

2017

# Systematic Review Protocol: The effects of glucocorticoids on selected hemodynamic and biochemical parameters in dogs and cats

Jessica Ward

*Iowa State University*, [jward@iastate.edu](mailto:jward@iastate.edu)

Allison Masters

Annette O'Connor

*Iowa State University*, [oconnor@iastate.edu](mailto:oconnor@iastate.edu)

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## Recommended Citation

Ward, Jessica; Masters, Allison; and O'Connor, Annette, "Systematic Review Protocol: The effects of glucocorticoids on selected hemodynamic and biochemical parameters in dogs and cats" (2017). *Veterinary Diagnostic and Production Animal Medicine Reports*. 7. [https://lib.dr.iastate.edu/vdpam\\_reports/7](https://lib.dr.iastate.edu/vdpam_reports/7)

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# Systematic Review Protocol: The effects of glucocorticoids on selected hemodynamic and biochemical parameters in dogs and cats

## **Abstract**

Objective: The objective of this scoping review is to define the scope of literature pertaining to the effects of glucocorticoids in dogs or cats on selected parameters that may affect cardiac function or fluid balance (blood glucose, blood pressure, sodium and potassium levels, echocardiographic or invasive hemodynamic indices, or indicators of volume status). It is our intention that after evaluating the available literature, we will then make a determination of the potential to conduct a systematic review and meta-analysis of the relevant literature for specific interventions.

## **Disciplines**

Small or Companion Animal Medicine | Veterinary Physiology | Veterinary Preventive Medicine, Epidemiology, and Public Health

# Systematic Review Protocol: The effects of glucocorticoids on selected hemodynamic and biochemical parameters in dogs and cats

Jessica Ward, Allison Masters, and Annette O'Connor

*Annette O'Connor*  
18<sup>th</sup> March 2017

**Objective:** The objective of this scoping review is to define the scope of literature pertaining to the effects of glucocorticoids in dogs or cats on selected parameters that may affect cardiac function or fluid balance (blood glucose, blood pressure, sodium and potassium levels, echocardiographic or invasive hemodynamic indices, or indicators of volume status). It is our intention that after evaluating the available literature, we will then make a determination of the potential to conduct a systematic review and meta-analysis of the relevant literature for specific interventions.

## Eligibility criteria:

- Population: dogs or cats (any age, any sex, any source [colony or client-owned], healthy or diseased)
- Intervention: glucocorticoid given systemically (PO, IV, IM, or SQ; NOT topical, inhaled, or other routes) OR hyperadrenocorticism diagnosed
- Comparator: parallel control group OR single arm pre/post
- Outcome variables:
  - Mean change from baseline in blood glucose
  - Mean change from baseline in blood pressure
  - Mean change from baseline in blood sodium or potassium
  - Mean change from baseline in echocardiographic or invasive hemodynamic measurements of cardiac structure or function
  - Mean change from baseline in indicators of volume status (blood volume, plasma volume, or body weight)
- Study: all study designs accepted
  - All years and languages eligible

## Information sources:

- MEDLINE – no year restrictions
- CABI – no year restrictions
- Conference proceedings: ACVIM Forum, ECVIM Convention, AVMA Convention, AAHA, AAVPT Symposium, AAFP Convention – past 3 years only
- Citations extracted to EndNote for further characterization

## Search strategy:

- POPULATION: (dog or canine or cat or feline)
  - Plurals not required (no difference in search results if plurals used)
- AND EXPOSURE: any of the following
  - General: (glucocorticoid or glucocorticoids or gluco-corticoid or gluco-corticoids or steroid or steroids or corticosteroid or corticosteroids)
    - Hyphens are needed for “glucocorticoid” but not for “corticosteroid”
    - Plurals are needed for all
  - Specific glucocorticoids: (prednisone or prednisolone or methylprednisolone or hydrocortisone or cortisol or cortisone or corticosterone or betamethasone or dexamethasone or triamcinolone or fludrocortisone or budesonide or flumethasone or isoflupredone)
    - Specific trade names are not needed (no difference in search from generic names only)

