

*Cats don't make it easy - helpful tools to assess,  
manage, and treat feline OA*

Margaret Gruen DVM PhD DACVB



# Disclosures

Consulting or sponsored CE: Zoetis, Boehringer-Ingelheim, Elanco, Assisi Animal Health

# Discussion Points



OA/DJD as a multidisciplinary  
condition



Behaviors affected by OA pain

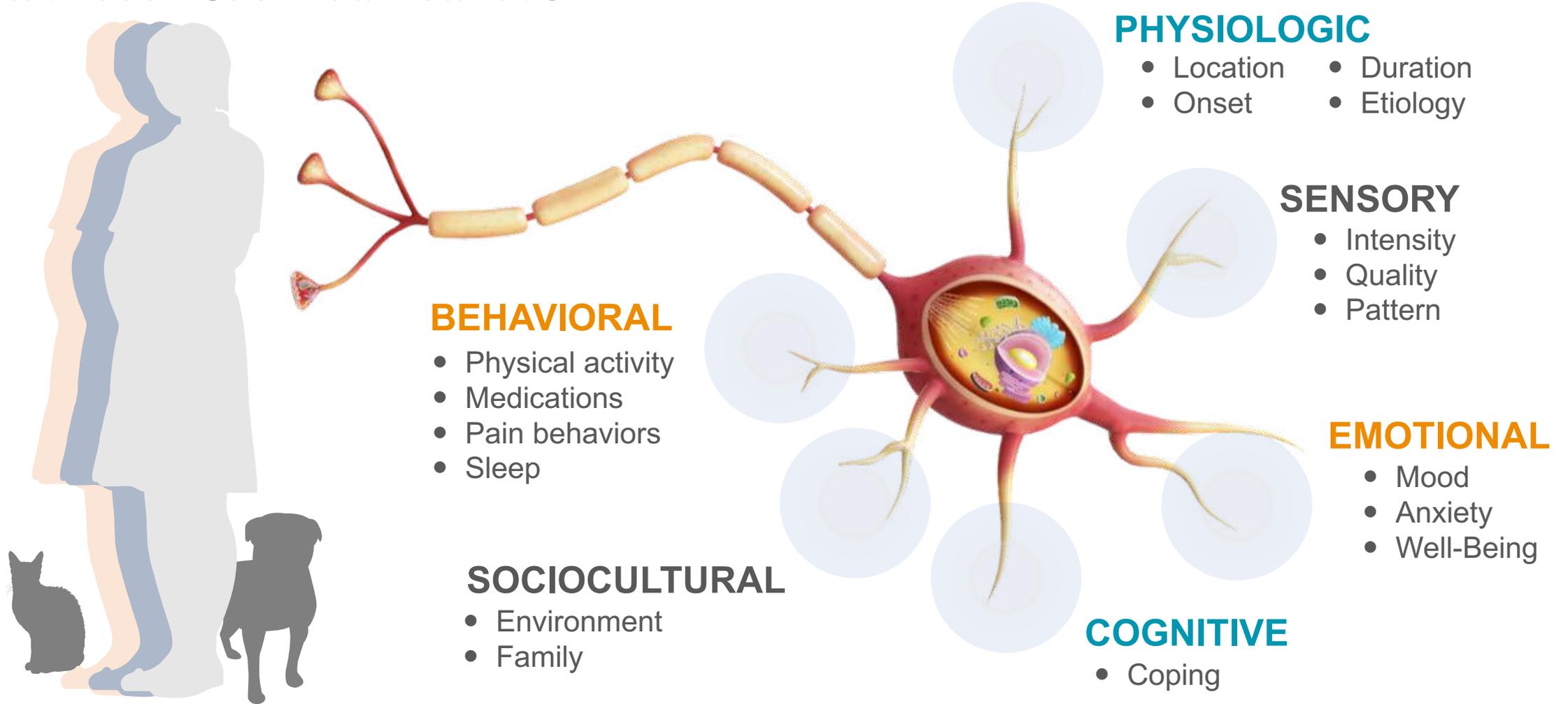


Why it matters: Quality of life



What's in the future for treatment

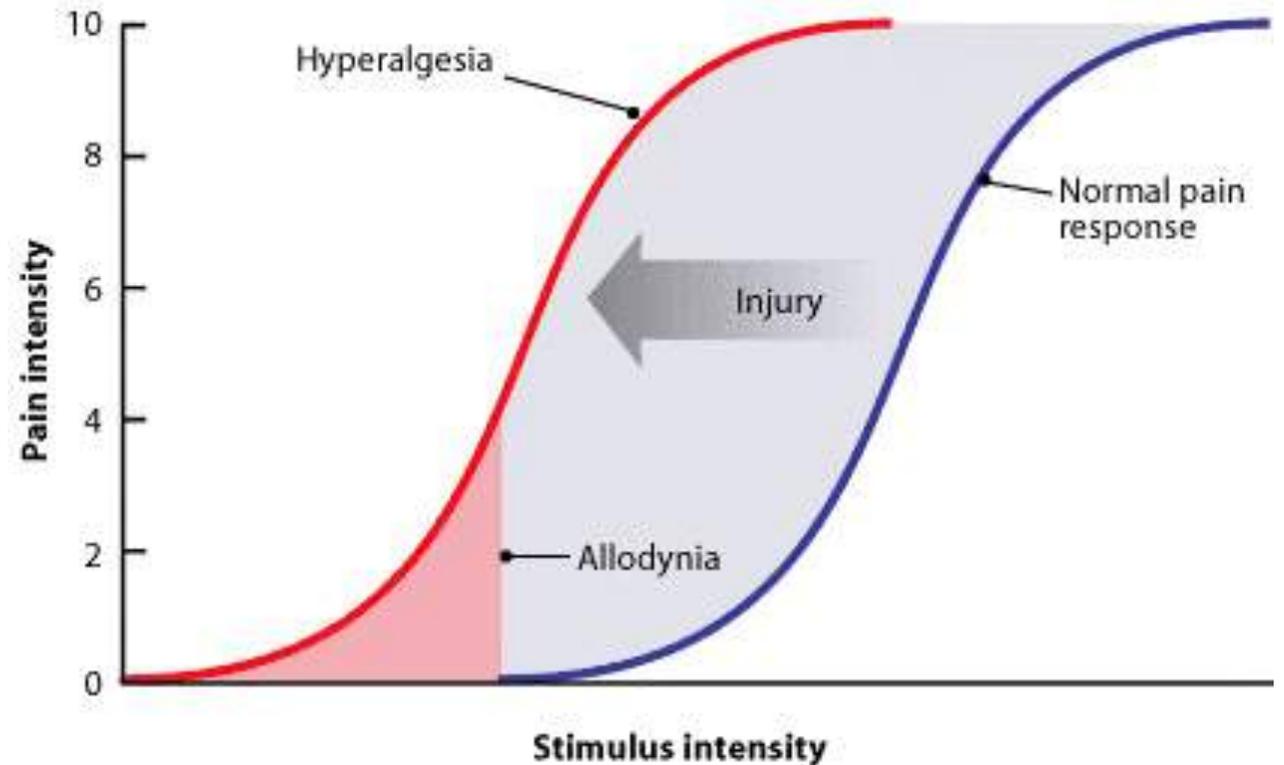
# PAIN IS MULTIDIMENSIONAL AND IS A UNIQUELY INDIVIDUAL EXPERIENCE



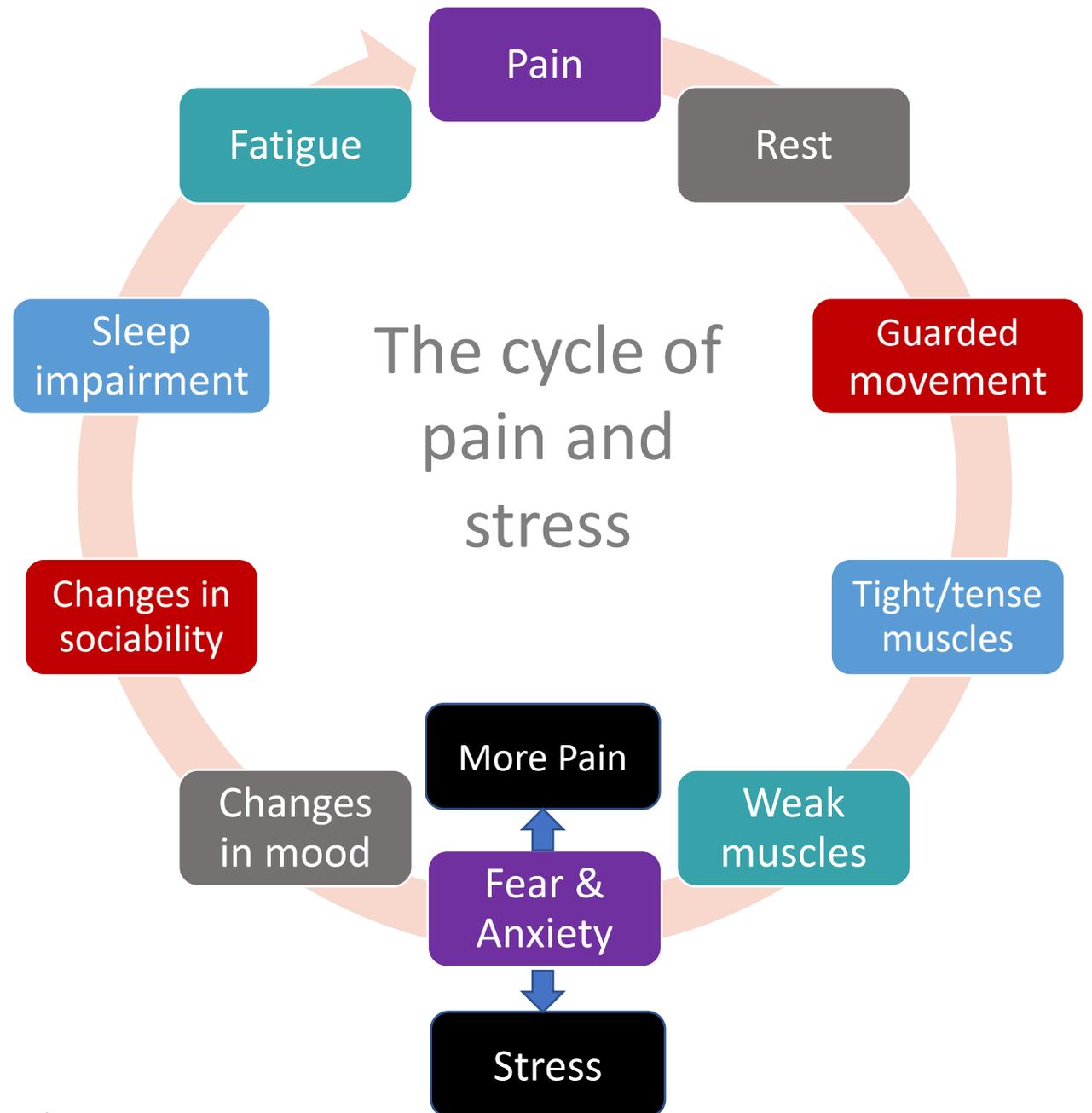
# Chronic pain has downstream consequences

Leads to changes reflective of:

- Defensive behavior
- Learned avoidance
- Peripheral and central sensitization



This complicates  
our management  
of patients



Decreased coping → Increased fear/avoidance

Tightened  
muscles

Tense

More  
inhibited  
behavior

Nervous

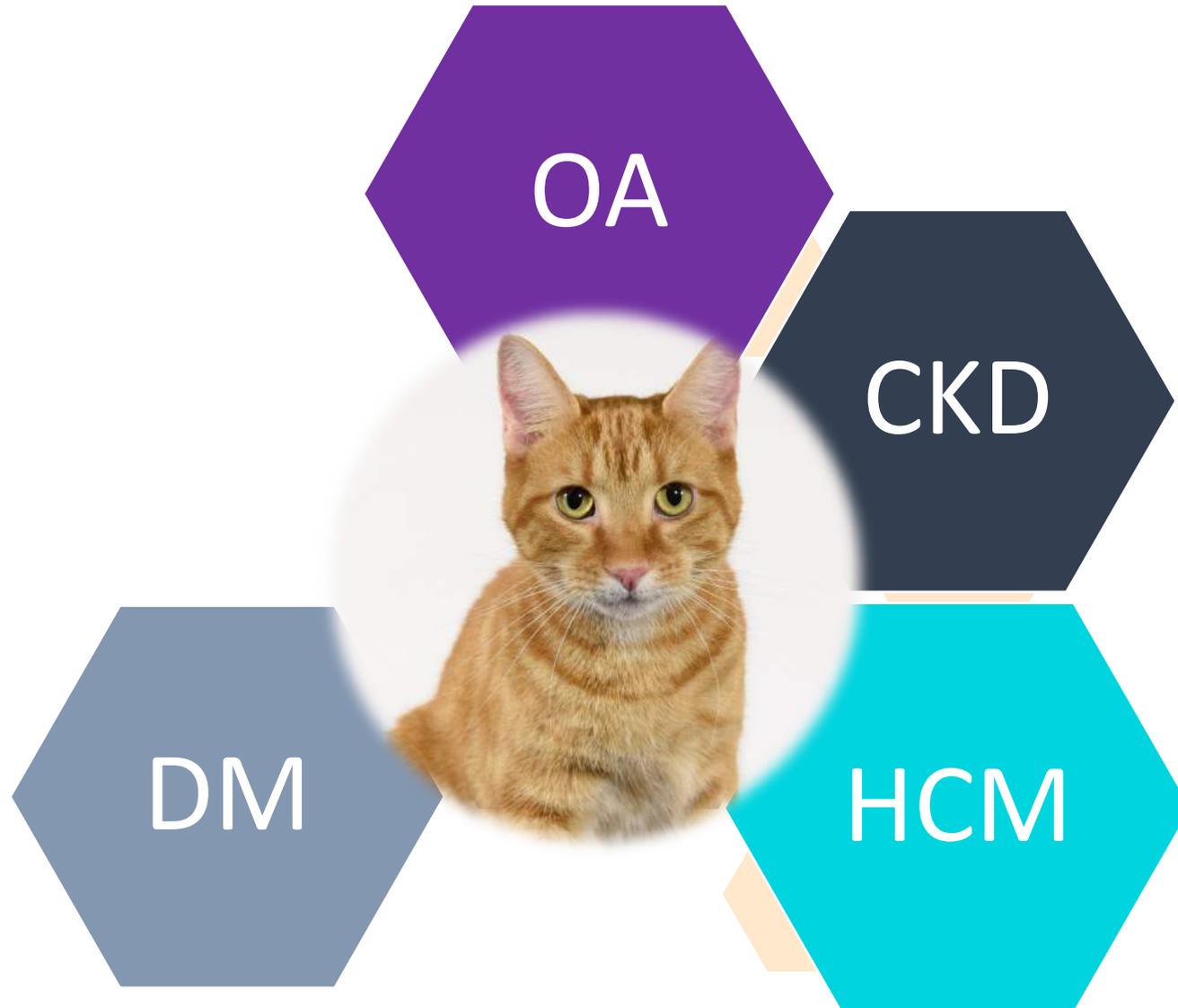
Vigilant



# OA is a multidisciplinary condition

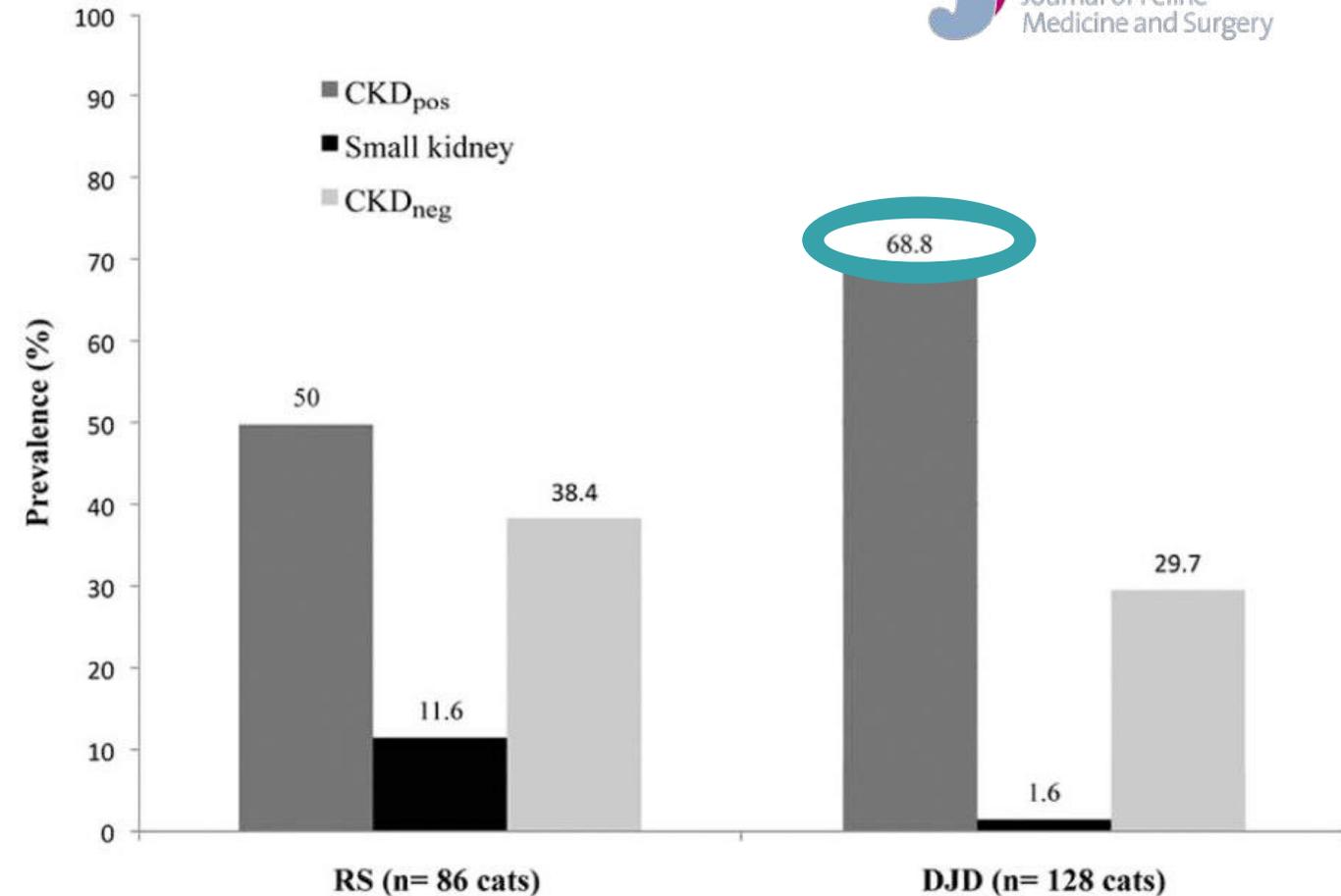


# With a multidisciplinary patient



# High overlap of DJD and CKD

Prevalence and classification of chronic kidney disease in cats randomly selected from four age groups and in cats recruited for degenerative joint disease studies



Marino *et al* 2014

Figure 1 Prevalence of cats with chronic kidney disease (CKD<sub>pos</sub>), small kidneys, and without CKD (CKD<sub>neg</sub>) in the randomly selected (RS) and degenerative joint disease (DJD) groups. Total prevalence (percentage) is shown above each bar. The prevalence was calculated as the number of cats in each category out of the total number of cats in the RS and DJD groups

# Prevalence of painful OA is high

- Middle-aged and older cats
  - 61%-92% of cats show radiographic evidence of DJD
  - ~40% of all cats will have DJD and associated pain
- More cats than are being treated





