and 60,184 FIV- controls. ORs compare the odds of at least one diagnosis in FIV+ versus FIV- cats. Adjusted ORs include sex and sterilization status. Estimates are shown with 95% CIs. Significance markers are *** $P < 0.001$, ** $P < 0.01$, and * $P < 0.05$; no marker indicates $P \geq 0.05$.

Table 3
Counts and prevalence of selected diagnoses in FIV+ cats and matched FIV- controls.

Specific Diagnosis	FIV+ Cats with Diagnosis	FIV+ Prevalence	FIV- Cats with Diagnosis	FIV- Prevalence
Underweight	2,497	8.3%	4,051	6.7%
Emaciated	93	0.3%	120	0.2%
Anorexia	843	2.8%	1,373	2.3%
Lymphadenopathy (All)	361	1.2%	239	0.4%
Generalized Lymphadenopathy	47	0.2%	27	0.05%
Chronic enteropathy/Enteritis	108	0.4%	221	0.4%
Lymphoma/Lymphoid Cancer	101	0.3%	125	0.2%
Uveitis	108	0.4%	120	0.2%
Conjunctivitis	2,966	9.9%	4,741	7.9%
Anemia	3,079*	10.2%	748	1.2%
Leukopenia or Neutropenia	89	0.3%	49	0.08%
Thrombocytopenia	177	0.6%	133	0.2%
Leukocytosis	309	1.0%	474	0.8%
Hemotropic Mycoplasma	26	0.09%	32	0.06%
Dermatitis	4,423	14.7%	5,938	10.0%
Otitis	6,419	21.4%	9,235	15.3%
Dermatitis/Otitis Externa** (3 or more dx)	907	3.0%	1,203	2.0%
Abscess	2,850	9.5%	2,419	4%
Rhinitis/Chronic Rhinitis	693	2.3%	1,010	1.7%
URI	4,194	14.0%	5,973	10.0%
URI (3 or more dx)**	301	1.0%	422	0.7%

Counts represent unique cats with at least one qualifying diagnosis recorded on or after the index FIV test. Denominators were 30,034 FIV+ cats and 60,184 FIV- controls; repeated visits did not increase counts. * Includes 2,383 cats assigned the FIV-specific diagnosis code “Anemia, FIV”; the remaining 696 anemia diagnoses arose from other anemia codes. ** Defined as at least 3 recorded diagnoses because no specific chronic diagnosis code was available.

Specific Diagnosis	FIV+ Cats with Diagnosis	FIV+ Prevalence	FIV- Cats with Diagnosis	FIV- Prevalence
Stomatitis	1,528	5.1%	943	1.6%
Tapeworm	2,618	8.7%	5,369	8.9%
Feline Leukemia Virus	1,417	4.7%	464	0.8%
Ear Mites	940	3.1%	2,393	4.0%
Roundworms	479	1.6%	1,057	1.8%
Feline Herpesvirus	335	1.1%	703	1.2%

Counts represent unique cats with at least one qualifying diagnosis recorded on or after the index FIV test. Denominators were 30,034 FIV+ cats and 60,184 FIV- controls; repeated visits did not increase counts. * Includes 2,383 cats assigned the FIV-specific diagnosis code “Anemia, FIV”; the remaining 696 anemia diagnoses arose from other anemia codes. ** Defined as at least 3 recorded diagnoses because no specific chronic diagnosis code was available.

Dermatological diagnoses showed a moderate positive association with FIV+ status (OR, 1.62; 95% CI, 1.57–1.67; adjusted OR, 1.68; 95% CI, 1.63–1.73; $P < 0.001$). Common dermatological diagnoses included otitis (21.4% of FIV+ cats vs 15.3% of FIV- cats), dermatitis (14.7% vs 10.0%), and abscesses (9.5% vs 4.0%).

The most notable difference in prevalence between the FIV + and FIV- cohorts was in the hematological diagnostic category, with FIV+ cats outnumbering FIV- cats by 8.5 percentage points (10.2% vs 1.7%). Anemia comprised the majority of the hematological abnormalities and was recorded in 10.2% of FIV+ cats and 1.2% of FIV- cats. Leukopenia or neutropenia was found in 0.3% of FIV + and 0.1% of FIV- cats, while thrombocytopenia was recorded in 0.6% of FIV + and 0.2% of FIV- cats. Hematological diagnoses showed a strong positive association with FIV+ status (OR, 6.55; 95% CI, 6.09–7.06; adjusted OR, 6.54; 95% CI, 6.07–7.04; $P < 0.001$).

