JAVMA

AVMA

# Horses diagnosed with pituitary pars intermedia dysfunction do not have shorter life expectancies but experience more medical events during their lifetime

Emma Stapley, DVM, DACVIM; Caroline Gillespie-Harmon, DVM, MS, DACVS; Sarah Waxman, DVM, MS, DACVS; Amanda Farr, DVM, DABVP; François-René Bertin, DVM, PhD, DACVIM*

Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Purdue University, West Lafayette, IN

*Corresponding author: Dr. Bertin (fbertin@purdue.edu)

**Objective**
The frequency of comorbidities in horses with pituitary pars intermedia dysfunction (PPID) in first-opinion practice is unknown. It is hypothesized that horses with PPID would have more frequent medical events and be euthanized at a younger age.

**Methods**
This was a case-control retrospective study. Medical records ranging from 1996 to 2024 including 132 horses diagnosed with PPID and 274 controls matched by age and breed were reviewed. Variables associated with PPID were evaluated with a Fisher exact or Mann-Whitney *U* test followed by conditional logistic regression. Results were reported as median (IQR) and percentage of total.

**Results**
Horses diagnosed with PPID were not euthanized at a younger age (median of 26 years [IQR, 22 to 31 years] vs median of 24 years [IQR, 21 to 29 years]). Factors independently associated with a diagnosis of PPID were poor healing, dental issues (including missing tooth or diagnosis of equine odontoclastic tooth resorption and hypercementosis), hyperinsulinemia-associated laminitis, and being prescribed NSAIDs.

**Conclusions**
The use of NSAIDs and occurrence of poor healing, hyperinsulinemia-associated laminitis, and dental issues were independently associated with a diagnosis of PPID.

**Clinical Relevance**
Horses diagnosed with PPID did not have shorter life expectancies but experienced more medical events during their lifetime compared to horses not diagnosed with PPID.

**Keywords:** pituitary pars intermedia dysfunction, laminitis, endocrinology, calcium, tooth

Pituitary pars intermedia dysfunction (PPID) is a common neurodegenerative condition in older horses, affecting approximately 20% of horses over 15 years of age.[1] The condition is associated with a constellation of clinical and clinicopathologic abnormalities including hypertrichosis, muscle atrophy, impaired athletic and reproductive performance, abnormal sweating, recurrent infections, desmitis, increased susceptibility to endoparasites and corneal ulcers, polyuria and polydipsia, and lethargy or otherwise abnormal behavior, as well as insulin dysregulation and an increased risk for hyperinsulinemia-associated laminitis (HAL).[2–7]

Received August 8, 2025
Accepted November 4, 2025
Published online December 17, 2025

doi.org/10.2460/javma.25.08.0533



Age is the most conclusively identified risk factor for the development of PPID; however, old age is also associated with increased risks for osteoarthritis, dental disease, ocular disorders, and exaggerated insulinemic responses to dietary carbohydrates.[4,8,9] Although hepatic, renal, pulmonary, and cardiac abnormalities have been identified histologically, and gastrointestinal intestinal dysbiosis and decreased lumbar bone mineral density have been documented in horses with PPID, the respective effects of PPID and old age are poorly understood.[10–12] Prior work has focused primarily on referral populations or owner-reported signs, both of which represent biases in the description of the clinical picture of PPID, and frequency of comorbidities of old horses with and without PPID in primary care practice.[3,10,13–15]

Comorbidities experienced over a horse's lifetime also play a major role in the owner's willingness to treat PPID, regardless of whether or not these conditions are actually linked to PPID.[16] Therefore,

information regarding the frequency and type of comorbidities experienced by horses diagnosed with PPID would be of significant benefit to equine veterinarians who must regularly help clients navigate treatment decisions in horses with PPID.

The aim of the current study was to assess the frequency and type of medical events in horses and ponies diagnosed with PPID in primary care practice. It was hypothesized that horses with PPID would have more frequent medical events and be euthanized at a younger age.

## Methods

### *Case selection*

Medical records obtained from the Purdue University Equine Field Service were reviewed. Records from the Purdue University Veterinary Hospital were only used when enrolled animals were treated at that hospital.

All horses and ponies diagnosed with PPID by any means were included, but donkeys and mules were excluded. A diagnosis of PPID was based on primary care veterinarian diagnosis including ACTH concentrations higher than seasonally adjusted diagnostic cutoff values at baseline and 10 or 30 minutes after administration of thyrotropin-releasing hormone (TRH), consistent clinical signs, and identification of a pituitary adenoma at necropsy.[17–19] Hormonal testing was performed at the institution's diagnostic laboratory on an Immulite 1000 Chemiluminescent Assay (Siemens Healthineers) and interpreted based on the seasonally adjusted reference ranges or overall reference ranges available to the attending veterinarians in the year of diagnosis.

