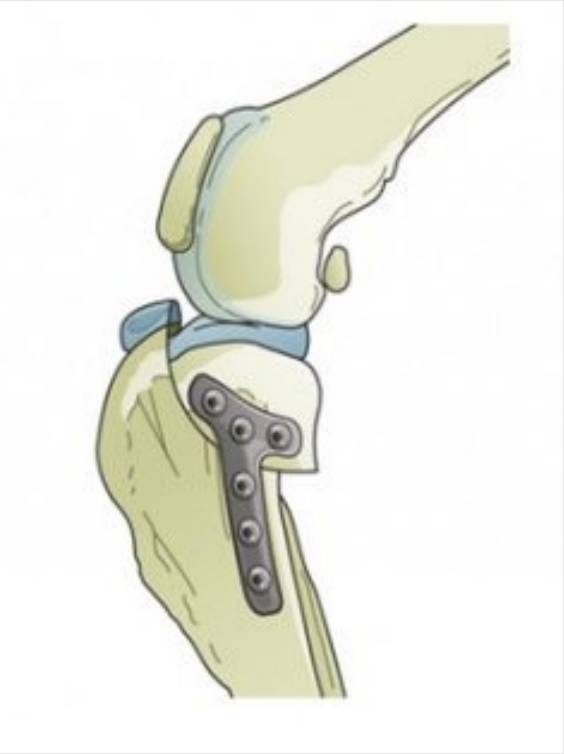
Clinical Research: How to Get Started

Jon Cheetham

Clinical SOP

TPLO Standard Operating Procedure

- History - co-morbidities and response to pain management and weight loss (if any)
- Physical exam –specifically the ortho exam critical
- Imaging – good quality CC and laterals –90/90 orientation for TPLO & measurements
- Client consent – risks, success rate, and importance of postop care
  - 40% owners don't follow postop surgical instructions
  - >1 in 10 dogs get chronic infection and need plate explanted
  - 50% of dogs rupture contralateral side in a year of first side
  - 25-50% of them have medial meniscal injury.
  - Cost
- OR scheduling
- Anesthesia assessment – resuscitation code written down. Peripheral nerve blocks. ±epidural. CBC/chem/UA if indicated. Preop gastric protectants
- Surgery – Timeout
- Perioperative and postop antibiotics
- Postop imaging ± rescue pain management.
- Communication: Surgeon calls owner, student calls when dog is awake.
- Student sets up discharge next day – they write the home instructions but we are lucky and have interns who review all that shit. Usually discharged day after sx



Research SOP

Research Standard Operating Procedure

1. Turn a clinical question into a hypothesis
2. Get the nugget of the trial right: PICOT approach
3. Draft one page summary – why, what, how; share, get feedback
4. Think about the figures – these tell the story
5. Ask for statistical analysis input
6. Request approvals – client consent, IACUC. Sequence them smartly
7. Consider a pilot animal or two
8. Start your project and review

"Over time an SOP becomes an algorithm, like clinics.
This is experience."

1) Turn a Clinical Question into a Hypothesis

A good hypothesis is:

- Answerable with a yes or no answer
- Represents a single unit or subset of the problem
- Is testable – quantitative measurement of outcome

Clinical Question: Is a renal prescription diet better for cats with chronic renal disease?

Hypothesis: *Cats with chronic renal disease loose less body weight when fed a renal prescription diet than the same population of cats fed a normal diet*

2) Get the nugget of the trial right: PICOT approach

Hypothesis: *Cats with chronic renal disease loose less body weight when fed a renal prescription diet than the same population of cats fed a normal diet*

Patient/Population:	Cats with naturally occurring chronic kidney disease
Intervention/exposure:	Renal prescription diet
Comparison/control:	Normal diet
Outcome:	Primary - Body weight; Secondary - Renal biochemistry
Time:	6 months after start diet

