WASHINGTON STATE UNIVERSITY
College of Veterinary Medicine

Caring for our Companion Pets:
Critical Research for Improving Companion Animal Health

"The interconnectedness of human and companion animal health"

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WSUVETMED
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Overview

Human and animal health are deeply connected

"The meeting is designed to explore...*data and research needs*, ... *policy* and *societal issues* in assessing, maintaining, and mitigating risks to the health of domesticated animals..."

- Overview most pressing needs for companion animal health

- Research challenges
  - Naturally occurring animal disease to inform human and animal health
  - Work through "regulatory reluctance barriers"
  - Need for centralized data hub for clinical trials and outcomes-based metrics for informed health care decision making

# Challenges for Companion Animal Health

- Significant shortage of Veterinarians nationally
  - Veterinary healthcare teams overwhelmed, high burnout
  - Markedly reduced access to care
    - Greater rates of morbidity/mortality
    - Increased pet surrender
    - Restricted access especially prominent for underserved communities/pet owners
    - Impacts human well-being, disruption of the human animal bond, especially for those most at risk
- The cost of health care for pets

Access to Care Challenges, all levels:

- High level referral clinics in urban areas

- Rural areas

- Native American nations

- Clinics that serve the pets of low-income people and people experiencing homelessness

- Inner city, care deserts
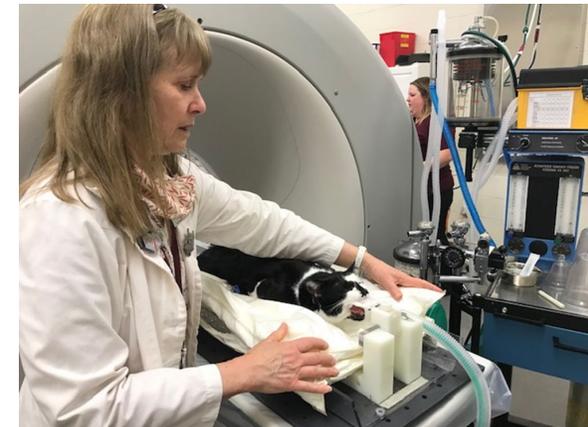
Access to Care

Persons experiencing homelessness with animals:

- Place a high value on the health and welfare of their pets
- Experience barriers to traditional health services and access to overall services
- Rely deeply on animal companionship and support.

With integrated health care:

- Medical care for humans increases if medical care for pets is provided
- The pet owner may seek care for their animal but stay for the human healthcare

https://www.onehealthclinic.org/

Research (1)
Harvesting naturally occurring animal disease models for *companion animal health*

- Most highly funded research in companion animals is used to inform human health care
  - Large public sources of money (e.g. NIH) are available for human health priorities
    - ★ Hard sell: "Relevant" naturally-occurring large animal models of human disease
    - Poor uptake in rodent-focused research study sections
  - Pharmaceutical companies also provide funding focused on human and/or animal health
    - Project based, rarely ongoing
    - Intellectual property and publication challenges when working with academia
    - ★ Success with animal "model" often removes the drug for companion animal use

How do we define "relevant" naturally occurring disease model?

Table 1. CIME and MS comparison

Most common among Pug, Yorkshire Terrier, Maltese, Chihuahua & German Shorthair Pointer	Most common among Caucasian and/or European ancestry
Females are more commonly affected	Sex ratio of men to women is 1:4
Highest occurrence among young adult, middle-aged dogs	Usually diagnosed post-puberty, ~20 years of age
Characterized by relapse-remission	Characterized by relapse-remission
Susceptibility loci for MHC II *DLA-chr4* and *DLA-chr15* among Maltese	Strong genetic association with MHC II *HLA-DRB1*15:01 allele*
Histology shows lymphocytic perivascular infiltrates with or w/o macrophages, astrogliosis and tissue necrosis	Histology shows lymphocytic perivascular infiltrates, white matter demyelination, astrogliosis and cortical atrophy
T2-weighted MRI shows hypertense foci	T2-weighted MRI shows hypertense foci
CSF shows lymphocytes, monocytes, ↑protein	CSF shows Th1 polarization, ↑IgG index, IgM oligoclonal bands, ↑protein