Control animals were selected from horses or ponies > 11 years of age not diagnosed with PPID by the attending veterinarian. Control cases were identified first from owners who had > 1 horse tested for PPID; if no horse met this criterion, controls were identified from the Purdue University Equine Field Service patient list, with each horse or pony diagnosed with PPID matched with 2 controls of the same breed type. If an owner had 1 horse diagnosed with PPID and more than 2 appropriate controls, all same-owner controls were included. If an owner had 1 horse with PPID and 1 control of a similar age of a moderately different breed type, the same-owner control was included and 2 additional breed-matched controls were added.

### *Data collection*

Medical records were reviewed from the start of each animal's record through the end of November 2024. Duration of the medical record, signalment (including base coat color), type of activity, location of boarding (at the time of diagnosis), reason for testing for PPID, medical events, treatments administered, and reason for euthanasia were recorded when available. Boarding location was recorded as *private residence* or *boarding facility* and classified as *rural* or *suburban* based on the Indiana demographic registry. Medical events were recorded as numbers (total and per year) and type. If a diagnosis of a medical event was considered likely by the attending veterinarian or the animal was treated for the condition, the medical event was considered to have occurred. If a medical event was reported to an attending veterinarian but managed by an owner without veterinary attention, it was considered to have occurred. A diagnosis of PPID was not counted as a medical event, as it was the variable that defined the groups, but a comorbidity prompting diagnostic testing for PPID was. Medical events were only considered as total counts and were not grouped as occurring before or after PPID diagnosis. Treatments administered were recorded as *antimicrobials*, *single course of NSAIDs* (which had a listed stop date or was not refilled), and *long-term daily administration of NSAID* (which was defined as a prescription for NSAID that was refilled regularly or otherwise described as intended for long-term use).

### *Statistical analysis*

Horses were grouped based on their PPID status. Shapiro-Wilk tests were used to assess the normality of continuous data. Nonnormally distributed continuous variables were reported as median (IQR) and normally distributed data were reported as mean ± SD. Categorical variables were reported as counts and percentages. Time-varying data were considered as fixed at the time of diagnosis, acknowledging the risk of misclassification and the possible time-dependent confounding. Univariable analysis was used to identify factors associated with a diagnosis of PPID by use of unpaired *t* tests or Mann-Whitney *U* tests, depending on distribution of continuous variables, and a Fisher exact test for categorical variables due to small observed counts. These analyses were performed without stratification, providing an initial overview of associations across the dataset. While independence of cases was not assumed, this approach allowed for a broad identification of potential variables of interest prior to more refined, matched multivariable analysis acknowledging the possibility of excluding variables that appeared nonsignificant when unmatched. Conditional multivariable logistic regression was then conducted to account for the matched case-control design, with *owner* specified as the stratification variable. Collinearity of continuous variables was checked with a correlation matrix of Spearman correlations to account for nonnormally distributed variables. An automated backward stepwise regression was used, with $P \leq .20$ in univariable analyses to enter and $P < .05$ to stay in the model. Model selection and fit were assessed with likelihood ratio tests and omnibus tests of model coefficients. The final model included only predictors that remained statistically significant after adjustment for the matching. Univariable analysis was performed with Prism (macOS version 10.4.1; GraphPad Software Inc), and conditional logistic regression was done with SPSS Statistics (macOS version 30; IBM Corp).

## Results

### *Signalment*

A total of 406 animals met the inclusion criteria, including 132 horses and ponies diagnosed with PPID and 274 controls. A total of 228 owners were included who owned a median of 1 horse (IQR, 1 to

2 horses). There was no significant difference in the birth year of horses diagnosed with PPID and controls (median of 1999 [IQR, 1994 to 2003] vs median of 1999 [IQR, 1996 to 2007]; *P* = .70), confirming age-matching, and the median age at the time of PPID diagnosis was 23 years (IQR, 18 to 25 years). Of the 132 horses diagnosed with PPID, there were 77 geldings (58.3%), 54 mares (40.9%), and 1 stallion (0.76%), while, of the 274 controls, there were 162 geldings (59.1%), 108 mares (39.4%), and 4 stallions (1.5%). Sex was not significantly different between the 2 groups (*P* = .75). Horses diagnosed with PPID and controls included a variety of breeds **(Supplementary Table S1)**, and breed type was not significantly different between the 2 groups (*P* = .90). Horses diagnosed with PPID and controls included a variety of coat colors, and base coat colors were not significantly different between horses with PPID and controls (*P* = .44). Ten horses diagnosed with PPID had 3 controls: 4 of 10 due to a control that was owner- but not breed-matched and 6 of 10 due to the owner having 3 equal quality controls.