3) Write a one page summary

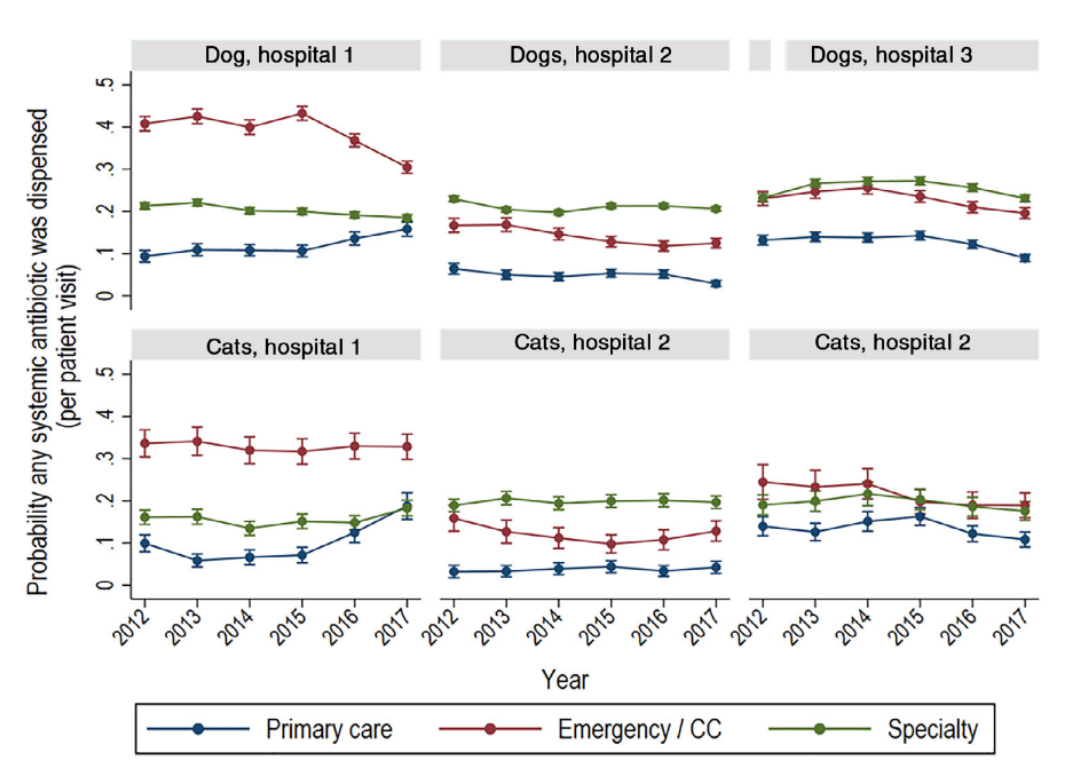
- Why does this / what is the knowledge gap
- What will change based on the results of this study? What's new?
- How are you going to do the study – PICOT structure

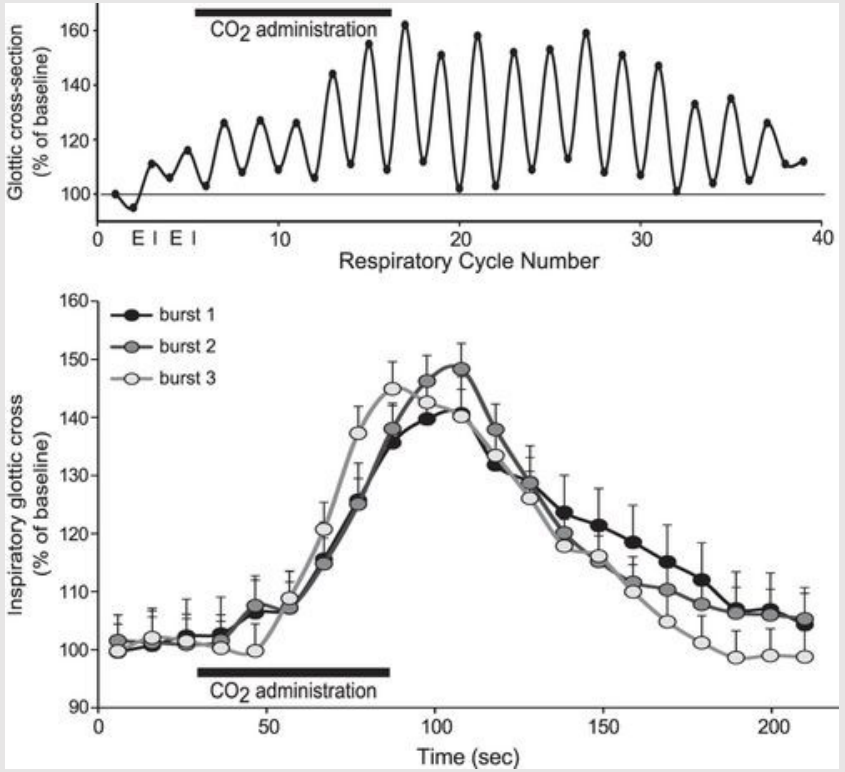
"Writing is how we realize we don't know what we are talking about"