CIME = Canine Immune-mediated encephalitis
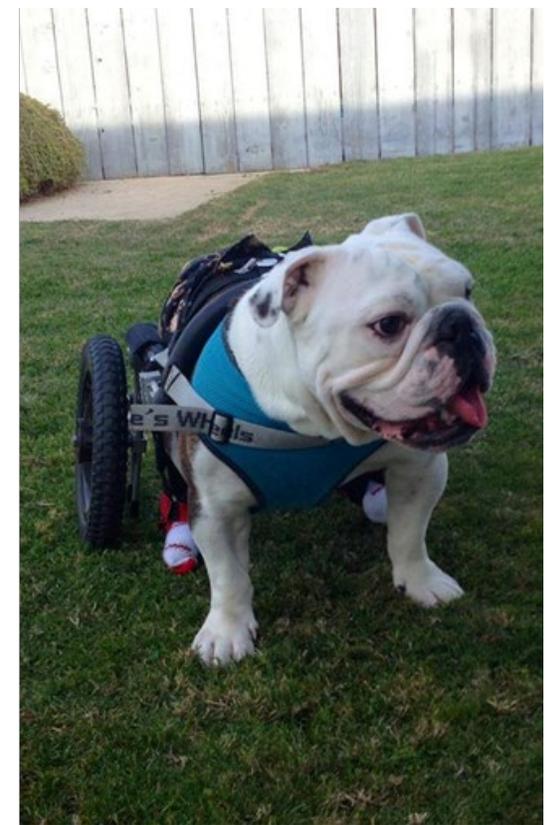
From an R21 summary statement:

"The use of house pets of variable age and gender and with naturally developing disease is powerful and relevant for translational research and closely mimics the environmental conditions and random gender and age of human patients with oral mucosal diseases."

AND

"The use of cats in household environments, with different lighting and diets…descriptive…not mechanistic…"

Research (2)
The removal of effective therapies for companion animal use "Regulatory Reluctance Barriers"

Feline Infectious Peritonitis (FIP)

https://www.theatlantic.com/science/archive/2020/05/remdesivir-cats/611341/

Canine Pemphigus Foliaceus

https://todaysveterinarypractice.com/dermatology/review-of-pemphigus-foliaceus-in-dogs-and-cats/

The FIP Example (fatal cat coronavirus)

People are paying as much as $10,000 for an unlicensed remdesivir variant for their cats, in a thriving black market linked to Facebook groups

https://www.businessinsider.com/coronavirus-treatment-cats-fip-sold-10k-black-market-2020-6

- Gilead invented and patented GS-441524

  - Gilead scientists co-authored the UC Davis studies showing effectiveness against FIP.

  - Cure rates between 80-100%!

- The company won't license GS-441524 for animal use, out of fear that its *similarity to remdesivir* could interfere with the human drug's FDA-approval process, remdesivir now approved for COVID-19

- Gilead worried that the cat research could impede the approval process for remdesivir. Because GS-441524 and remdesivir are so similar, *any adverse effects uncovered in cats might have to be reported and investigated* to guarantee remdesivir's safety in humans.

- *Gilead's caution about generating unnecessary cat data is **standard industry practice**. "One of the rules in drug development is never perform a test you don't have to, if the results could be problematic"*

The Canine PF example
Most common canine autoimmune skin disorder

Efficacy of a Bruton's Tyrosine Kinase Inhibitor (PRN-473)
in the treatment of canine pemphigus foliaceus

- Rilzabrutinib, small molecule, Bruton's tyrosine kinase (BTK) inhibitor important in B-cell signaling.

- In company funded clinical trial: "In canines with naturally occurring pemphigus, rilzabrutinib treatment resulted in rapid clinical improvement demonstrated by anti-inflammatory effects visible within 2 weeks and all animals proceeding to complete or substantial disease control."

  - Pretty cool

- *Removed from veterinary market* (same reason as for GS-441524)

  - Eventually commercialized for human ITP with "revenue expected to reach an annual total of $154 million by 2034"

  - Interestingly...failed phase 3 human PF clinical trial

- *Not approved for veterinary use*

  - *Too expensive without insurance AND veterinary market not big enough*

Research (3)
Need for centralized data hub for clinical trials and outcomes-based metrics for informed health care decision making

Mars Veterinary Health

Mars Veterinary Health established the Medical Affairs Science Team. Focused on outcomes-based healthcare and clinical studies ...will leverage strategic partnerships and the breadth and depth of our data-driven insights....

Dottie Brown, MS, DVM, DACVS, VP of Science and Healthcare Innovation and leader of the Mars Veterinary Health Medical Affairs Science Team