### *Boarding and use*

Of the 132 horses diagnosed with PPID, 67 (50.8%) were kept in suburban areas and 65 (49.2%) in rural areas; of the 274 controls, 120 (43.8%) were kept in suburban areas and 154 (56.2%) in rural areas. Urbanization was not significantly different between the 2 groups (*P* = .20). Horses diagnosed with PPID were significantly more likely to be kept at the owner's home, with 82 of 132 (62.1%) kept at home and 50 of 132 (37.9%) boarded. Of the 274 controls, 139 (50.7%) were boarded and 135 (49.3%) were kept at home (*P* = .02).

The 132 horses diagnosed with PPID included 121 (91.7%) that were or had been used for light work and 7 (5.3%) that were or had been used for moderate to intense work. The 274 control horses included 263 (95.9%) that were or had been used for light work and 11 (4.0%) that were or had been used for moderate to intense work. Activity level was not significantly different between groups (*P* = .61).

### *Diagnosis of PPID*

Of 132 horses with PPID, 125 (94.7%) were diagnosed following hormonal testing. The reason for testing included abnormal haircoat in 47 of 125 (37.6%), diagnosis of insulin dysregulation in 28 of 125 (22.4%), unexplained infections in 15 of 125 (12.0%), muscle atrophy in 11 of 125 (8.8%), changes in behavior in 6 of 125 (4.8%), age-related screening in 3 of 125 (2.4%), and abnormal sweating in 1 of 125 (.8%). In 12 of 125 (9.6%), no reason for testing could be identified in the medical record, and 10 of 125 (8.0%) included a reason categorized as *other*.

Of the 132 horses diagnosed with PPID, 90 (68.2%) were initially diagnosed based on the results of baseline ACTH concentrations, 35 (26.5%) were diagnosed based on the results of ACTH concentrations 10 minutes after TRH stimulation (7 of 35 included only after TRH ACTH concentrations; none used the 30-minute time point), 5 (3.8%) had been diagnosed before entering the practice with reasons for and results of initial testing not transferred, 2 (1.5%) were diagnosed based on clinical signs without concurrent hormonal testing, and 1 (0.8%) had an antemortem diagnosis of PPID confirmed at necropsy. For cases in which only baseline ACTH was measured, the median ACTH concentration at the time of PPID diagnosis was 114.5 pg/mL (IQR, 70.1 to 253.8 pg/mL). Some horses were diagnosed despite ACTH concentrations below the diagnostic threshold because of severe clinical signs consistent with PPID. The median baseline ACTH concentration that led to a diagnosis of PPID when a TRH stimulation was performed was 34.0 pg/mL (IQR, 28.0 to 43.4 pg/mL), and the median ACTH concentration that led to a diagnosis of PPID after TRH stimulation was 376 pg/mL (IQR, 235 to 518 pg/mL). Of the 127 horses diagnosed with PPID by the Purdue University Equine Field Service, 1 (0.8%) was diagnosed in 2008, 1 (0.8%) was diagnosed in 2014, 3 (2.4%) were diagnosed in 2015, 2 (1.6%) were diagnosed in 2016, 6 (4.7%) were diagnosed in 2017, 9 (7.1%) were diagnosed in 2018, 9 (7.1%) were diagnosed in 2019, 11 (8.7%) were diagnosed in 2020, 17 (13.4%) were diagnosed in 2021, 20 (15.7%) were diagnosed in 2022, 25 (19.7%) were diagnosed in 2023, and 23 (18.1%) were diagnosed in 2024.

### *Medical events*

Horses diagnosed with PPID had significantly more total medical events than controls (median of 7 events [IQR, 4 to 11 events] vs median of 5 events [IQR, 3 to 9 events]; *P* = .01) but no more medical events per years of records (median of 0.7 events/y [IQR, 0.4 to 1.2 events/y] vs median of 0.6 events/y [IQR, 0.3 to 1.2 events/y]; *P* = .3). Horses diagnosed with PPID had significantly fewer medical events per year before compared to after diagnosis (median of 0.5 events/y [IQR, 0.3 to 0.92 events/y] vs median of 1.5 events/y [IQR, 0.5 to 2.8 events/y]; *P* < .001; **Table 1**).

**Table 1**—Factors considered in the multivariable analysis.

| Variable | *P* value |
|---|---|
| Boarding | .02* |
| Urbanization | .2 |
| Hoof abscess | .2 |
| High fecal egg count | .03* |
| Loose manure | .2 |
| Poor healing | .05 |
| Antimicrobial use | .07 |
| Equine odontoclastic tooth resorption and hypercementosis[a] | .006* |
| Missing tooth[a] | .1 |
| Dental issue | < .001* |
| Hyperinsulinemia-associated laminitis | < .001* |
| Adiposity | .1 |
| Osteoarthritis | .2 |
| NSAID use | .006* |
| Phenylbutazone use[a] | .002* |
| Fever of unknown origin | .2 |
| Neurologic disease (spinal/peripheral nerve) | .03* |
| No. of medical events | .004* |

*$P < .05$ with univariable analysis.

[a]Variable removed for collinearity or as part of a composite variable.