A first draft will be imperfect, that's normal and OK. Just write something.
It helps to:
1. Clarify your thinking, get feedback, iterate and improve the design.
2. Build the collaboration study matter

4) Think about the figures – these tell the story

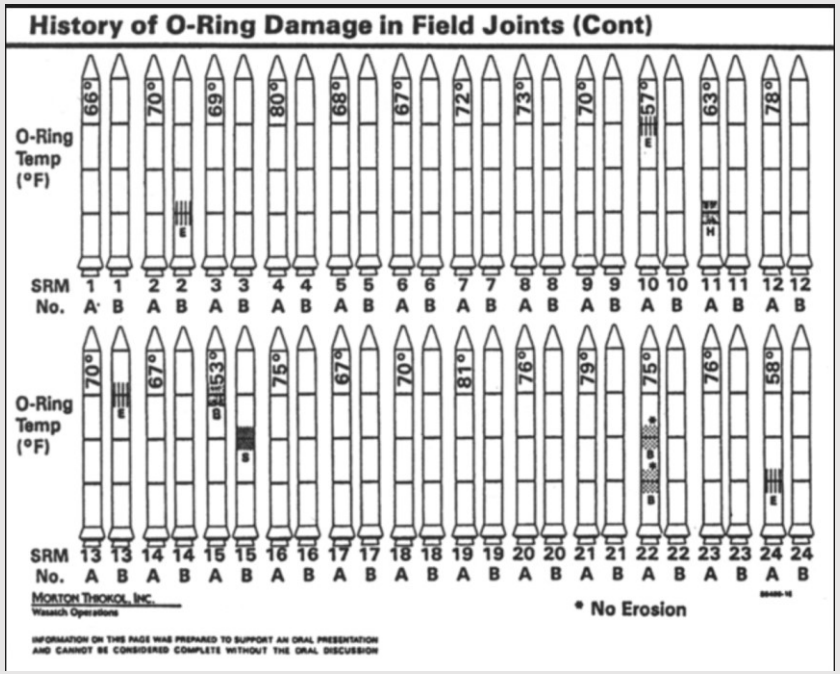
- Begin with the end in mind – what will the figure look like?