A weak negative association was found between FIV+ status and renal/urinary diagnoses (OR, 0.87; 95% CI, 0.83–0.92) and weight/nutrition diagnoses (OR, 0.89; 95% CI, 0.87–0.92). Following adjustment for sex and sterilization status, the weak negative association with renal/urinary diagnoses remained (adjusted OR, 0.94; 95% CI, 0.89–1.00; $P < 0.05$), whereas the association with the overall weight/nutrition category was not maintained (adjusted OR, 0.99; 95% CI, 0.96–1.02; $P > 0.05$). Although the overall weight/nutrition category was not associated with FIV+ status after adjustment, underweight was recorded in 8.3% of FIV+ cats and 6.7% of FIV- cats.

ORs for conditions listed as other, oral/dental, neoplastic, infectious/immune, ophthalmic, and respiratory categories showed a weak positive association with FIV+ status, ranging from 1.12 to 1.43. These associations were maintained following adjustment for sex and sterilization status, with adjusted ORs ranging from 1.12 to 1.45 (all $P < 0.001$). Cardiovascular and neurologic diagnoses were not

associated with FIV+ status after adjustment (cardiovascular: adjusted OR, 1.07; 95% CI, 0.89–1.27; neurologic: adjusted OR, 1.07; 95% CI, 0.88–1.28; both P > 0.05).

Discussion

The principal finding of this large retrospective cohort study was that FIV+ cats did not exhibit the broad pattern of multisystem disease historically attributed to FIV infection. Although FIV seropositivity was positively associated with 8 of the 12 diagnostic categories evaluated, the associations based on the adjusted ORs were weak positive in 6 categories. Associations were weak negative in renal/urinary and not present in cardiovascular, neurologic, and overall weight/nutrition diagnoses. The only larger associations were concentrated in dermatological diagnoses, particularly abscesses and dermatitis, and the hematological diagnosis of anemia, conditions that share environmental, behavioral, and infectious risk factors with FIV acquisition.

Chronic kidney disease and related renal syndromes have historically been proposed as sequelae of FIV infection, largely by analogy with HIV and on the basis of renal lesions described in naturally infected cats [15]. In this cohort, however, renal/urinary diagnoses were slightly less common in FIV+ than FIV- cats (6.7% vs 7.6%) and a weak negative association between FIV seropositivity and renal/urinary diagnoses was found (adjusted OR, 0.94; 95% CI, 0.89–1.00).

Cardiac muscle lesions have likewise been described in FIV+ cats and interpreted as FIV-associated injury [16, 17]. This study found no association with FIV seropositivity (adjusted OR, 1.07; 95% CI, 0.89–1.27) and the same prevalence (0.7%) in FIV + and FIV- cats. While subclinical cardiac lesions were not evaluated in this study, detecting FIV-infected cells within such lesions would not by itself establish causation because infected inflammatory cells may migrate to tissue injured by an unrelated process [2].

Neurologic diagnoses were recorded in 0.6% of each cohort and were not associated with FIV seropositivity (adjusted OR, 1.07; 95% CI, 0.88–1.28). Previous estimates of neurologic disease in FIV+ cats have ranged from approximately 5% to 40%, with the highest estimates derived from experimental inoculation studies [6, 18, 19]. Although these studies demonstrate that FIV can affect the nervous system under experimental conditions, differences in viral dose, inoculation route, and study population limit their applicability to naturally acquired infection and may help explain the marked discrepancy with the present findings. Earlier studies also lacked current molecular diagnostic methods for identifying other pathogens capable of producing similar neurologic signs.

The overall weight/nutrition category was not associated with FIV seropositivity after adjustment, but because the category combined diagnoses in opposing directions, prevalence was determined for both underweight and emaciated cats separately after the primary analysis. Very few cats were emaciated (0.3% of FIV + and 0.2% of FIV-) but 8.3% of FIV + and 6.7% of FIV- cats were classified as underweight. The 1.6-percentage-point difference in underweight cats warrants clinical awareness but these data do not support the broadly prevalent wasting syndrome historically attributed to FIV.

