



**IDEXX DecisionIQ™**

**Feline hyperthyroidism  
disease risk indication**



**IDEXX**

1

Use of artificial intelligence  
in medicine

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2

Feline hyperthyroidism  
disease risk

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Methods

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Results and discussion

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Clinical utility of the model

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**The Feline Hyperthyroidism Disease Risk Indication feature offered through IDEXX DecisionIQ™ provides insights into patients with an increased likelihood of a diagnosis of hyperthyroidism (based on an increased total T<sub>4</sub>) compared to other cats within 1 of 3 different time frames:**

- **Current disease**
- **Within the next 6 months**
- **Within the next 18 months**



**Collaborative human-machine teams, veterinarians, and artificial intelligence (AI) systems can actively enhance each other's complementary strengths.<sup>1</sup>**

New research shows that significant performance improvements can be achieved when humans and machines work together. Through such collaborative human-machine teams, veterinarians, and artificial intelligence (AI) systems can actively enhance each other's complementary strengths.<sup>1</sup>

In medicine, applications of AI use machine-learning models to search medical data and uncover insights aimed at improving health outcomes and patient experiences. Thanks to recent advances in computer science and informatics, AI is quickly becoming an integral part of modern healthcare.<sup>2</sup> Clinical decision support is one of the most common applications of AI in medicine, and it forms the basis of human-machine teams that seek to raise the standard of care for veterinary patients.

Today, new data sources create opportunities to improve the services we provide to animals by fusing information from both digital and physical worlds. Insights from electronic health records, genomic data, and point-of-care information create new forms of insight into an animal's life. This form of "augmented" intelligence empowers veterinarians and deepens traditional insights in ways that are only recently becoming clear. The Feline Hyperthyroidism Disease Risk machine-learning AI model developed by IDEXX is one such example.





**Predictive modeling provides an opportunity to identify cats with a higher risk of developing hyperthyroidism.**

Hyperthyroidism is the most common endocrine disease in cats and occurs in approximately 10% of senior and geriatric cats.<sup>3-7</sup> Although annual screening of total T<sub>4</sub> (TT4) is recommended for older cats as a component of preventive care, not all older cats receive annual wellness care and not all pet owners approve recommended testing. In fact, TT4 measurements are only performed for 1 in 4 cases where blood is tested in senior cats and 1 in 2 cases in geriatric cats.<sup>8</sup>

This suggests that diagnosis of hyperthyroidism may be delayed in some cats. Undiagnosed and untreated hyperthyroidism can have systemic effects, including hypertension and damage to the heart, eyes, kidneys, and brain. In addition, prolongation of the disease interval prior to curative therapy with disease control has been associated with higher risk of severe hyperthyroidism, increased number of thyroid nodules, and increased risk of malignant transformation of thyroid adenomas.<sup>9</sup>



**The Feline Hyperthyroidism Disease Risk Indication feature is a machine-learning AI model.**

Early identification of cats that have an increased risk for developing elevated TT4 levels may reduce the risk of systemic complications from untreated hyperthyroidism and improve therapeutic outcomes. Predictive modeling may provide an opportunity to identify cats with a higher risk of developing hyperthyroidism, even if the cat has not yet had a TT4 measurement or if increased TTF levels develop between recommended annual screening tests.<sup>1,2</sup>

The Feline Hyperthyroidism Disease Risk Indication feature is a machine-learning AI model that assesses commonly measured biochemical and hematology values as well as patient data to predict the probability of an elevated TT4 level if measured today or of an elevated TT4 level sometime in the medium- to longer-term future. Recommendations based on a positive prediction differ depending on the time frame in which the disease is expected to develop, presence of concurrent disease, and presence or absence of clinical signs.



**Set criteria for inclusion or exclusion in the data sets, as well as the definition of positive, are predetermined by human medical experts.**

## Overview

There are many variations in machine-learning model development. The Feline Hyperthyroidism Disease Risk Indication model uses a form of machine learning that involves utilizing very large sets of anonymized patient data to provide a training set of defined positive cases (patients who have the attribute of interest) and negative cases (patients without that attribute).

Set criteria for inclusion or exclusion in the data sets, as well as the definition of positive, are predetermined by human medical experts. The machine, presented with the training set, looks backwards at patient results in the months prior to the diagnosis. From this data, the machine uses mathematical algorithms to learn the patterns and relationships of weighted analytes and trends, along with other patient data, such as signalment, until it finds the model that best predicts the eventual diagnosis. Once the model is defined, it is reviewed from a medical perspective and validated for performance requirements.



**The model was trained to predict an elevated total T<sub>4</sub> test (> 4.7 µg/dL) using approximately 2.6 million cats who had diagnostic results available for a biochemistry profile, a complete blood count (CBC), and a total T<sub>4</sub> test.**

## Algorithm development

Using a large database of results performed either at IDEXX Reference Laboratories or in-clinic on IDEXX analyzers, the model was trained to predict an elevated total T<sub>4</sub> test (> 4.7 µg/dL) using approximately 2.6 million cats who had diagnostic results available for a biochemistry profile, a complete blood count (CBC), and a total T<sub>4</sub> test. The minimum requirements for the chemistry profile were commonly assessed parameters as found in a chem 10 with electrolytes.

The prediction model was trained using a training set consisting of positive cases defined as cats with a TT4 level above the reference interval (upper limit 4.7 µg/dL) and negative cases defined as cats with a TT4 level within the reference interval ( $\leq$  4.7 µg/dL). Data from the 18 months prior to the elevated TT4 level for positive cats or the most recent 18 months for negative cats was used to train the algorithm. The predictive algorithms provide independent predictions of whether a TT4 level is likely to be > 4.7 µg/dL: 1) today, 2) in 1–6 months, and 3) in 13–18 months. The model parameters were optimized in order to meet predetermined performance criteria of sensitivity  $\geq$  70% and specificity  $\geq$  95%.