# Why do we miss feline OA signs?

- Most cats do not exhibit lameness<sup>1</sup>
  - Frequently bilateral<sup>2,3</sup>
  - Tendency to be less demonstrative about pain as a protective mechanism<sup>4</sup>
- Cats compensate for severe disease because they are small and agile
- Radiographic changes are variable<sup>1</sup>
  - Cats with early disease may be very painful yet show no radiographic changes

1. Bennett D, et al. Osteoarthritis in the Cat: How common is it and how easy to recognize *JFMS* 2012, (14) 65-75

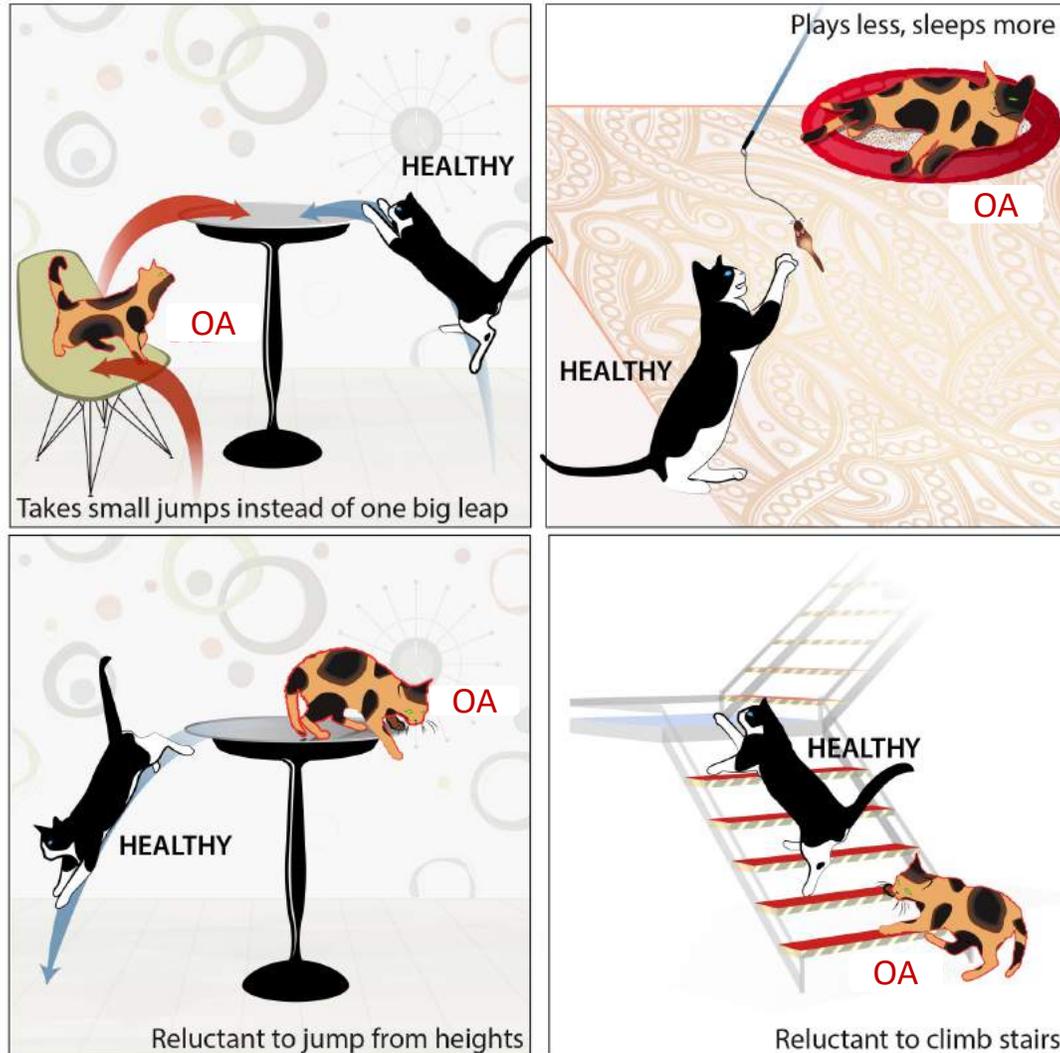
2. Lascelles BD et al, Feline degenerative joint disease. *Vet Surg* 39:2-13, 2010

3. Godfrey DR, Osteoarthritis in cats: a retrospective radiological study. *J Small Anim Pract* 2005 46(9); 425-429

4. Hardie EM et al, Radiographic evidence of degenerative joint disease in geriatric cats: 100 cases (1994–1997) *JAVMA* 2002;220:628–632

Behavior is the single best way to assess for the presence and progression of pain

# Painful OA affects cat behavior



- Changes in mobility
  - Gait or activity
  - Ability to maneuver and perform daily routines
  - Loss of smoothness/fluidity
- Changes in behavior
  - Decreased sociability
    - Hiding, changes in mood/demeanor/tolerance of handling

How do we  
identify this cat?