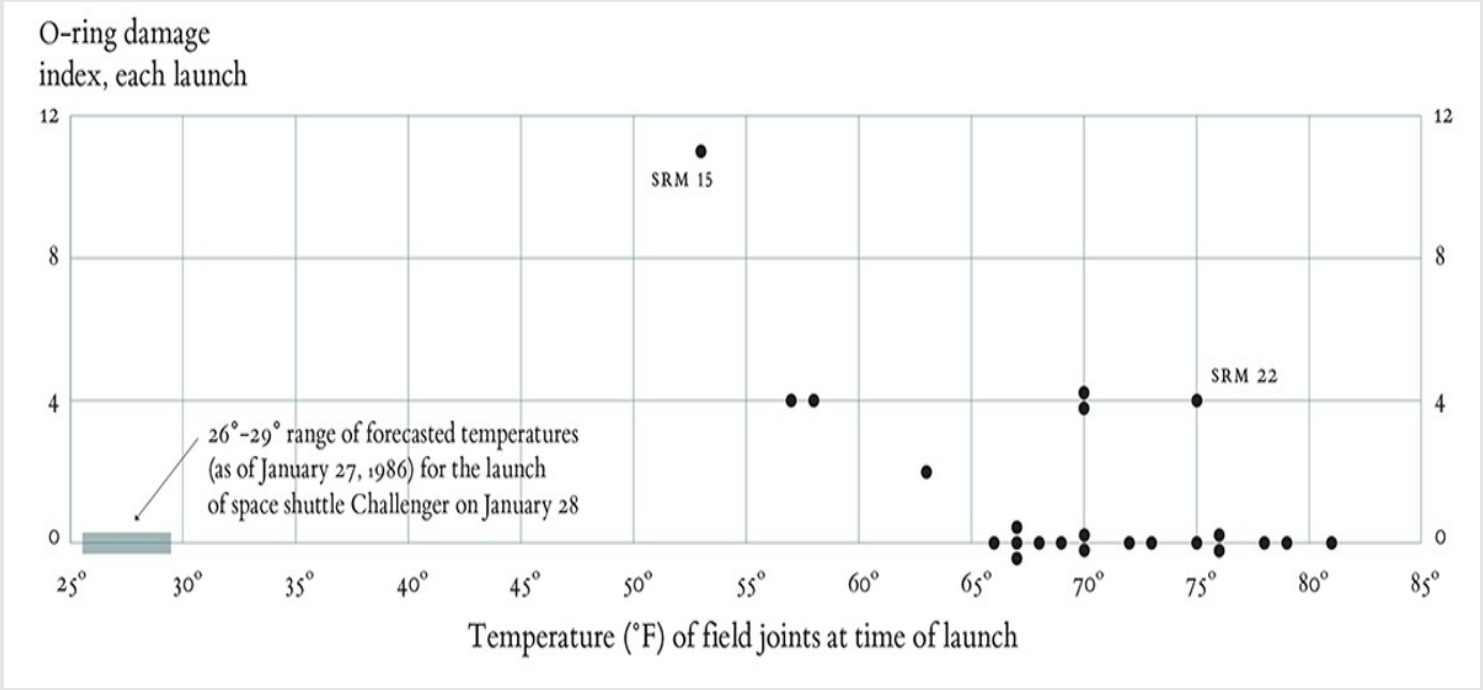




Goggs, Menard et al JVIM 2020

4) Think about the figures – these tell the story





5) Ask for statistical analysis input

The People

- **Mark Rishniw (mr89)** – invaluable resource within DCS.
- **CSCU -** clinically relevant assistance on study design and data analysis
  - CSCU's Stephen Parry (stephen.parry@cornell.edu) works with many of our clinicians and may be contacted directly.
  - Free consulting or analysis for a fee

The Software

JMP Pro - available without cost for DCS faculty through a departmental license. Contact vmithelpdesk@cornell.edu

GraphPad for figures – it's the best – email dcs-it@cornell.edu to access

6) Request approvals – client consent, IACUC

Client consent form

- Required for all studies that are not retrospective or using leftover/residual samples
- A single letter or form can be used for organizations such as zoos, shelters, farms
- 5 business days turnaround time (Contact: Carol Frederick c.frederick@cornell.edu)

Exemption from IACUC or IACUC approval:

1) Exemption: retrospectives, residual samples (CUVCSC committee). This helps demonstrating correct approvals obtained for many journals.

2) IACUC approval is needed if:

- You are collecting **any** sample that is not required for standard of care treatment **OR**
- You are performing **any** procedure that is not part of standard of care treatment

- Applications due by the end of business the third Thursday of every month
- Protocols are reviewed in the following month, to be approved at the following month's meeting
- 2-3 month turnaround time. Contact: Rob Felt (rjf243)for help

The Clinical Trials Team

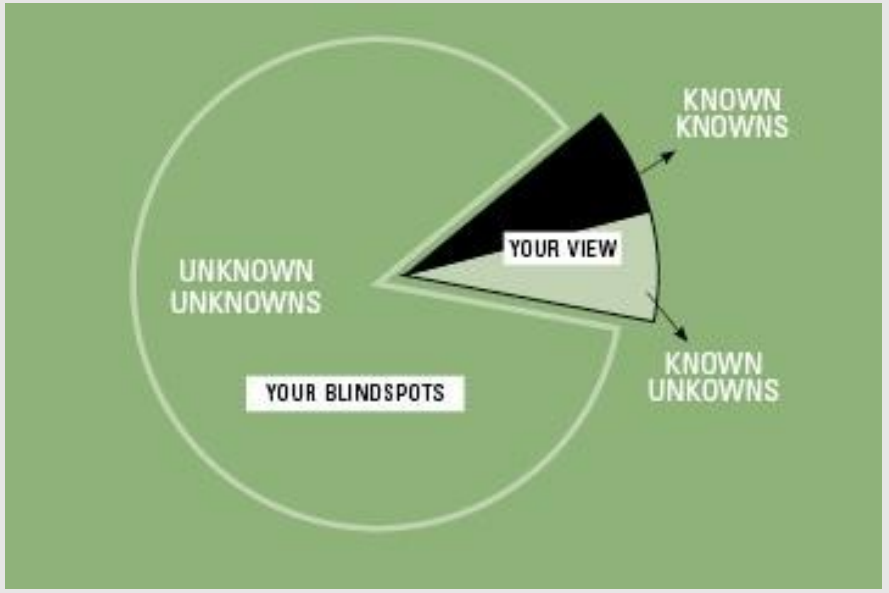
Carol Frederick, LVT, VTS (ECC)
Section Supervisor
(c.frederick@cornell.edu)