Medical events included endocrine (regional adiposity and HAL), musculoskeletal (subsolar abscess, tendinopathy, osteoarthritis, nondental bone fracture, and lameness not attributed to other included causes), dental (equine odontoclastic tooth resorption and hypercementosis [EOTRH], dental extraction, diastema, fractured tooth, and missing tooth), ocular (corneal ulcer, immune-mediated keratitis, conjunctivitis, and enucleation), gastrointestinal (fecal egg count [FEC] > 200 eggs/g, medically managed colic, gastric ulcers, and loose manure or excess fecal water without other reported clinical abnormalities), allergic (asthma, insect bite hypersensitivity, and other allergic reactions), integument (dermatopathy, evidence of ectoparasites, cellulitis, and melanomas), and other medical events (fever of unknown origin, weight loss, peripheral or central neurologic deficit, cardiac murmur, esophageal obstruction, poor healing, anxious personality, and systemic inflammatory response syndrome) as well as general anesthesia (elective and emergent conditions; Supplementary Table S1).

When only animals diagnosed with HAL were considered, there was no significant difference in the number of times HAL reoccurred between PPID and control groups (median of 1 [IQR, 2 to 1] vs median of 1 [IQR, 1 to 1]; $P = .10$). When only animals with ≥ 1 high FECs were considered, there was no significant difference in the number of times high FECs reoccurred between horses with PPID and controls (2 [1 to 4] vs 2 [1 to 5]; $P = .15$; Table 1).

### *Treatment*

Of the 132 horses diagnosed with PPID, 125 (94.7%) received pharmaceutical treatment for PPID. Of these 125 horses, 120 (96.0%) received the labeled form of pergolide (Prascend) and 5 (4.0%) received compounded pergolide, including 4 animals where < 0.5 mg was indicated and 1 horse where rationale was not listed. No horse received cabergoline. Of the horses not receiving pharmaceutical treatment, 3 of 7 (42.9%) had treatment delayed at the attending veterinarian's discretion due to a combination of mild clinical signs and a mild increase (< 5 pg/mL) in ACTH concentration, 2 of 7 (28.6%) had owners decline treatment for financial reasons, and 2 of 7 (28.6%) did not have a reason reported. No control horses received treatment for PPID.

Nonsteroidal anti-inflammatory drugs were prescribed to 73.5% (97 of 132) of PPID horses and 59.5% (163 of 274) of controls ($P = .006$). Phenylbutazone was the only type of NSAID that was more frequently prescribed to horses diagnosed with PPID. Of the 132 horses diagnosed with PPID, 76 (57.6%) received ≥ 1 course of phenylbutazone; of the 274 controls, 114 (41.6%) received ≥ 1 course of phenylbutazone ($P = .002$). Horses with PPID received more courses of phenylbutazone than controls (median of 1 course [IQR, 0 to 2 courses] vs median of 0 courses [IQR, 0 to 1 course]; $P < .001$) and more courses of phenylbutazone per years of records (median of 0.08 courses/y [IQR, 0.00 to 0.12 courses/y] vs median of 0.00 courses/y [IQR, 0.00 to 0.00 courses/y]; $P = .002$) but were not more likely to be on long-term treatment (29 of 132 [22.0%] vs 40 of 274 [14.6%]; $P = .07$). Of the 132 horses diagnosed with PPID, 60 (45.5%) received ≥ 1 course of any systemic antimicrobial agent; of the 274 controls, 111 (40.5%) received ≥ 1 course ($P = .39$; Table 1; Supplementary Table S1).

### *Survival*

Horses with PPID alive at the end of the study period were significantly older than surviving controls (median of 24 years [IQR, 21 to 28 years] vs median of 20 years [IQR, 16 to 23 years]; $P < .001$). At the end of the study period, 34 of 132 horses with PPID (25.8%) and 33 of 274 controls (12.0%) had been euthanized; the age at euthanasia was not significantly different between animals diagnosed with PPID and controls (median of 26 years [IQR, 22 to 31 years] vs median of 24 years [IQR, 21 to 29 years]; $P = .39$). Horses diagnosed with PPID that were euthanized had a median survival time of 2 years after diagnosis (IQR, 1 to 4 years). Reasons for euthanasia in horses diagnosed with PPID included colic in 10 of 34 (29.4%), nonemergent quality-of-life concerns excluding HAL in 9 of 34 (26.5%), emergent reasons other than colic in 7 of 34 (20.6%), HAL in 4 of 34 (11.8%), and being down and unable to rise in 4 of 34 (11.8%). Reasons for euthanasia in controls included emergent reasons other than colic in 13 of 33 (39.4%), colic in 8 of 33 (24.2%), nonemergent quality-of-life concerns excluding HAL in 6 of 33 (18.2%), being down and unable to rise in 4 of 33 (12.1%), and HAL in 2 of 33 (6.0%). There was no significant difference in reason for euthanasia between horses with PPID and controls ($P = .53$). Only 2 of 34 euthanized horses (5.9%) had PPID listed as a major reason for euthanasia.