Many reports have stated that chronic gingivostomatitis is one of the most common clinical conditions in FIV-infected cats, with severe oral inflammatory disease described in approximately 50% of affected cats in some early reports [6, 11]. The present data corroborated an association between FIV and oral/dental disease, although its overall strength was weak positive (adjusted OR, 1.32; 95% CI, 1.28–1.36). Gingivostomatitis was diagnosed in 5.1% of FIV+ cats and 1.6% of FIV- cats. Thus, gingivostomatitis deserves clinical attention in FIV+ cats, but its absolute prevalence was substantially below that suggested by some early descriptions. Earlier studies may also have overestimated effects attributable specifically to FIV because molecular testing to identify other pathogens was less robust. Coinfection with feline calicivirus, a well-supported contributor to feline chronic gingivostomatitis, could not be evaluated in this dataset [20, 21].

Across reviews and guidelines, FIV has frequently been framed as an oncogenic cofactor, with tumor prevalence in FIV+ cats reported to be as high as 20% [22]. Lymphoma and leukemia have been discussed specifically, with some studies reporting substantially increased odds among FIV+ cats [23, 24]. In the present study, neoplastic diagnoses had a weak positive association with FIV seropositivity (adjusted OR, 1.42; 95% CI, 1.31–1.55). However, lymphoma or leukemia was diagnosed in only 0.3% of FIV+ cats and 0.2% of FIV- cats. The weak association and low absolute prevalence do not support the conclusion that lymphoma and leukemia are substantially more common among FIV+ cats.

Ophthalmic disease, particularly uveitis, has frequently been portrayed as part of the FIV clinical spectrum, based mainly on a small case series, experimental research, and a postmortem study [25–27]. A study of 120 cats referred for uveitis found FIV seropositivity in 7.3%, whereas prevalences of feline coronavirus, *Toxoplasma gondii*, and *Bartonella spp.* were substantially higher [28]. In the present study, ophthalmic diagnoses had a weak positive association with FIV seropositivity (adjusted OR, 1.34; 95% CI, 1.28–1.41), occurring in 11.6% of FIV + and 8.9% of FIV- cats. Most of this difference involved conjunctivitis, whereas uveitis was recorded in only 0.4% of FIV+ cats. These results corroborate a weak association with ophthalmic disease but do not support uveitis as a common manifestation of natural FIV infection. Shared exposure to other pathogens is a plausible contributor, although the effects of FIV and environmental exposure cannot be separated in this dataset [29].

The weak positive association with respiratory disease (adjusted OR, 1.45; 95% CI, 1.40–1.51) was primarily due to upper respiratory infection diagnoses, which were recorded in 14.0% of FIV + and 10.0% of FIV- cats. Although previous studies have reported chronic upper respiratory infection in as many as 25% of FIV+ cats [4], chronicity could not be formally assessed with this dataset. However, with repeated diagnostic codes examined as a proxy, only 1.0% of FIV + and 0.7% of FIV- cats had 3 or more upper respiratory infection diagnoses. The shared exposure patterns associated with outdoor access and contact with other cats provide a plausible explanation for part of the difference, but this study cannot determine the relative contributions of FIV, lifestyle, and pathogen exposure [30].

Diagnoses in the “other” category had a weak positive association with FIV seropositivity (adjusted OR, 1.21; 95% CI, 1.15–1.27) and were recorded in 9.5% of FIV + and 8.2% of FIV- cats. Chronic enteritis

associated with diarrhea and weight loss has been estimated to occur in at least 10% of cats infected with FIV [4]. In the present dataset, chronic enteritis or enteropathies were uncommon (0.4%) and occurred at the same prevalence in FIV + and FIV- cats. Generalized lymphadenopathy was commonly described in early FIV research and was considered persistent for as long as 9 months following acute infection [4]. In this cohort of 30,034 FIV+ cats, only 47 had a diagnosis of generalized lymphadenopathy, indicating that it was a rare finding.

The infectious/immune category had a weak positive association with FIV seropositivity (adjusted OR, 1.12; 95% CI, 1.09–1.16). Endoparasites, ear mites, FHV-1, and FeLV accounted for most diagnoses in this category. Most occurred at similar prevalences in FIV + and FIV- cats, whereas FeLV was recorded in 4.7% of FIV+ cats and 0.8% of FIV- cats. This difference was similar in direction to a multicenter cross-sectional study in which 13% of FIV + and 2% of FIV- cats tested positive for FeLV [31]. The higher prevalence of FeLV among FIV+ cats is consistent with shared behavioral and environmental risk factors for acquiring both viruses.