Ethos Discovery

A cure for one is a cure for all
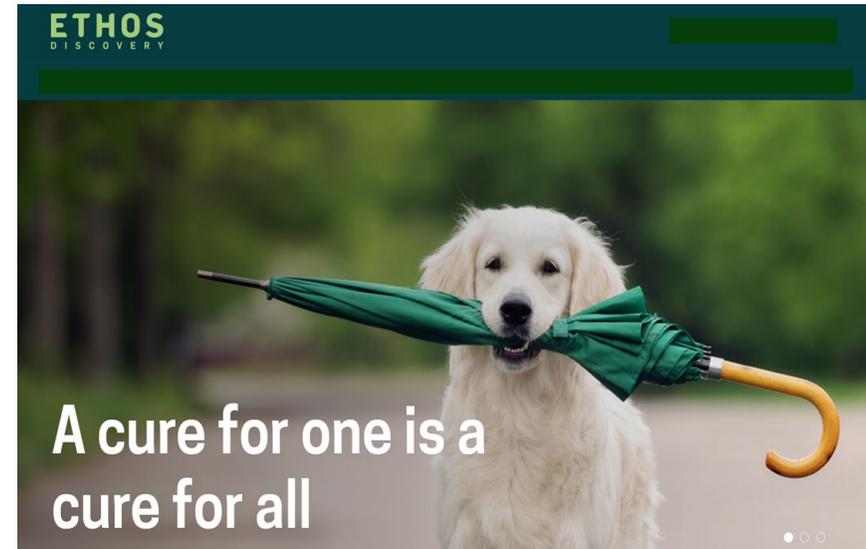
Ethos Discovery acts as an incubator for Scientific Innovations addressing unmet diagnostic and therapeutic needs. Ethos Discovery is a stand-alone not for profit created to fulfill unmet needs that hold the potential to improve outcomes for veterinary and human health care patients.

Veterinary Corporate Practices

Goals:

- Focused on outcomes-based health care
  - How do we assess efficacy?
  - Build a road map in medical records, monitoring clinical support, benchmark care
- Clinical studies
  - Build a network of clinics that are "plug and play" for studies
- Use real-world data in a meaningful way

Needs:

- Data Scientists
  - Tools and platforms
- Library of medical outcomes
- Professional alignment
  - How to coalesce language and definitions
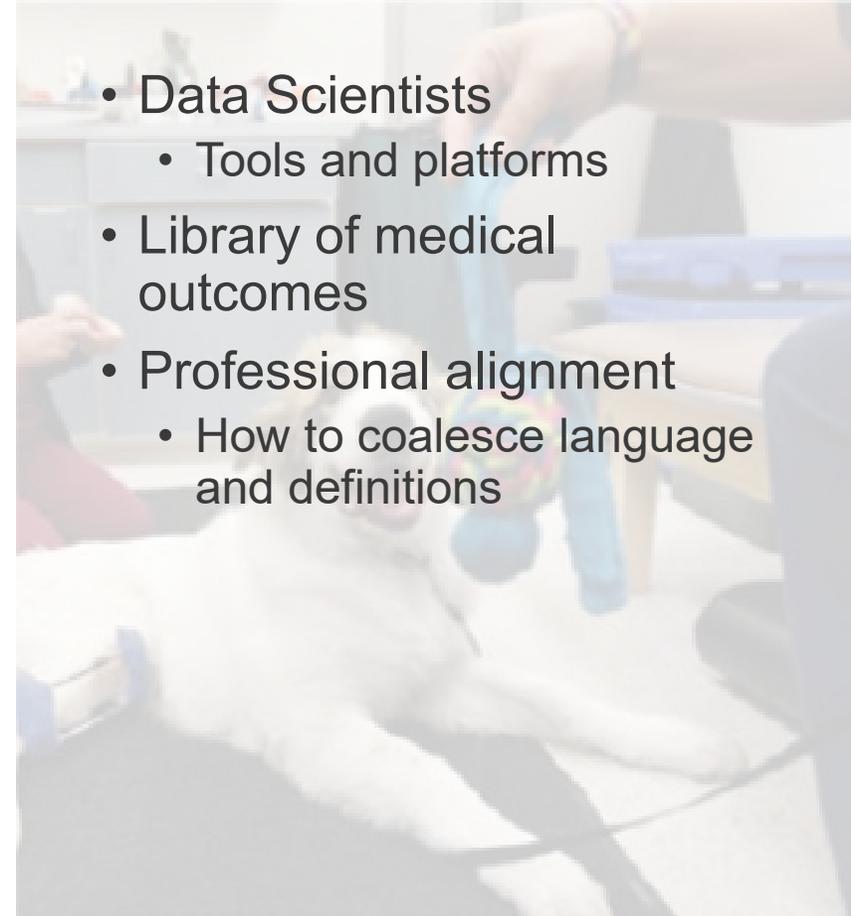
Bold Ideas—Companion Animal Health

For scientific community engagement in research policy, processes and panels

1

Assemble a panel of experts that could define a process by which naturally occurring disease models in large animals could be evaluated for "relevancy" to specific human health disorders

2

Work with the veterinary and human FDA to understand and work through the barriers limiting the use of drugs that have demonstrated efficacy in companion animals

3

Engage large veterinary healthcare companies (e.g. Mars, Ethos) to build data-informed, outcome-based healthcare processes and practices

4

Support state and federal solutions to address the veterinary shortage