### *Multivariable analysis*

Independent factors associated with a diagnosis of PPID in primary care practice included poor wound healing, dental issue (including missing tooth and EOTRH), HAL, and use of NSAIDs **(Table 2)**.

**Table 2**—Factors associated with a diagnosis of pituitary pars intermedia dysfunction in primary care practice per a conditional logistic regression with *owner* specified as the stratification variable and based on 125 cases and 132 controls.

| Variable | OR | 95% CI | *P* value |
|---|---|---|---|
| Intercept | N/A | N/A | < .001 |
| Poor healing | | | |
| No | Ref | Ref | Ref |
| Yes | 2.36 | 1.12–4.97 | .024 |
| Dental issue | | | |
| No | Ref | Ref | Ref |
| Yes | 1.89 | 1.01–3.54 | .047 |
| Hyperinsulinemia-associated laminitis | | | |
| No | Ref | Ref | Ref |
| Yes | 2.98 | 1.48–6.03 | .002 |
| NSAID use | | | |
| No | Ref | Ref | Ref |
| Yes | 2.12 | 1.14–3.97 | .018 |

N/A = Not applicable. Ref = Reference.

## Discussion

The results of the study indicated that horses diagnosed with PPID are not euthanized at a younger age and do not have more medical events per year. However, the results indicated they are more likely to have been prescribed NSAID and suffer from HAL, poor wound healing, and dental issue (including missing tooth and EOTRH).

No difference in reasons for euthanasia between horses diagnosed with PPID and controls was detected. While PPID status appeared to be a consideration when deciding to euthanize an animal, many control horses had old age listed as a reason for euthanizing in the face of critical illness. This is consistent with previous reports[20,21] that old age is a risk factor for nonsurvival in critical illness, a common reason for elective euthanasia, and a common reason for euthanizing a horse instead of treating a critical illness. There could be little practical difference between an owner's decision to euthanize a horse with a critical illness or quality-of-life concerns due to the animal's PPID status versus the animal's age. The time of 2 years between diagnosis and euthanasia was shorter than the previously reported[15,22] 3.6 to 4.5 years. Horses in our sample were slightly older at diagnosis compared to prior reports,[3,15,22] but those reports were drawn from referral populations. A greater appreciation for the range of potential clinical signs associated with PPID has likely resulted in PPID testing being included in the diagnostic plan for a greater range of conditions, leading to improved recognition of the disease in animals with comorbidities that independently necessitate euthanasia, as evidenced by the greater number of total medical events in the PPID group.[2–6] The increasing number of positive test results over the included time period likely reflected the improved practitioner, and possibly client, recognition of PPID beginning in the late 2010s.[1,8,13,16]

The use of NSAIDs is considered protective in the development of human Parkinson disease (PD), a similar α-synucleinopathy, due to a reduction in systemic inflammation and neuroinflammation, but the use of NSAIDs was found to be associated with a diagnosis of PPID in the current study, although they could not be considered protective or a risk factor in the current study design.[23–25] It is possible that NSAIDs are used later in the progression of any inflammatory process in horses compared to people or that this finding simply represented a greater number of veterinary-attended inflammatory conditions occurring during the animal's lifetime.

Insulin resistance in people is a risk factor for PD, and up to 76.5% horses with PPID were found to have insulin dysregulation.[1,3,7,26] The current study further supported that PPID is more closely associated with insulin dysregulation and HAL than could be explained by age-related changes alone.[9] Horses diagnosed with PPID that became laminitic once did not reoccur more frequently than controls that became laminitic. These results suggested that pergolide is insufficient as a monotherapy in horses with PPID that develop HAL and that concurrent specific insulin dysregulation management strategies should be considered.[3,27]

Poor healing of any lesion was associated with a diagnosis of PPID. The role of altered cortisol production and metabolism in the clinical manifestations of PPID remains poorly understood.[6,28] While cortisol concentrations are not consistently increased in animals with PPID, there appears to be markedly increased metabolite excretion and significant alterations in tissue-level cortisol metabolism in the skin, suspensory ligaments, adipose tissue, and liver in horses with PPID.[6,28] The effects of glucocorticoids on both the inflammatory and proliferative phases of wound healing are well documented, and this finding supports the clinical significance of the documented alterations in cortisol metabolism in horses with PPID.[6,28–30]

There is an increasingly recognized connection between PPID and dental issues, with horses with EOTRH having PPID more frequently than age-matched horses without EOTRH.[31] Hypovitaminosis D and altered calcium metabolism are proposed causes of EOTRH and have been strongly implicated in the development of PD.[12,31–33] This could be representing a potential etiologic link between the PPID and PD, if hypovitaminosis D is a feature of both neurodegenerative conditions.[31,34] However, glucocorticoids significantly alter calcium metabolism and this might also account for the increased frequency of structural dental abnormalities in PPID animals.[35,36]