Dermatological conditions had a moderate positive association with FIV seropositivity (adjusted OR, 1.68; 95% CI, 1.63–1.73), with diagnoses recorded in 38.1% of FIV + and 27.6% of FIV- cats. This 10.5-percentage-point difference was one of the more apparent differences between the cohorts. The principal diagnoses contributing to the category were otitis (21.4% of FIV + vs 15.3% of FIV- cats), dermatitis (14.7% vs 10.0%), and abscesses (9.5% vs 4.0%). Early reports linked FIV infection to dermatitis and chronic infections of the skin and ear canals, citing prevalences as high as 15% [32], whereas a later review emphasized that infectious dermatoses in cats often have overlapping, nonspecific presentations and require identification of the underlying cause [33]. Although chronicity could not be formally assessed, only 3.0% of FIV + and 2.0% of FIV- cats had 3 or more dermatological diagnostic codes. Outdoor access, ectoparasite exposure, fighting, and bite wounds may have contributed to the excess of dermatitis and abscess diagnoses. Thus, the moderate positive association identifies a notable difference between cohorts but does not establish that FIV itself caused these conditions.

Progressive CD4 + cell depletion has been documented in experimental and natural FIV infection and is consistent with the virus's tropism for this cell population [2, 6]. Despite this biological effect, clinical signs may remain inapparent in naturally infected populations, and an experimental long-term study found that some cats remained clinically well despite very low CD4 + counts [12, 34]. Hematological diagnoses provided the strongest positive association identified in this study (adjusted OR, 6.54; 95% CI, 6.07–7.04). At least one hematological diagnosis was recorded in 10.2% of FIV + and 1.7% of FIV- cats. The association was primarily due to anemia, which was recorded in 10.2% of FIV+ cats and 1.2% of FIV- cats; leukopenia or neutropenia was recorded in only 0.3%, and thrombocytopenia in 0.6%, of FIV+ cats. Thus, the pattern was predominantly one of anemia rather than generalized cytopenia.

This distribution of hematological abnormalities differed from that reported in several previous studies. In an early study by Shelton et al [35], numerous hematological abnormalities were reported in a group

composed primarily of clinically ill FIV+ cats, including anemia (36%), lymphopenia (53%), neutropenia (34%), and thrombocytopenia (8%). Fifty asymptomatic FIV+ cats evaluated by Fujino et al [36] had similarly high prevalences of anemia (30%), leukopenia (26%), and thrombocytopenia (24%). Gleich and Hartmann, however, found a higher prevalence of neutropenia among 90 FIV+ cats but did not identify significant associations with lymphopenia, thrombocytopenia, or anemia [7]. A study of 278 FIV+ cats in 3 cohorts identified hemoglobin concentrations below the reference interval but did not find evidence of generalized cytopenia [9].

The dataset did not permit systematic evaluation of the causes of anemia. The predominance of anemia, with little leukopenia, neutropenia, or thrombocytopenia, did not resemble generalized bone marrow suppression. Hemoplasma infections can cause anemia and share risk factors with FIV infection, including outdoor access and aggressive interactions [37]. However, hemoplasma testing was not standardized, and diagnostic codes were uncommon. FeLV coinfection, although uncommon overall, could account for some cases of nonregenerative anemia, and chronic inflammatory disease may have contributed to others. Surveillance bias is also possible because CBCs may be performed more frequently in FIV+ cats. Additionally, 2,383 FIV+ cats received the FIV-specific diagnostic code “Anemia, FIV,” which was unavailable for FIV- cats and may have inflated the hematological OR. Even with these limitations, the magnitude of the association and absolute difference in anemia prevalence support hematological evaluation and monitoring for anemia in FIV+ cats.

FIV was identified during the HIV/AIDS epidemic, and early research appropriately explored the biological similarities between FIV and HIV, including the potential use of FIV as a model for lentiviral infection [1, 2]. This early analogy, however, may have encouraged concurrent diseases to be broadly attributed to FIV. Many of the clinical syndromes described in the original report [1] can also result from other pathogens commonly encountered in densely housed cat populations, and the infectious disease testing available at the time could not exclude these alternative causes [38–40]. Likewise, findings from subsequent experimental studies using high viral doses or unnatural inoculation routes should not be assumed to represent the usual consequences of naturally acquired infection. Taken together, findings from more than 30,000 FIV+ cats did not reveal the severe, progressive multisystem disease historically attributed to FIV, indicating that this is not a characteristic population-level outcome of naturally acquired infection.