- Plurals are not needed
  - Endogenous hypercortisolemia: (hyperadrenocorticism or hypercortisolism or hypercortisolemia or hypercortisolaemia or cushings or cushing's or hyper-adrenocorticism or hyper-cortisolism or hyper-cortisolemia or hyper-cortisolaemia)
    - Hyphens are needed

**FINAL SEARCH PROTOCOL:**

**CABI:**

Set	<input type="button" value="Run Search"/> <b>CABI</b> Search History - " CABI steroid pop/exp"
#4	#1 and (#2 or #3) <i>DocType=All document types; Language=All languages;</i>
#3	TS=(corticosteroid or corticosteroids or steroid or steroids or glucocorticoid or gluco-corticoid or glucocorticoids or gluco-corticoids or prednisone or prednisolone or methylprednisolone or hydrocortisone or betamethasone or dexamethasone or triamcinolone or fludrocortisone or budesonide or flumethasone or isoflupredone) <i>DocType=All document types; Language=All languages;</i>
#2	TS=(hyperadrenocorticism or hypercortisolism or hypercortisolemia or hypercortisolaemia or cushings or cushing's or hyper-adrenocorticism or hyper-cortisolism or hyper-cortisolemia or hyper-cortisolaemia) <i>DocType=All document types; Language=All languages;</i>
#1	TS=(dog or cat or canine or feline) <i>DocType=All document types; Language=All languages;</i>

**MEDLINE:**

Set	<input type="button" value="Run Search"/> <b>MEDLINE</b> Search History - " MEDLINE pop/exp"
#4	#1 and (#2 or #3) <i>DocType=All document types; Language=All languages;</i>
#3	TS=(hyperadrenocorticism or hypercortisolism or hypercortisolemia or hypercortisolaemia or cushings or cushing's or hyper-adrenocorticism or hyper-cortisolism or hyper-cortisolemia or hyper-cortisolaemia) <i>DocType=All document types; Language=All languages;</i>
#2	TS=(corticosteroid or corticosteroids or steroid or steroids or glucocorticoid or glucocorticoids or gluco-corticoid or gluco-corticoids or prednisone or prednisolone or methylprednisolone or hydrocortisone or betamethasone or dexamethasone or triamcinolone or budesonide or flumethasone or isoflupredone) <i>DocType=All document types; Language=All languages;</i>
#1	TS=(dog or canine or cat or feline) <i>DocType=All document types; Language=All languages;</i>

**SCREENING PROTOCOL**

**Level 1: Title/Abstract Relevance Screening (2 independent reviewers, JW + AM)**

**Screening questions:**

- Is this primary research?
  - Yes → go forward
  - No → exclude
  - Can't tell → go forward
  - Can't tell → exclude
  - Is this a Proceedings >5yrs old → exclude automatically
- Are the study subjects dogs or cats?
  - Yes → go forward
  - No → exclude
  - Can't tell → go forward
  - Can't tell → exclude
- Did study subjects have a glucocorticoid administered OR hyperadrenocorticism diagnosed?
  - **Highlight relevant words used in the search for easy identification:**
    - *Corticosteroid or corticosteroids or steroid or steroids or glucocorticoid or gluco-corticoid or glucocorticoids or gluco-corticoids or prednisone or prednisolone or methylprednisolone or*

*hydrocortisone or betamethasone or dexamethasone or triamcinolone or fludrocortisone or budesonide or flumethasone or isoflupredone*

- *Hyperadrenocorticism or hypercortisolism or hypercortisolemia or hypercortisolaemia or cushings or cushing's or hyper-adrenocorticism or hyper-cortisolism or hyper-cortisolemia or hyper-cortisolaemia*
- Yes → go forward
- No → exclude
- Can't tell → go forward
- Can't tell → exclude