Lucinda (Cindy) Bennett, LVT
(llb11@cornell.edu)

Sydney Kraus-Malett, LVT
(sk2395@cornell.edu)

7) Consider a pilot animal or two?

- Begin the study and consider if the first one or two animals may be treated as pilot.
- Also works for retrospectives – look back at 10 cases first
- Smooths the processes, data collection, xl sheet formatting, variables to collect
- Identify things you didn't think of
- Determine ahead of time if animals will be pilot



8) Start your project and review

- Review project process at ~ 5, 10, 25, 50% of the way through
  - Is data collection capturing everything you need?
- Collate and format correctly from the start
  - Avoids the hump of “sorting out my data” before beginning data analysis
  - Lower case for all excel - step reduces data hygiene clean up of data at the end
- Useful tools to consider
  - Google forms
  - Google sheets
  - Prelude
  - Redcap

Additional Resources

- DCS Research & Grant Planning Information
  - https://www.vet.cornell.edu/departments/clinical-sciences/dcs-research-and-grant-planning

- Clinical Trials
  - If you plan to conduct a clinical trial on client owned animals contact our Clinical Trials Coordinators (Carol Frederick; Cindy Bennett) or visit the Clinical Trials Faculty Resource page for details for setting up a new clinical trial, patient recruitment, and sample collection

- DCS Innovation Laboratory Contact Suzin Webb (VMC C1118).
  - Services Available: Project Planning, Supply Purchasing, Experimentation, Data Summary/Analysis

- DCS Research Drop-In Session
  - Immediately after the DCS Department Meeting (4th Tuesday of each month).Informal discussion of your research idea and help navigating our research ecosystem. 9:00-10:00AM. Please contact Maria Hopko for the Zoom link.

Internal funding opportunities

Cornell College of Veterinary Medicine Resident Research Grant Programs: <$10,000