## Algorithm testing

A testing set was identified using results from adult cats over 6 years of age from 891,000, 881,000, and 840,000 visits for the 0-, 6-, and 18-month time points, respectively. No data from the training data set was reused in the testing data set. Model performance was evaluated for sensitivity and specificity and to determine whether the model accurately predicted the likelihood that a cat would develop an elevated TT4 level at various time points as outlined above.



**Table 1.**  
Model performance including accuracy, sensitivity, and specificity in predicting elevated TT4 results for different time points.

Excellent performance was found for the immediate-term (today), medium-term (within 6 months) and long-term (within 18 months) predictions. Model accuracy was 95%, 93%, and 91% for the immediate-term, medium-term, and long-term predictions, respectively. The model exceeded the performance requirements for a high specificity  $\geq 95\%$  with sensitivity  $\geq 70\%$  (table 1).

	Accuracy	Sensitivity	Specificity
Immediate (today)	95%	72%	98%
Within 6 months	93%	71%	96%
Within 18 months	91%	71%	95%

**Table 2.**  
Accuracy of the model for predicting elevated TT4 levels for different time points and with and without prior TT4 results.

Accuracy was also measured for cats with or without prior TT4 results (table 2). The medium and long-term models performed with equivalent accuracy regardless of whether prior TT4 results were available. For the immediate model, the presence of prior TT4 results further increased the accuracy to 98%.

	Immediate (today)	Within 6 months	Within 18 months
All cats	95%	93%	91%
Cats without prior TT4 results	94%	93%	91%
Cats with prior TT4 results	98%	94%	91%



**Discordancy rates are based solely on identifying a  $T_4 > 4.7$  and do not account for hyperthyroid cats with high normal  $T_4$  values commonly seen with concurrent disease.**

The rate of discordant results, where the model predicted an elevated TT4 level, but the measured TT4 was within the reference interval, was low at 9% for the immediate-term, 12% for medium-term, and 17% for long-term predictions. Discordancy rates are based solely on identifying a  $T_4 > 4.7$  and do not account for hyperthyroid cats with high normal  $T_4$  values commonly seen with concurrent disease.

Clinical history, medication history, and information about concurrent nonthyroidal illness were not available; therefore, it was not possible to determine how many of these cats may have been hyperthyroid with artificially or physiologically depressed TT4 levels due to concurrent illnesses.

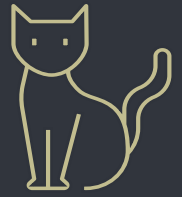


**The Feline Hyperthyroidism Disease Risk Indication model has demonstrated excellent predictive accuracy when identifying cats at increased risk of developing TT4, even if the cat has not previously had a TT4 result.**

This model was developed with the goals of enabling earlier detection of feline hyperthyroidism as well as identifying those cats who may be at increased risk of developing hyperthyroidism in the future compared to other senior cats and who would therefore benefit from more frequent preventive care visits and bloodwork. Knowledge of this increased risk may facilitate conversations with pet owners who may be reluctant to bring their cats in for regular wellness checks.

The Feline Hyperthyroidism Disease Risk Indication model has demonstrated excellent predictive accuracy when identifying cats at increased risk of developing elevated TT4, even if the cat has not previously had a TT4 result.

The model requires only those basic analytes commonly measured during preventive care bloodwork, such as those found in a chem 10 with electrolytes and a CBC. The presence of historical TT4 results is not required for accurate predictions for any of the time frames, but historical TT4 results do enhance the accuracy of identification of cats at immediate risk.



**Concurrent systemic illness may artificially decrease TT4 levels due to “euthyroid sick syndrome.”**

While an increased TT4 level in a cat with consistent clinical signs is generally considered diagnostic of hyperthyroidism, not all cats with clinical hyperthyroidism will have a TT4 level above the reference interval. In some cases, the apparent discordance between TT4 levels and clinical signs may be associated with biological variation in TT4 levels within the patient due to fluctuations of the hormone throughout the course of the day. This biological variation may be especially apparent early in the course of disease. Of perhaps greater importance, however, is the impact of concurrent systemic illnesses that may commonly be found in older cats.

Concurrent systemic illness may artificially decrease TT4 levels due to “euthyroid sick syndrome.” These cats may have TT4 levels at the middle to high end of the reference interval, making it more challenging to diagnose hyperthyroidism in cats with comorbidities. In cases where model predictions, clinical signs, and measured TT4 do not align, further investigation of thyroid function, such as free T<sub>4</sub> testing, technetium scan (<sup>99m</sup>TcO<sub>4</sub><sup>-</sup>), or T<sub>3</sub> suppression testing, is recommended.



**Only the veterinarian, with their deeper insights into each specific patient, can diagnose hyperthyroidism.**

**It is important to recognize that AI machine-learning models are not a replacement for human experts.**

The predictive models have access to limited information about each patient, and therefore, they can only provide information regarding the relative risk of disease. A positive prediction is not a guarantee of an elevated TT4 level now or in the future. Only the veterinarian, with their deeper insights into each specific patient, can diagnose hyperthyroidism or determine the best course of action for their patient at increased risk of developing hyperthyroidism in the future.

**The model predictions instead provide additional data for veterinarians to consider when creating a personalized diagnostic and monitoring plan to achieve earlier diagnosis and treatment of hyperthyroid cats.**

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