How do we  
quantify the  
behavior?

How do we  
monitor  
treatment?



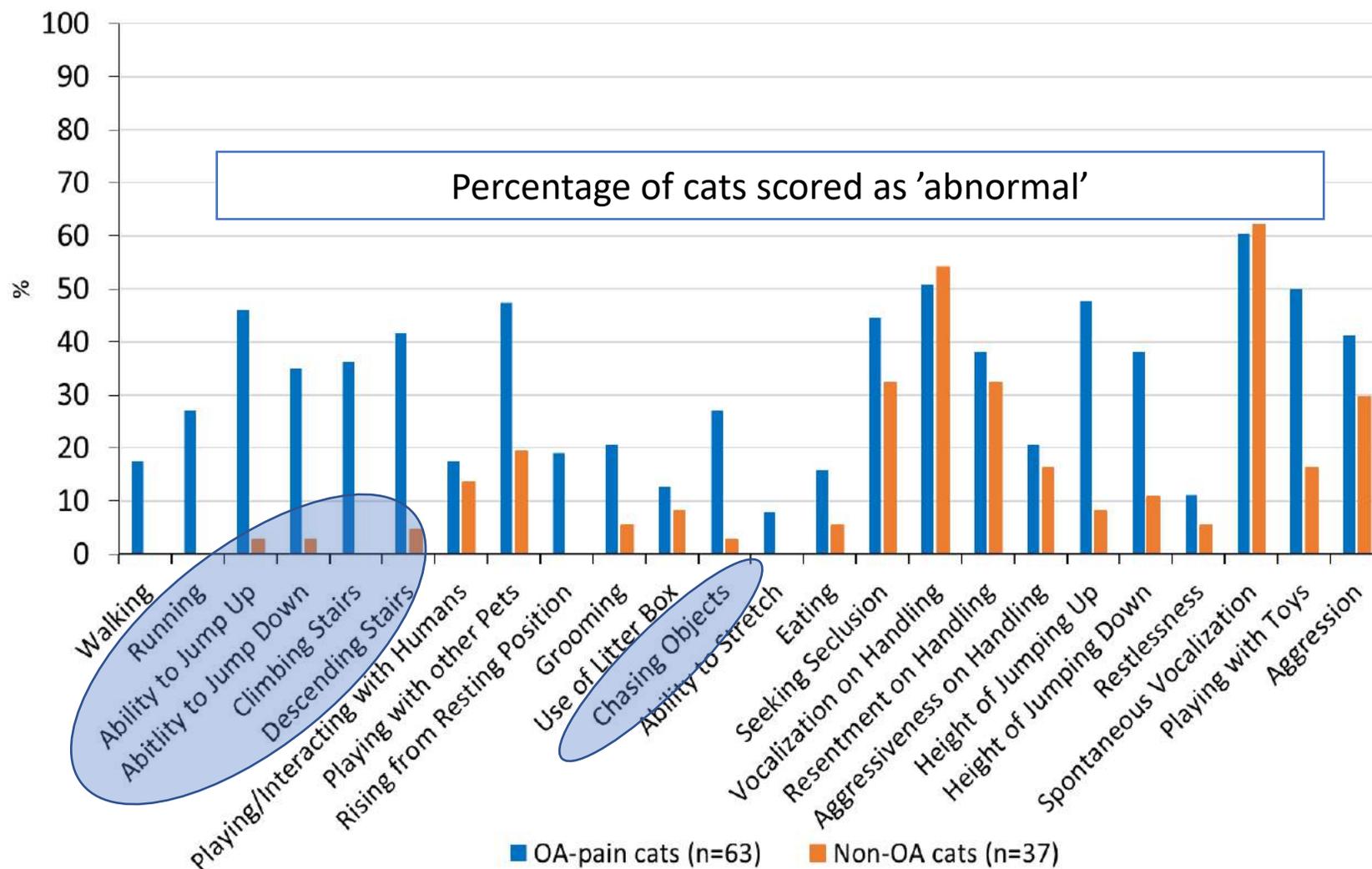
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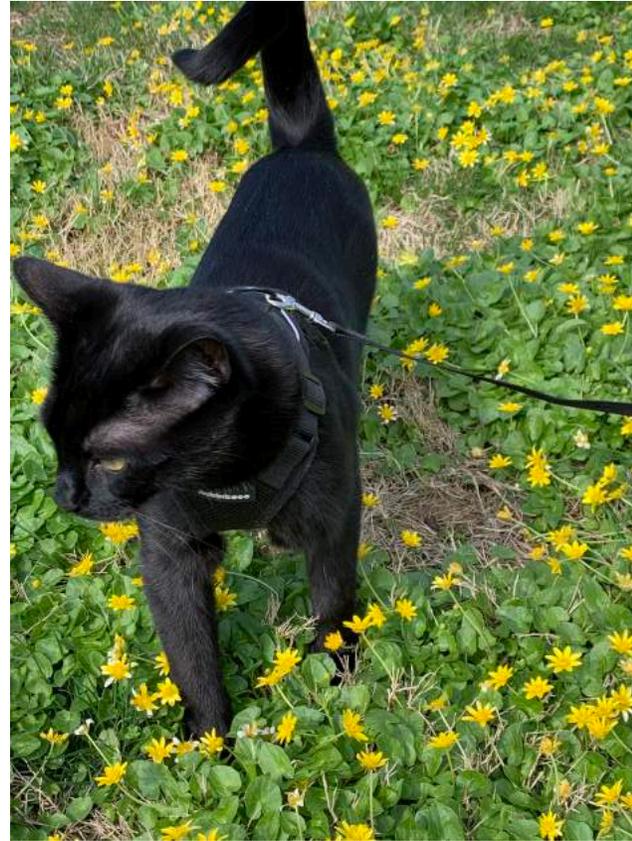
How do we  
monitor  
treatment?