Horses diagnosed with PPID were not more likely to be diagnosed with corneal ulcers, tendinopathies, or subsolar abscesses. Horses with PPID were found to have lower corneal sensitivity compared to both young and old controls, and these changes are correlated with impaired corneal healing in other species.[4] Increasing age, stable fly management practices, allergies, and environmental hazards might account for the similar number of corneal ulcers diagnosed in the PPID and control groups in our sample.[4,37] However, age, sex, breed, work intensity and type, and poor footing have all been associated with tendinopathies and likely accounted for the similar rates of occurrence between the PPID and control groups.[38,39] Increased risk of infections, including subsolar abscesses, has been documented in horses with PPID, but infections and subsolar abscesses were not diagnosed more frequently in the PPID group.[1] The similar frequency of systemic antimicrobial usage between horses with and without PPID in the current sample further supported that bacterial infections were not more frequent with PPID. While PPID might increase an individual's risk for these conditions, increasing age and the presence of other risk factors mean that overall rate of occurrence does not appear to differ in old horses with and without PPID.[4,6,38–40]

The most significant limitation of the study was the inability to assess whether medical events occurred before or after onset of clinical signs of PPID, meaning that none of the associated factors can be considered risk factors. However, chronic inflammation resulting in prolonged oxidative stress is a major risk factor for PD and the current study did support a greater prevalence of chronic inflammatory conditions in horses with PPID.[23–25]

The detail recorded for any given medical event and diagnostic and treatment decisions was frequently limited, making it difficult to determine an exact timeline of the development of clinical signs and follow changes in treatment regimens. However, it was possible to confirm the broad categories of medical events evaluated in the current study.

Diagnoses were frequently based on equivocal ACTH concentrations or a previous veterinarian's diagnosis, and most controls had not been tested. As such, horses could only be compared as *diagnosed* and *not diagnosed*. Owner matching was intended to reduce the risk of controls with undiagnosed PPID, as an owner that had tested 1 horse for PPID was considered likely to consent to testing if it was suggested for another animal. The fact that the univariable analyses were conducted without accounting for the matched design might have led to the exclusion of variables that appeared nonsignificant in the unmatched analysis but could have been relevant within matched pairs. However, this limitation was mitigated by the subsequent use of conditional multivariable logistic regression, which appropriately accounted for the matching structure. The sample size and lack of detail regarding follow-up clinical signs prevented classification of horses as having controlled or uncontrolled PPID, which would have been clinically relevant. Consequently, our analysis compared only diagnosed and undiagnosed horses.

Another major limitation of the relatively small sample size was that uncommon medical events might have been too infrequent to allow for the detection of differences between the 2 groups. The occurrence of minor medical events and the use of NSAIDs and antibiotics was likely significantly underrepresented in both groups due to the reliance on owner reporting of these events. However, the data did reflect the frequency with which veterinarians could expect to be consulted on these decisions in horses with and without PPID. Finally, perceptions of and testing recommendations for PPID changed dramatically over the study period, as shown by the larger number of cases diagnosed in later years of the study, meaning that milder cases might have been missed in the earlier portion of the study period.

Overall, horses diagnosed with PPID had more total medical events and a greater likelihood of being treated with NSAID and having HAL, poor wound healing, and dental issues. However, in a mostly treated population, horses diagnosed with PPID were not likely to be euthanized at a younger age or have more frequent adverse events when their full medical record was considered. Potentially related medical events such as high FEC, insulin dysregulation, corneal ulceration, desmitis, and subsolar abscessation should be managed on an individual and multimodal basis and not attributed exclusively to the presence of PPID when they occur.

## Acknowledgments

The authors would like to thank the Purdue University veterinary students who contributed to the initial recording of the medical records used in this study during clinical rotations with the Purdue University Equine Field Service.

## Disclosures

The authors have nothing to disclose. No AI-assisted technologies were used in the composition of this manuscript.

## Funding

The authors have nothing to disclose.