Cornell Riney Canine Health Center Research Grants Program: <$100,000

Cornell Feline Health Center Research Grants Program: $75,000

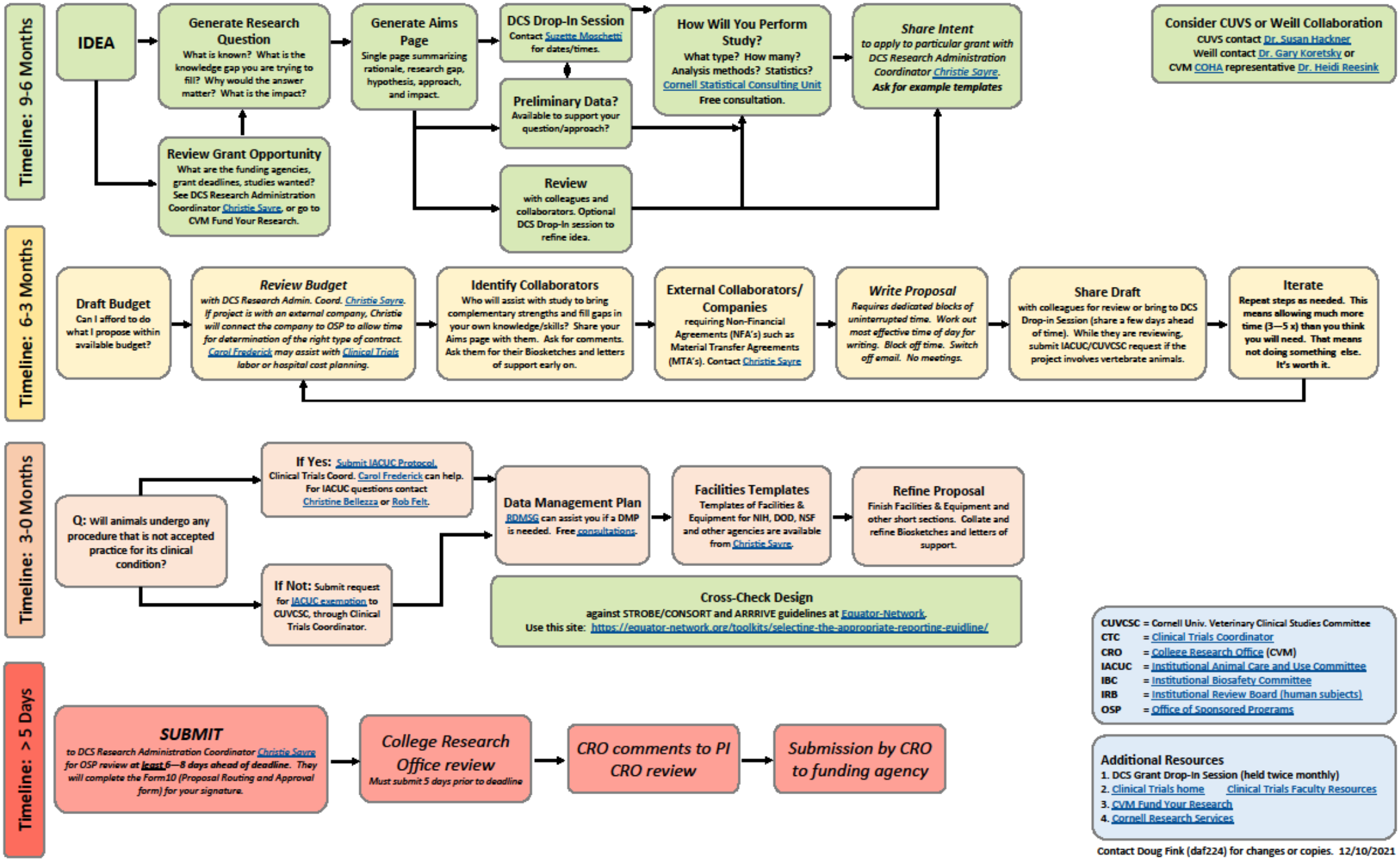
Harry M. Zweig Memorial Fund for Equine Research: <$100,000

The John T. and Jane A. Wiederhold Foundation Wildlife Conservation and Shelter Medicine Program: <$100,000

Cornell College of Veterinary Medicine Research Grants Program in Animal Health: <$50,000

Christie Sayre
cms44@cornell.edu

CVM Clinical Sciences Research Grant Process



Contact Doug Fink (daf224) for changes or copies. 12/10/2021

Dogs

- Determine the transcriptome of canine soft tissue sarcoma
- Drug repurposing to aid tx of canine lymphoma
- Identifying Clotting Risk Factors in IMHA
- Radiofrequency therapy for dogs with chronic osteoarthritis hind limb pain
- C1INCH-complement inhibition in IMHA
- Surgical Site Infection Surveillance in soft tissue and orthopedic surgeries in dogs and cats
- Comparing a novel insulin CRI to standard of care in DKA
- Randomized controlled trial of resource efficient interventions in traumatic wounds
- Investigating use of CPAP helmet in brachycephalics during recovery from anesthesia
- Investigating accuracy and utility of ultrasound for diagnosing acute hip luxation
- Analyzing PK/PD of unasyn and baytril in critically ill patients
- A new chemotherapeutic combo for splenic HSA
- Cell-free DNA in B-cell lymphoma
- Lab-Supported Antimicrobial Stewardship
- GLS-1027 canine uveitis medication
- A new chemo combination for B-cell LSA
- RTX for dogs with chronic elbow pain
- Investigating pannexins in chronic pain
- Investigating cause of blood clotting in IMHA
- Genetic sequencing of dogs with AML
- Investigating pre-stretching for laparoscopy
- Animos anti-itch spray
- OKV-1001 in IMHA and chronic atopy

Cats

- Investigating dietary intervention in chronic enteropathy
- Metabolomics before and after RAIT
- Determining the optimal approach to chest compressions
- Cyclosporine as a first line tx in FCGS
- Investigating genetics of DM in cats
- Culturing macrophages in cats with FCGS