Strengths of this study include the large sample of 90,218 cats, standardized electronic medical records from more than 1,000 primary care clinics, coverage of an 11-year period, and inclusion of approximately 2 sex- and birth-year–matched controls for each FIV + cat. The per-cat analysis prevented repeated diagnostic coding from allowing a small number of frequently evaluated cats to dominate the results. The broad primary care population also complements experimental studies and studies based on referral or clinically selected populations.

Several limitations should be acknowledged. FIV status was based on antibody test results from a single point-of-care test. The test used has reported sensitivity of 97.9% and specificity of 99.0%, limiting but

not eliminating a potential misclassification [13]. A cat could also have tested negative before seroconversion or could have become infected after an earlier negative test. Although vaccine-induced antibodies can persist for more than 7 years, vaccine-associated antibody interference was expected to be uncommon because FIV vaccination was classified as non-core and recommended only for cats at high risk of exposure, was not routinely administered within the Banfield network during most of the study period, and was discontinued in the United States and Canada in 2015 [12].

Data were collected retrospectively from a large clinical database, and diagnostic categorization relied on medical record coding rather than standardized case definitions. Coding practices varied across clinicians and clinics, diagnoses were not always definitive, chronic conditions may have been coded only at initial presentation, and resolved conditions may not have been formally documented as such. These inconsistencies may have introduced misclassification in either direction.

Follow-up time and the number of post-index visits varied among cats. Available visit data indicated that FIV+ cats had slightly more post-index visits than FIV- controls, providing greater opportunity for diagnoses to be detected. This difference may have increased some positive associations through surveillance bias but would not explain the absence of broad associations across multiple organ systems. The per-cat analysis prevented repeated diagnoses from inflating prevalence but could not eliminate differences in the opportunity to receive a diagnosis.

Residual confounding from indoor/outdoor status, colony exposure, socioeconomic factors, diet, dental care, and viral coinfections likely remained despite matching and adjustment. Testing prompted by a concurrent illness may also have increased the apparent association between FIV and the diagnosis that led to testing. Finally, because the dataset was derived primarily from general practice, diagnoses made exclusively in specialty or referral settings may have been underrepresented.

Conclusions

In this large primary care cohort of more than 30,000 FIV+ cats, FIV seropositivity was not broadly associated with disease across multiple organ systems. Among the 12 diagnostic categories evaluated, cardiovascular, neurologic, and overall weight/nutrition diagnoses were not associated with FIV seropositivity, and renal/urinary diagnoses showed a weak negative association. Six categories showed weak positive associations, dermatological diagnoses showed a moderate positive association (principally due to otitis, dermatitis, and abscesses) and hematological diagnoses showed a strong positive association largely due to anemia. Several of these positive associations may reflect the same behavioral and environmental factors that increase the likelihood of FIV exposure—including outdoor access, fighting, ectoparasites, and contact with other cats—rather than direct effects of the virus, although their relative contributions could not be separated in this dataset. Taken together, these findings indicate that historical descriptions substantially overstate the usual clinical impact of naturally acquired FIV. An FIV test result should be interpreted in the context of the individual cat's clinical condition rather than as a prognosis in itself. A positive result should prompt hematological evaluation

for anemia but, by itself, does not justify euthanasia or exclusion from adoption or return-to-field programs.

Declarations

Ethics approval and consent to participate

The study analyzed existing, completely de-identified electronic veterinary medical records from client-owned cats and involved no prospective enrollment, interventions, specimen collection, or access to identifying information about owners. The Pennsylvania State University Human Research Protection Program determined that the project did not meet the definition of human subjects research because no information about humans was collected. Institutional animal care and use committee approval and owner consent were not required for this secondary analysis of de-identified clinical records.

Consent for publication

Not applicable.

Competing Interests

MTR and KT are affiliated with Banfield Pet Hospital, which provided the data analyzed in this study. The other authors declare that they have no competing interests.