## ORCID

François-René Bertin https://orcid.org/0000-0002-2820-8431

Emma Stapley https://orcid.org/0009-0009-5731-8996

## References

1. Ireland JL, McGowan CM. Epidemiology of pituitary pars intermedia dysfunction: a systematic literature review of clinical presentation, disease prevalence and risk factors. *Vet J*. 2018;235:22–33. doi:10.1016/j.tvjl.2018.03.002
2. McFarlane D, Hale GM, Johnson EM, Maxwell LK. Fecal egg counts after anthelmintic administration to aged horses and horses with pituitary pars intermedia dysfunction. *J Am Vet Med Assoc*. 2010;236(3):330–334. doi:10.2460/javma.236.3.330
3. Horn R, Bamford NJ, Afonso T, et al. Factors associated with survival, laminitis and insulin dysregulation in horses diagnosed with equine pituitary pars intermedia dysfunction. *Equine Vet J*. 2019;51(4):440–445. doi:10.1111/evj.13041
4. Miller C, Utter ML, Beech J. Evaluation of the effects of age and pituitary pars intermedia dysfunction on corneal sensitivity in horses. *Am J Vet Res*. 2013;74(7):1030–1035. doi:10.2460/ajvr.74.7.1030
5. Keen JA, McLaren M, Chandler KJ, McGorum BC. Biochemical indices of vascular function, glucose metabolism and oxidative stress in horses with equine Cushing's disease. *Equine Vet J*. 2004;36(3):226–229. doi:10.2746/0425164044877215
6. Hofberger SC, Gauff F, Thaller D, Morgan R, Keen JA, Licka TF. Assessment of tissue-specific cortisol activity with regard to degeneration of the suspensory ligaments in horses with pituitary pars intermedia dysfunction. *Am J Vet Res*. 2018;79(2):199–210. doi:10.2460/ajvr.79.2.199
7. de Laat MA, McGowan CM, Sillence MN, Pollitt CC. Equine laminitis: induced by 48 h hyperinsulinaemia in Standardbred horses. *Equine Vet J*. 2010;42(2):129–135. doi:10.2746/042516409X475779
8. Herbst AC, Coleman MC, Macon EL, Harris PA, Adams AA. Owner-reported health and disease in U.S. senior horses. *Equine Vet J*. 2024; 57(3):684–702. doi:10.1111/evj.14200
9. Rapson JL, Schott HC II, Nielsen BD, McCutcheon LJ, Harris PA, Geor RJ. Effects of age and diet on glucose and insulin dynamics in the horse. *Equine Vet J*. 2018;50(5):690–696. doi:10.1111/evj.12812
10. Glover CM, Miller LM, Dybdal NO, Lopez A, Duckett WM, McFarlane D. Extrapituitary and pituitary pathological findings in horses with pituitary pars intermedia dysfunction: a retrospective study. *J Equine Vet Sci*. 2009;29(3):146–153. doi:10.1016/j.jevs.2009.01.004
11. Wang W, Gibson J, Horsman S, Mikkelsen D, Bertin FR. Characterization and comparison of fecal microbiota in horses with pituitary pars intermedia dysfunction and age-matched controls. *J Vet Intern Med*. 2025;39(1):e17288. doi:10.1111/jvim.17288
12. Colbath AC, Fortin JS, Burglass CM, et al. Lumbar vertebral bone density is decreased in horses with pituitary pars intermedia dysfunction. *Equine Vet J*. 2024;56(2):368–376. doi:10.1111/evj.14039
13. McGowan TW, Pinchbeck GP, McGowan CM. Prevalence, risk factors and clinical signs predictive for equine pituitary pars intermedia dysfunction in aged horses. *Equine Vet J*. 2013;45(1):74–79. doi:10.1111/j.2042-3306.2012.00578.x