Horses

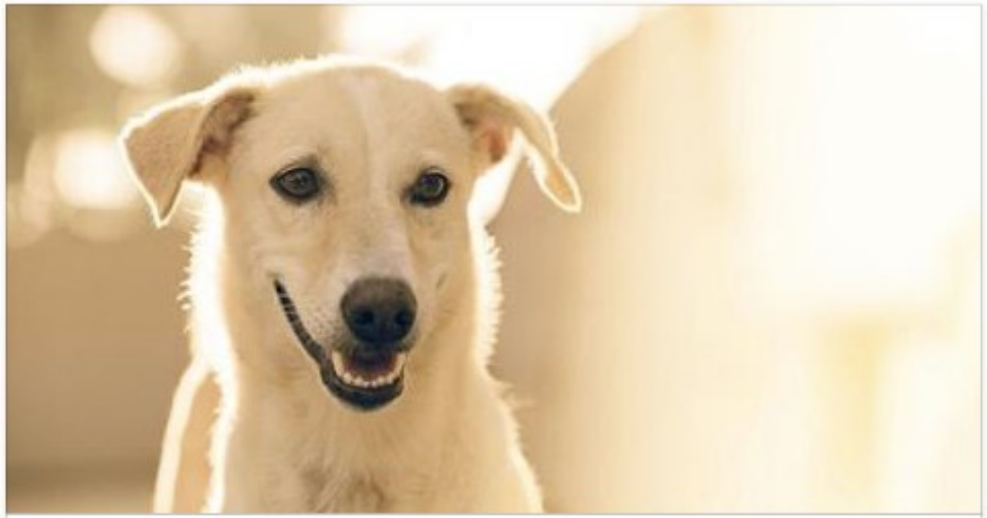
- Novel ventilation in anesthetized horsees
- Treatment response for equine fungal endometritis
- Looking for diagnostic markers in mares with placentitis
- Investigating low-volume uterine lavage as a diagnostic tool in mares with endometrial fibrosis or acute inflammation

And more coming!

Patient Recruitment

Cornell University College of Veterinary Medicine
July 15 at 7:40 AM ·

Traditional chemotherapeutic drugs have been used to extend quality of life for dogs diagnosed with lymphoma, but additional safe, low cost therapies are needed for these canine patients, which is the purpose of this clinical trial currently running at the Cornell University Hospital for Animals.



Drug Repurposing to Aid Treatment of Canine Lymphoma

Drug Repurposing to Aid Treatment of Canine Lymphoma Canine Lymphoma is one of the most common cancers in dogs with few treatment options available....

WWW2.VET.CORNELL.EDU

Open Veterinary Clinical Trial

Complement Inhibition in IMHA (C_1INCH)

GOALS Immune-mediated hemolytic anemia (IMHA) is a common disease that affects all breeds of dogs and can be fatal. In the severe form of the disease complement activation causes red blood cells to be broken down in the bloodstream. At present no therapies for IMHA target this complement activation. We have confirmed that an FDA licensed formulation of C_1-INH is safe for dogs and effectively inhibits canine complement mediated hemolysis. We hope this will translate into a beneficial effect in dogs with intravascular red cell breakdown due to IMHA. In this trial, we aim to assess the efficacy of C_1-INH for management of intravascular IMHA.

ELIGIBILITY Dogs presenting to the Cornell University Hospital for Animals for intravascular IMHA

COMPENSATION Your dog will benefit from the provision of diagnostic testing and follow-up monitoring at zero cost to you. The drug or placebo will be provided free of charge. Any tests or procedures unrelated to the study will be your responsibility.

OWNER RESPONSIBILITIES If you agree to let your dog participate in this study, your dog will receive the same diagnostic tests and treatments as for any other dog with this disease and will receive standard of care therapies. In addition, your dog will be randomly assigned to receive either an infusion of C_1-INH or a saline placebo. We will perform daily blood sampling on your dog for up to 5 days or when he/she leaves the hospital (whichever is sooner).

Principal Investigators
Robert Goggs, BVSc, DACVECC, DECVECC, PhD, MRCVS

Contact Information
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College of Veterinary Medicine
Education. Discovery. Care.