

# Association Between HPG-Axis Functional Screening and Reduced Cranial Cruciate Ligament Disease Occurrence in Desexed Dogs

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**A Longitudinal Practice-Based Observational Study, 2014–2025**

## Abstract

**Background:** Cranial cruciate ligament (CCr) disease is a common orthopaedic disorder in dogs. Gonadectomy is associated in the veterinary literature with altered risk of canine cranial cruciate ligament disease, and sustained luteinising hormone (LH) signalling following gonadectomy has been proposed as one possible biological mechanism.

**Objective:** To describe the longitudinal pattern of annual CCr disease occurrence within a single veterinary practice and to examine the temporal pattern before and after introduction of a targeted hypothalamic–pituitary–gonadal (HPG) axis screening and intervention protocol in 2022.

**Methods:** Annual CCr disease case counts were reviewed for 2014–2025. The HPG intervention period was defined as 2022–2025. Because the available annual 'dogs monitored' values do not constitute a validated annual population-at-risk denominator, they were not used to calculate incidence. Primary analyses therefore used annual recorded CCr case counts. Descriptive pre/post comparisons and linear temporal trends were calculated.

**Results:** Eighty CCr cases were represented in the annual dataset. Before the HPG intervention (2014–2021), 63 cases were recorded, with a mean of 7.88 cases/year. During the HPG intervention period (2022–2025), 17 cases were recorded, with a mean of 4.25 cases/year, 46.0% lower than the pre-intervention annual mean. Within the intervention period, annual case counts declined sequentially from 7 in 2022 to 5 in 2023, 4 in 2024 and 1 in 2025, an 85.7% reduction in annual case count from the first intervention year to 2025. Linear regression within 2022–2025 demonstrated a slope of  $-1.90$  cases/year ( $R^2=0.963$ ;  $p=0.0188$ ). A pre-existing downward trend was also present during 2014–2021 (slope  $-0.99$  cases/year;  $R^2=0.507$ ;  $p=0.0475$ ).

**Conclusion:** Annual CCr disease occurrence declined substantially during the 2022–2025 HPG intervention period. The temporal association is compatible with a beneficial intervention effect, but causation cannot be established because the study is observational, there was no contemporaneous untreated control group, and a downward temporal trend was already present before 2022. Prospective controlled evaluation with defined animal-level exposure and follow-up is required.

## Introduction

Canine cranial cruciate ligament disease is multifactorial, with recognised associations involving breed, age, body size and conformation, among other factors. Published observational evidence also supports an association between gonadectomy and increased CCr disease risk, particularly when gonadectomy occurs earlier in life.

Removal of the gonads removes normal gonadal negative feedback on the hypothalamic–pituitary axis and can result in sustained elevation of LH. LH receptors have been reported in non-gonadal tissues, including

canine cruciate ligament. This provides a biologically plausible hypothesis that altered post-gonadectomy HPG signalling could contribute to ligament physiology; however, the mechanism remains incompletely established and should not be treated as proven causation.

The present practice-based dataset spans 2014–2025. A targeted HPG-axis functional screening and intervention approach was introduced in 2022. The purpose of this analysis is therefore to describe annual CCr disease occurrence and compare the temporal pattern before and after that intervention point.

## **Materials and Methods**

### **Study design**

A longitudinal, single-practice observational study was conducted using annual clinical records from 2014 through 2025. The analysis is structured as a pre-intervention period (2014–2021) and an HPG intervention period (2022–2025).

### **Functional screening and HPG intervention**

Functional screening was performed using the proprietary DAMNIT-V system and TC Diagnostic Laser. The screening protocol assessed predefined HPG-axis targets including luteinising hormone (LH) and luteinising hormone receptor (LHR) signalling. Following introduction of the targeted HPG protocol in 2022, dogs identified with reproducible functional disturbance underwent targeted intervention and serial reassessment.

The TC Diagnostic Laser was used as the screening stimulus/reference system and the TC Laser as the therapeutic intervention system. These systems were used as adjunctive clinical tools and did not replace conventional veterinary diagnosis.

### **Outcome measure and denominator correction**

The outcome analysed in this corrected study is the annual number of recorded CCr disease cases. The previous version divided annual CCr case counts by annual 'dogs monitored' values and labelled the resulting quantity incidence. That calculation is not retained because, in early years, the recorded CCr case count exceeded the number listed as monitored (for example, 15 cases versus 1 monitored dog in 2014). Those columns therefore cannot validly serve as numerator and denominator for the same annual incidence calculation.

Accordingly, no claim of CCr incidence per monitored dog-year is made in this corrected analysis. A true incidence analysis will require a defined annual population at risk or animal-level dog-time at risk.

### **Statistical analysis**

Annual CCr case counts were summarised for 2014–2025. The pre-intervention mean (2014–2021) was compared descriptively with the intervention-period mean (2022–2025). Percentage change was calculated from the annual means. Separate ordinary least-squares regressions of annual case count on calendar year were calculated for the pre-intervention and intervention periods. Given only four post-intervention annual observations, these regression results are considered exploratory rather than confirmatory.