14. Miller MA, Moore GE, Bertin FR, Kritchevsky JE. What's new in old horses? Postmortem diagnoses in mature and aged equids. *Vet Pathol*. 2016;53(2):390–398. doi:10.1177/0300985815608674
15. Rohrbach BW, Stafford JR, Clermont RS, Reed SM, Schott HC II, Andrews FM. Diagnostic frequency, response to therapy, and long-term prognosis among horses and ponies with pituitary par intermedia dysfunction, 1993–2004. *J Vet Intern Med*. 2012;26(4):1027–1034. doi:10.1111/j.1939-1676.2012.00932.x
16. Ballou ME, Mueller MK, Dowling-Guyer S. Aging equines: understanding the experience of caring for a geriatric horse with a chronic condition. *J Equine Vet Sci*. 2020;90:102993. doi:10.1016/j.jevs.2020.102993
17. Adams AA, Siard-Altman MH, Reedy SE, et al. Evaluation of seasonal influences on adrenocorticotropic hormone response to the thyrotropin-releasing hormone stimulation test and its accuracy for diagnosis of pituitary pars intermedia dysfunction. *Vet J*. 2023;300–302:106035. doi:10.1016/j.tvjl.2023.106035
18. Durham AE, Clarke BR, Potier JFN, Hammarstrand R, Malone GL. Clinically and temporally specific diagnostic thresholds for plasma ACTH in the horse. *Equine Vet J*. 2021;53(2):250–260. doi:10.1111/evj.13292
19. Durham AE, Potier JF, Huber L. The effect of month and breed on plasma adrenocorticotropic hormone concentrations in equids. *Vet J*. 2022;286:105857. doi:10.1016/j.tvjl.2022.105857
20. van Proosdij R, Frietman S. Retrospective analysis of cause-of-death at an equine retirement center in the Netherlands over an eight-year period. *J Equine Vet Sci*. 2022;110:103824. doi:10.1016/j.jevs.2021.103824
21. Southwood LL, Dolente BA, Lindborg S, Russell G, Boston R. Short-term outcome of equine emergency admissions at a university referral hospital. *Equine Vet J*. 2009;41(5):459–464. doi:10.2746/042516409X385823
22. Schott HC II, Strachota JR, Marteniuk JV, Refsal KR. Long-term response of equids with pituitary pars intermedia dysfunction to treatment with pergolide. *J Vet Intern Med*. 2025;39(3):e70109. doi:10.1111/jvim.70109
23. Noyce AJ, Bestwick JP, Silveira-Moriyama L, et al. Meta-analysis of early nonmotor features and risk factors for Parkinson disease. *Ann Neurol*. 2012;72(6):893–901. doi:10.1002/ana.23687
24. Gonzalez-Latapi P, Bayram E, Litvan I, Marras C. Cognitive impairment in Parkinson's disease: epidemiology, clinical profile, protective and risk factors. *Behav Sci (Basel)*. 2021;11(5):74. doi:10.3390/bs11050074
25. Belvisi D, Pellicciari R, Fabbrini A, et al. Risk factors of Parkinson disease: simultaneous assessment, interactions, and etiologic subtypes. *Neurology*. 2020;95(18):e2500–e2508. doi:10.1212/WNL.0000000000010813
26. Ruiz-Pozo VA, Tamayo-Trujillo R, Cadena-Ullauri S, et al. The molecular mechanisms of the relationship between insulin resistance and Parkinson's disease pathogenesis. *Nutrients*. 2023;15(16):3585. doi:10.3390/nu15163585
27. Durham AE, Frank N, McGowan CM, et al. ECEIM consensus statement on equine metabolic syndrome. *J Vet Intern Med*. 2019;33(2):335–349. doi:10.1111/jvim.15423
28. Morgan RA, Keen JA, Homer N, et al. Dysregulation of cortisol metabolism in equine pituitary pars intermedia dysfunction. *Endocrinology*. 2018;159(11):3791–3800. doi:10.1210/en.2018-00726
29. Christian LM, Graham JE, Padgett DA, Glaser R, Kiecolt-Glaser JK. Stress and wound healing. *Neuroimmunomodulation*. 2006;13(5–6):337–346. doi:10.1159/000104862
30. Guo S, Dipietro LA. Factors affecting wound healing. *J Dent Res*. 2010;89(3):219–229. doi:10.1177/0022034509359125
31. Tretow M, Hain AM, Bienert-Zeit A. Aetiological relevance of haematological, biochemical and endocrine parameters on equine odontoclastic tooth resorption and hypercementosis (EOTRH). *Equine Vet J*. 2025;evj.14555. doi:10.1111/evj.14555
32. Zaichick SV, McGrath KM, Caraveo G. The role of $Ca^{2+}$ signaling in Parkinson's disease. *Dis Model Mech*. 2017;10(5):519–535. doi:10.1242/dmm.028738
33. James O. Equine odontoclastic tooth resorption and hypercementosis. *J Vet Dent*. 2022;39(4):346–357. doi:10.1177/08987564221120715
34. Suzuki M, Yoshioka M, Hashimoto M, et al. Randomized, double-blind, placebo-controlled trial of vitamin D supplementation in Parkinson disease. *Am J Clin Nutr*. 2013;97(5):1004–1013. doi:10.3945/ajcn.112.051664
35. Glade MJ, Krook L, Schryver HF, Hintz HF. Calcium metabolism in glucocorticoid-treated pony foals. *J Nutr*. 1982;112(1):77–86. doi:10.1093/jn/112.1.77
36. Compston J. Glucocorticoid-induced osteoporosis: an update. *Endocrine*. 2018;61(1):7–16. doi:10.1007/s12020-018-1588-2
37. Ludwig C, Barr E, Gilger BC. Relationship between stable management practices and ocular disease in horses. *Equine Vet Educ*. 2025;37(2):84–89. doi:10.1111/eve.13963
38. Crișan MI, Damian A, Ștefănuț LC, Dezdrobitu CC, Neagu DM, Denoix JM. Global epidemiological analysis of prevalence and risk factors associated with the deep digital flexor tendinopathy in the equine distal limb: 100 cases. *J Equine Vet Sci*. 2018;67:55–60. doi:10.1016/j.jevs.2018.03.005
39. Mero JL, Scarlett JM. Diagnostic criteria for degenerative suspensory ligament desmitis in Peruvian Paso horses. *J Equine Vet Sci*. 2005;25(5):224–228. doi:10.1016/j.jevs.2005.04.001
40. Cole SD, Stefanovski D, Towl S, Boyle AG. Factors associated with prolonged treatment days, increased veterinary visits and complications in horses with subsolar abscesses. *Vet Rec*. 2019;184(8):251. doi:10.1136/vr.104138

## Supplementary Materials

Supplementary materials are posted online at the journal website: avmajournals.avma.org.