# Six activities can help identify cats with OA



Unlike dogs, these behaviors are best observed in the home



Without owner engagement, many of these behaviors are attributed to aging

# Why it matters: Quality of life

## Five pillars of a healthy feline environment

A safe place

Multiple and separate resources for food, water, toileting, scratching, resting/sleeping

Opportunity for play and predatory behavior

Positive and predictable social interactions

Respect for the importance of a cat's sense of smell



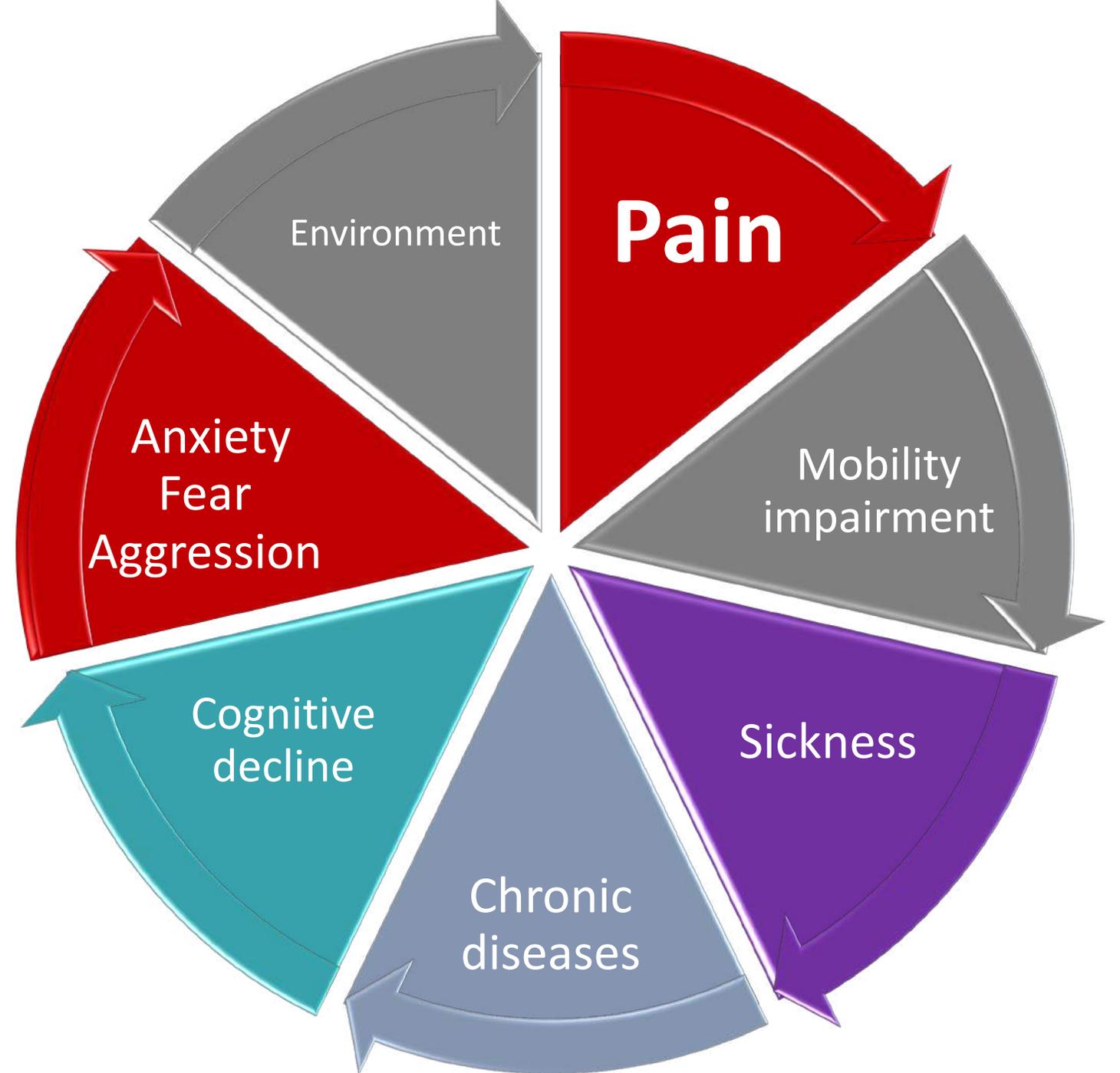
## With OA:

- Coping ability decreases
- Modifications needed to ensure access



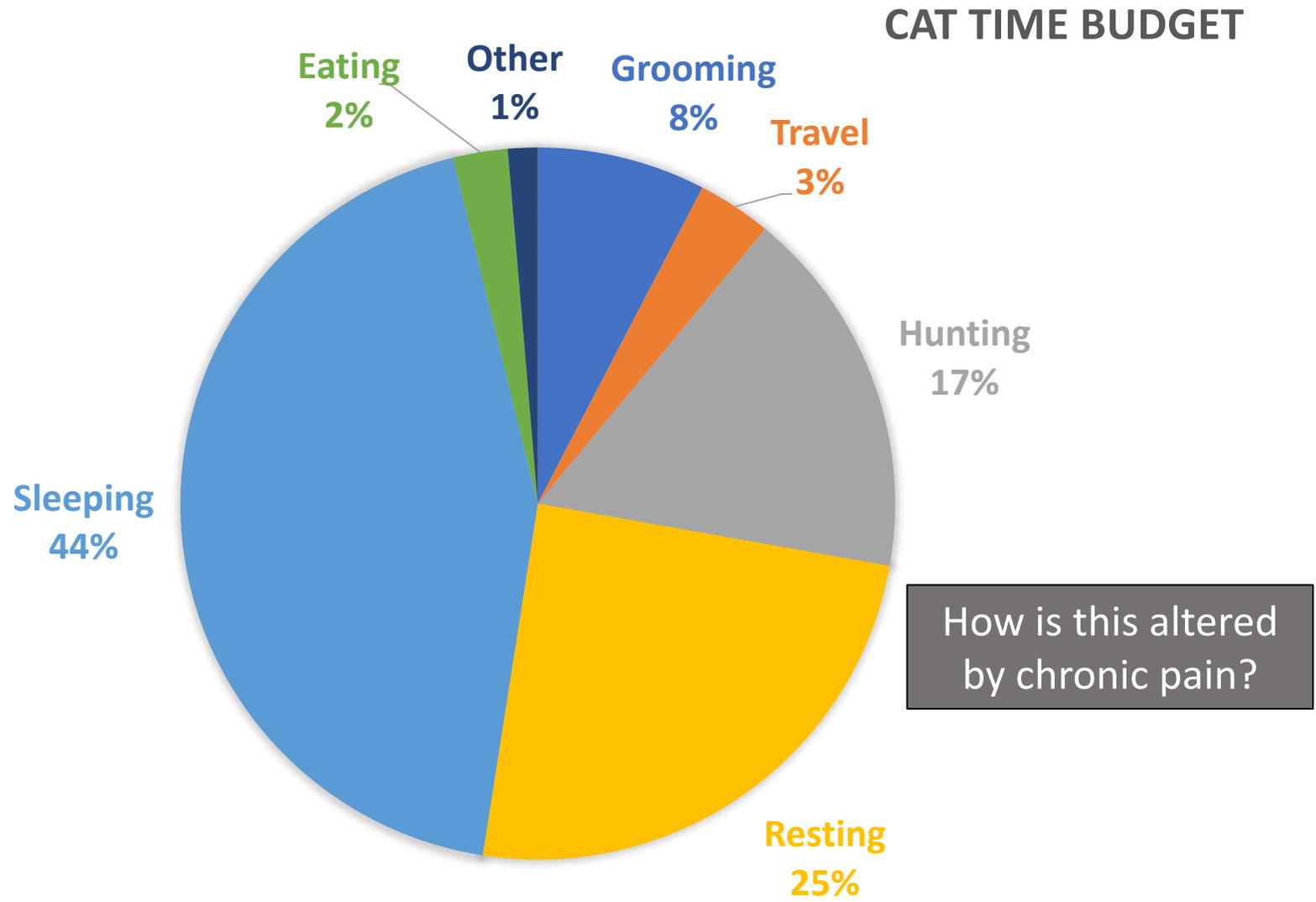
Because quality  
of life is more  
than just  
absence of  
pain...

Many impacts  
on **quality of life**



To understand  
what to provide,  
we need to  
understand cat  
needs





To understand *cat needs*, we need to understand their history

- Solitary hunters
- Social structure is both solitary and community
- “Time-share” resources
- People are a part of cats’ social structure
- Use scent for communication