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Author Contribution

BLM contributed to study design, developed the diagnostic body-system categories with MTR, interpreted the findings, and led the writing and revision of the manuscript. MTR contributed to the initial study design and data acquisition, developed the diagnostic categories with BLM, prepared an initial manuscript draft, and reviewed and edited the manuscript. KT contributed to the initial study design, data acquisition, and manuscript review and editing. BT contributed to the initial study design and manuscript review and editing. OLB and DL contributed to study design, performed the statistical analyses, and reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Data Availability

The data that support the findings of this study are owned by Banfield Pet Hospital and were used under a data collaboration agreement. Because the records are confidential and proprietary, they are not publicly available. Requests for access must be directed to Banfield Pet Hospital and require its prior written permission.

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Figures

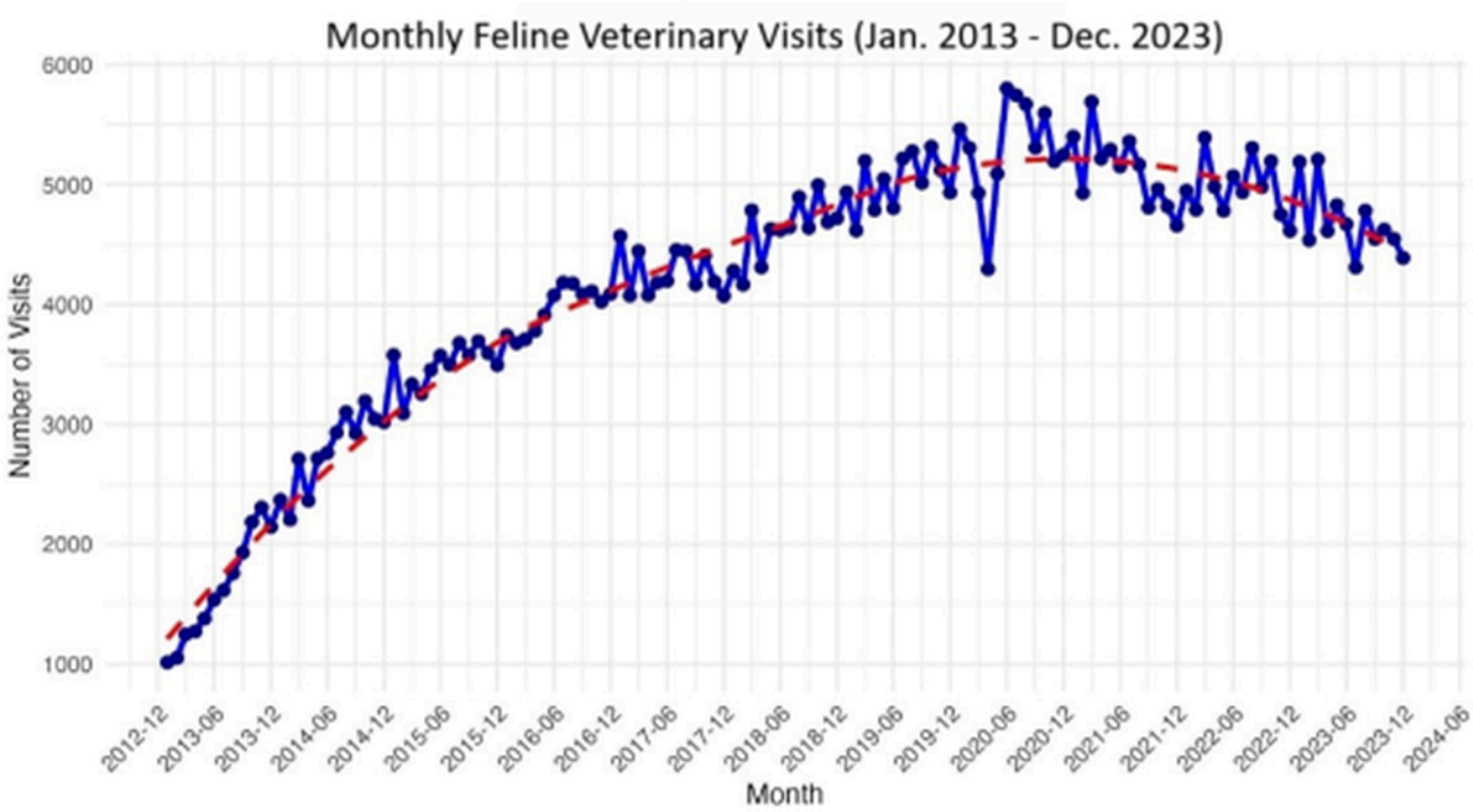

Figure 1

Feline visits per month from January 2013 through December 2023.