## **Level 2: Full Text Relevance Screening and Initial Extraction (2 independent reviewers, JW + AM)**

### **Level 2 screening questions**

- Does this study still reach relevance based on level 1? (Should this have been excluded at level 1?)
  - Yes → go forward
  - No → exclude
- Was glucocorticoid administered systemically (PO, IV, IM, or SQ – i.e. not topically/inhaled)?
  - Yes → go forward
  - No → exclude
- Does the study include some type control/comparison group?
  - Yes → go forward
  - No → exclude
- Does the study report results for at least one outcome variable of interest?
  - **Highlight relevant words for easy identification:**
    - *Glucose OR glycosuria OR glycosuric OR glucosuric OR diabetogenic OR diabetes OR diabetic OR insulin OR fructosamine*
    - *Pressure OR hypertension OR volume OR fluid OR water OR edema OR diuretic OR diuresis OR blood OR plasma OR intravascular OR extracellular*
    - *Heart OR cardiac OR failure OR echocardiography OR echocardiogram OR echocardiograph OR hemodynamic OR hemodynamics OR ventricular OR ventricle OR hypertrophy OR hypertrophic OR myocardium OR myocardial*
    - *Sodium OR potassium OR mineralocorticoid OR mineralo-corticoid*
  - Yes → go forward
  - No → exclude

### **Level 2 data extraction questions**

- What species was studied? (check all that apply)
  - Dogs
  - Cats
- What was the intervention? (check all that apply)
  - Glucocorticoid administered
  - Hyperadrenocorticism
- What was the route of GC administration? (check all that apply)
  - PO
  - IV
  - IM
  - SQ

- What is the control/comparison group (check all that apply):
  - Study animals at baseline before glucocorticoid/hyperadrenocorticism
  - Study animals after washout post-glucocorticoid/hyperadrenocorticism
  - Parallel group of untreated/unaffected dogs
  - Parallel group of dogs treated with medication other than GC
  - Other type of comparison group
- Which outcome measures were investigated? (check all that apply **OR add new**)
  - Blood glucose metabolism
  - Blood pressure
  - Na/K (mineralocorticoid effect)
  - Echocardiography
  - Radiographic/CT/MRI heart size
  - Fluid balance: plasma volume, total body water, extracellular water
  - Invasive hemodynamics (cardiac output, stroke volume, etc)

### Level 3: Full Text Data Extraction (worksheet)

Study subjects	<input type="radio"/> Domestic dogs <input type="radio"/> Domestic cats		
Intervention	<input type="radio"/> GC <input type="radio"/> HAC (this choice triggers which shaded boxes below are shown)		
Route of GC	<input type="radio"/> PO <input type="radio"/> IV <input type="radio"/> IM <input type="radio"/> SQ		
Comparison group	<input type="radio"/> Control group (untreated) <input type="radio"/> Control group (treated with medication other than GC) <input type="radio"/> Treatment animals before/after GC <input type="radio"/> Other comparison group <input type="text"/>		
Comparison group	<input type="radio"/> Control group <input type="radio"/> HAC before/after treatment of HAC <input type="radio"/> Other <input type="text"/>		
Year published	<input type="text"/>		
Country where work performed	<input type="text"/>		
Study setting	<input type="radio"/> Veterinary school <input type="radio"/> Specialty referral hospital <input type="radio"/> General practice <input type="radio"/> Research lab (not vet school) Setting not discussed or unclear <input type="radio"/> Other <input type="text"/>		
Source of animals	<input type="radio"/> Client-owned <input type="radio"/> Experimental/Research colony <input type="radio"/> Shelter <input type="radio"/> Other		
Data collection	<input type="radio"/> Prospective <input type="radio"/> Retrospective <input type="radio"/> Other/Unclear		
Total # of study groups (including control)	①   ②   ③   ④   ⑤   ⑥		
Assign labels to all treatment groups indicated above	① <input type="text"/> Control (untreated) ② <input type="text"/> ③ <input type="text"/> (Can add more if needed based on # of treatment groups) (These choices then populate the columns in "subject data" and "GC data" or "HAC data" below)		
Crossover design?	<input type="radio"/> Yes <input type="radio"/> No <i>If yes:</i> Washout period between groups (d): _____ Total # of study subjects: _____ # of treatment arms in crossover: _____ Other details of crossover: _____		
Allocation of treatment groups	<input type="radio"/> Randomized to treatment group <input type="radio"/> Allocated to treatment group but not random <input type="radio"/> Approach to allocation not clear <input type="radio"/> N/A (only 1 treatment group) <input type="radio"/> N/A (retrospective study)		
Subject data: record for each study group	① Control (untreated)	②	③
Number of subjects			
Health status			
Age at enrollment (yr) (mean/med, SD/range)			
Sex	Female: ( ) # altered: ( ) Male: ( ) # altered: ( )	Female: ( ) # altered: ( ) Male: ( ) # altered: ( )	Female: ( ) # altered: ( ) Male: ( ) # altered: ( )
Body weight (kg) (mean/med, SD/range)			
Breed			
GC data: record for each study group	①	②	③
Name of GC/other drug			
Route			
Initial dose (mg/kg)			
Initial frequency (qXhr)			
Duration of GC at initial dose			
Taper of GC? (y/n)			
Description of taper			