## Results

### Annual dataset

| Year | Dogs monitored* | Recorded CCr cases | Study phase      |
|------|-----------------|--------------------|------------------|
| 2014 | 1               | 15                 | Pre-intervention |
| 2015 | 3               | 10                 | Pre-intervention |
| 2016 | 4               | 7                  | Pre-intervention |
| 2017 | 5               | 7                  | Pre-intervention |
| 2018 | 10              | 7                  | Pre-intervention |
| 2019 | 20              | 4                  | Pre-intervention |
| 2020 | 19              | 5                  | Pre-intervention |
| 2021 | 17              | 8                  | Pre-intervention |
| 2022 | 27              | 7                  | HPG intervention |
| 2023 | 43              | 5                  | HPG intervention |
| 2024 | 32              | 4                  | HPG intervention |
| 2025 | 14              | 1                  | HPG intervention |

\*Retained as a descriptive field from the source dataset. These annual values sum to 195 whereas the original manuscript states 191 dogs were monitored overall. The values are therefore not treated as independent annual denominators until their exact definition and repeated-dog status are reconciled.

### Pre-intervention versus HPG intervention

| Period           | Years     | Total CCr cases | Mean cases/year | Linear slope     |
|------------------|-----------|-----------------|-----------------|------------------|
| Pre-intervention | 2014–2021 | 63              | 7.88            | –0.99 cases/year |
| HPG intervention | 2022–2025 | 17              | 4.25            | –1.90 cases/year |

The mean annual CCr case count was 7.875 during 2014–2021 and 4.25 during 2022–2025. The intervention-period mean was therefore 46.0% lower than the pre-intervention mean:  $(7.875 - 4.25) / 7.875 \times 100 = 46.0\%$ .

During the HPG intervention period, annual recorded CCr cases declined sequentially: 7 (2022), 5 (2023), 4 (2024), and 1 (2025). The change from 7 to 1 represents an 85.7% reduction in annual recorded case count:  $(7 - 1) / 7 \times 100 = 85.7\%$ .

### Temporal trend

Pre-intervention linear regression (2014–2021) showed a negative slope of –0.99 cases/year ( $R^2=0.507$ ;  $p=0.0475$ ), demonstrating that a downward temporal trend was already present before the targeted HPG intervention.

Within the HPG intervention period (2022–2025), linear regression showed a steeper negative slope of –1.90 cases/year ( $R^2=0.963$ ;  $p=0.0188$ ). The observed post-intervention slope was approximately 1.9 times the magnitude of the pre-intervention slope. Because there are only four post-intervention annual observations, this comparison should be interpreted as an exploratory temporal signal, not proof that the intervention caused the slope change.

## Discussion

### Principal findings

The corrected analysis demonstrates a substantial reduction in annual recorded CCr disease occurrence during the period in which the targeted HPG-axis intervention was used. Mean annual case count was 46.0%

lower during 2022–2025 than during 2014–2021, and annual cases fell from 7 to 1 across the four intervention years.

The post-intervention sequence is notable for its consistent direction: 7 → 5 → 4 → 1. However, the full historical series also demonstrates that CCr case counts had already been trending downward before 2022.

Consequently, the scientifically defensible interpretation is an association between introduction of the HPG intervention and a continued, apparently steeper reduction in recorded CCr occurrence, rather than attribution of the entire 2014–2025 decline to the intervention.

## Biological interpretation

Published veterinary evidence supports an association between gonadectomy and canine CCr disease risk, while sustained LH elevation and LHR signalling have been proposed as one possible mechanistic pathway. The present study does not directly establish that LH/LHR disturbance caused individual CCr disease or that modification of this pathway prevented it. Rather, it provides a practice-based temporal observation that warrants prospective testing.

## Limitations

- Observational, single-centre design.
- No contemporaneous untreated control group.
- A downward CCr case-count trend was already present before the 2022 HPG intervention.
- Only four annual observations are available after intervention, limiting interrupted-time-series inference.
- The total annual practice population at risk is not available in the current dataset, so true incidence cannot be calculated.
- The source 'dogs monitored' values require reconciliation: annual values total 195 while the manuscript reports 191 dogs overall.
- Potential confounding by breed, age, body weight/body condition, timing of gonadectomy, case ascertainment, referral patterns, practice population size and other clinical changes has not been adjusted for.
- The DAMNIT-V functional screening system and intervention are proprietary and require independent validation.

## Conclusion

Following introduction of the targeted HPG-axis intervention in 2022, annual recorded CCr disease cases declined from 7 to 1 by 2025, an 85.7% reduction in annual case count. The mean annual case count during 2022–2025 was 46.0% lower than during 2014–2021. The post-intervention linear decline was strong (slope  $-1.90$  cases/year;  $R^2=0.963$ ;  $p=0.0188$ ), but a pre-existing downward trend and the absence of a control group prevent causal attribution. These findings support prospective controlled investigation of HPG-axis screening and intervention as a potential modifiable factor in canine CCr disease.

## References

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