Total duration of GC (d)			
Other drug(s) given to study group			
<b>HAC data: record for each study group</b>	①	②	③
Etiology of HAC	<input type="radio"/> Spontaneous <input type="radio"/> Drug-induced <input type="radio"/> N/A	<input type="radio"/> Spontaneous <input type="radio"/> Drug-induced <input type="radio"/> N/A	<input type="radio"/> Spontaneous <input type="radio"/> Drug-induced <input type="radio"/> N/A
How was HAC diagnosed?	<input type="radio"/> ACTH stim <input type="radio"/> LDDS <input type="radio"/> Other <input type="text"/>	<input type="radio"/> ACTH stim <input type="radio"/> LDDS <input type="radio"/> Other <input type="text"/>	<input type="radio"/> ACTH stim <input type="radio"/> LDDS <input type="radio"/> Other <input type="text"/>
Duration of HAC prior to study			
HAC controlled medically at d0 of study?	<input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> N/A <input type="radio"/> Not recorded How HAC treated/controlled: <input type="text"/>	<input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> N/A <input type="radio"/> Not recorded How HAC treated/controlled: <input type="text"/>	<input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> N/A <input type="radio"/> Not recorded How HAC treated/controlled: <input type="text"/>
HAC treated during study?	<input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> N/A Treatment: <input type="text"/>	<input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> N/A Treatment: <input type="text"/>	<input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> N/A Treatment: <input type="text"/>
Outcome measures assessed; description of outcome measure	<input type="radio"/> Blood glucose metabolism <input type="text"/> <input type="radio"/> Blood pressure <input type="text"/> <input type="radio"/> Electrolytes <input type="text"/> <input type="radio"/> Echocardiography <input type="text"/> <input type="radio"/> Heart size on CXR, CT, MRI <input type="text"/> <input type="radio"/> Fluid balance, plasma volume total body water <input type="text"/> <input type="radio"/> Invasive hemodynamics (CO, SV, etc) <input type="text"/> <input type="radio"/> Other (add if needed): <input type="text"/> (These choices then populate the columns in "Outcome measure data" below)		
<b>Outcome measure data: record for each outcome measure assessed</b>	(A)	(B)	©
Treatment groups in which outcome measure was assessed (y/n)	① ② ③	① ② ③	① ② ③
Time points (d0-dX) outcome measure was assessed for each treatment group	Group ①: _____ Group ②: _____ Group ③: _____	Group ①: _____ Group ②: _____ Group ③: _____	Group ①: _____ Group ②: _____ Group ③: _____
Timing of outcome measure assessment (time during day)	<input type="radio"/> Fasted (y.n) <input type="radio"/> # hours post-tx: _____ <input type="radio"/> Other timing: _____ <input type="radio"/> Not specified	<input type="radio"/> Fasted (y.n) <input type="radio"/> # hours post-tx: _____ <input type="radio"/> Other timing: _____ <input type="radio"/> Not specified	<input type="radio"/> Fasted (y.n) <input type="radio"/> # hours post-tx: _____ <input type="radio"/> Other timing: _____ <input type="radio"/> Not specified
Was outcome assessment blinded?	<input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> Not recorded	<input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> Not recorded	<input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> Not recorded
<b>Other notes</b>			



*And Lee*  
18<sup>th</sup> March 2017