Solitary hunters — Midlevel predators



Cats have a  
flexible social  
structure

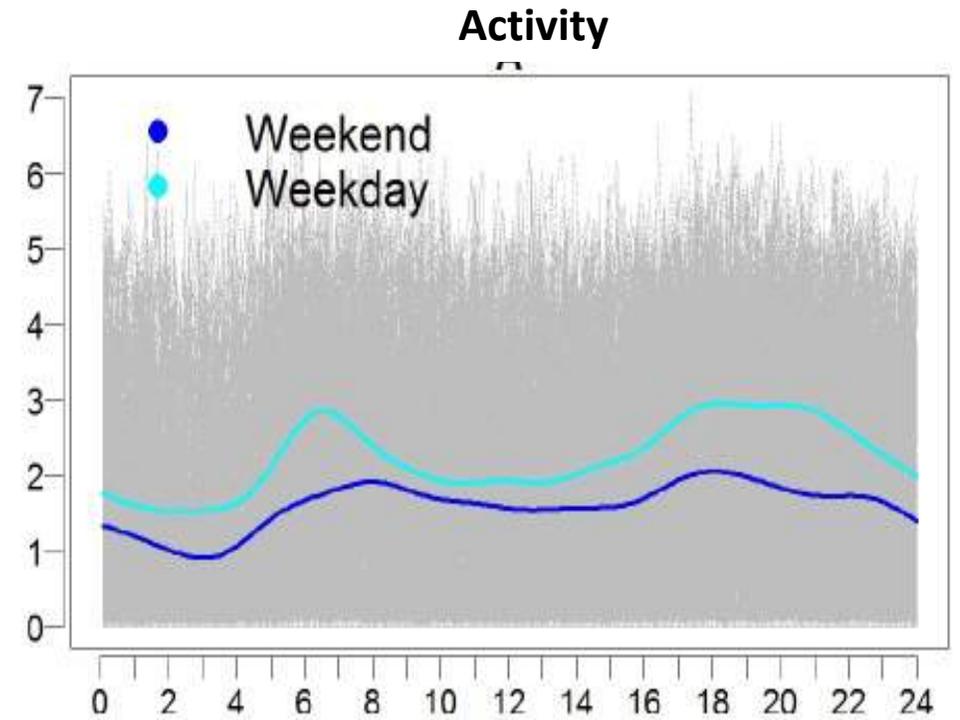
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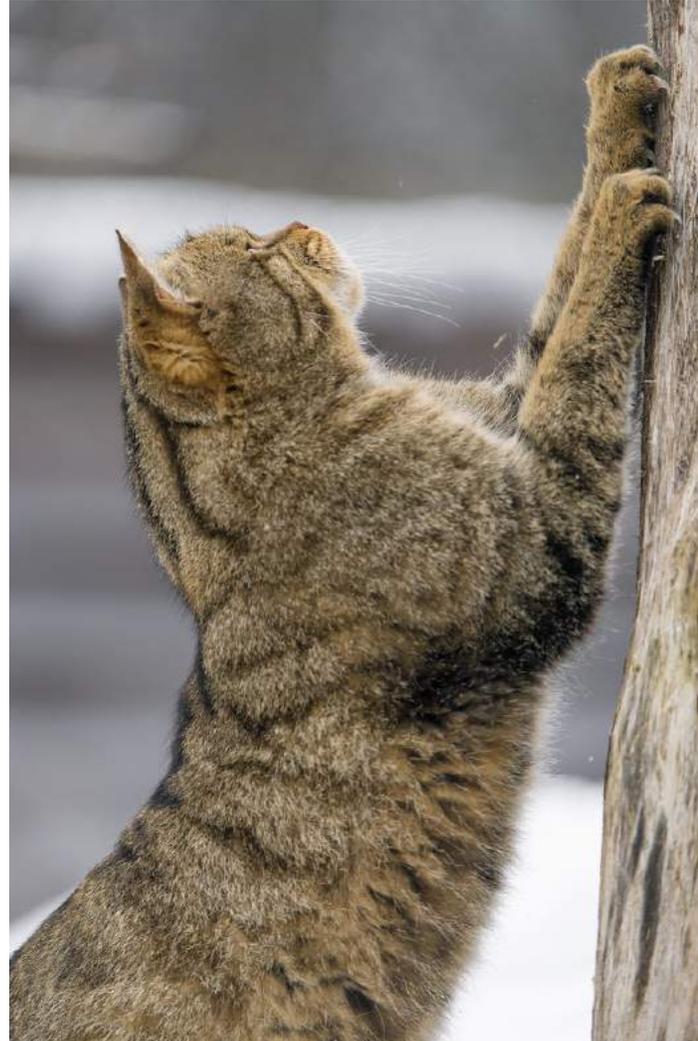
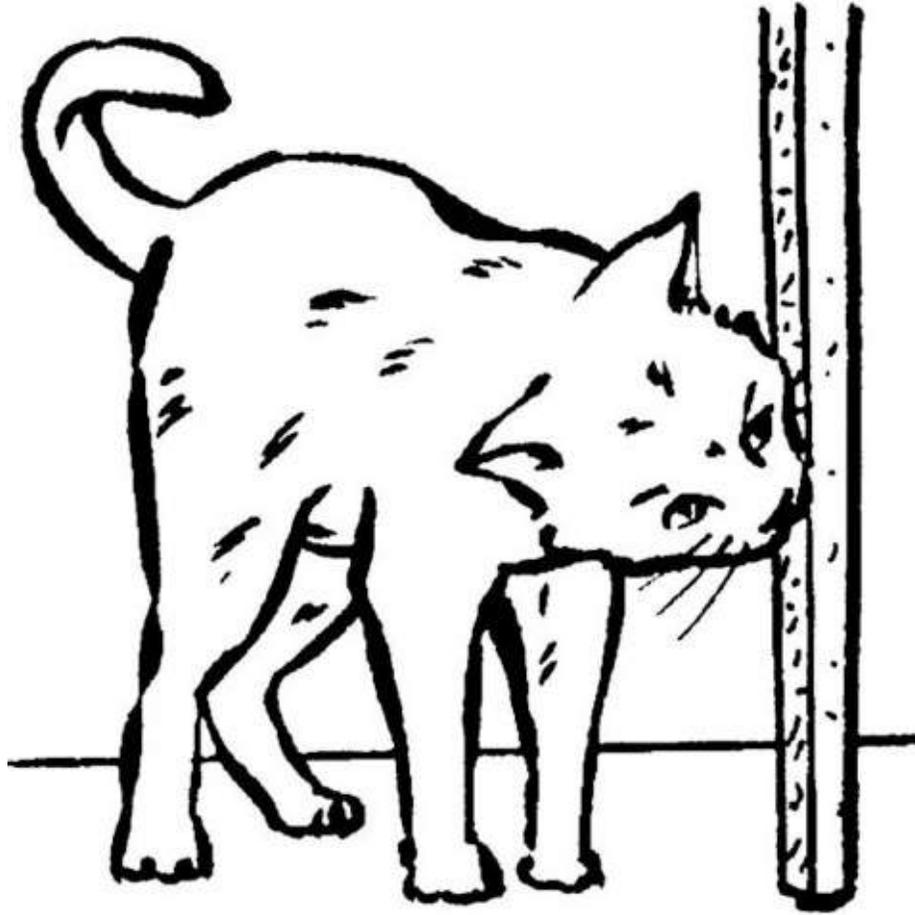
Time-sharing of  
resources

System of communication designed to  
avoid conflict

# Social interactions with people are important



# Cats use scent for communication





## Cats depend on us to meet their needs

- Lack of activity and enrichment could lead to a variety of health and behavioral issues
  - Obesity
  - Inappropriate play
  - Boredom/frustration
  - Potential for behavior problems

# The importance of 3-D space

- Increased 3-D space
  - Increased use of space and
  - Decreased agonistic encounters



- Cats treated with effective analgesic will resume use of vertical space
- What accommodations must be made to preserve access?



Safe places – Ability to ‘get away’ may be compromised

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Cats with OA pain need  
consistent access to safe,  
comfortable spaces

## How do we identify this cat?



Owner engagement is crucial – they know their own cats' behavior and notice changes earlier

BUT, they often dismiss the changes as “slowing down” or normal aging



## Learning about OA and associated pain motivates action among owners

### Owners:

- Can detect behavioral changes in their cats
- Do not want their cats to be in pain
- Must understand that these behavioral changes may indicate disease

# When we ask about pain...

- This requires a shift in our language



Current emphasis for 'pain' is weighted on extreme behaviors





Need to shift to awareness

Less extreme behavioral changes are still indicative of painful disease

**CAT OSTEOARTHRITIS PAIN CHECKLIST**



Your Cat's Name: \_\_\_\_\_

Your Name: \_\_\_\_\_

Osteoarthritis pain can be a serious health problem for your cat. And cats hide almost everything, especially pain. You know your cat's playful ways and what she loves better than anyone. Changes in these behaviors could be signs of osteoarthritis pain. Your veterinarian relies on you to report changes in your cat's behavior for more accurate diagnoses. If it is found that your cat is showing signs of OA-related pain, helping your cat begins by talking to your vet.

**COULD MY CAT HAVE OSTEOARTHRITIS?**

This checklist will help your veterinary team identify your cat's activities and behaviors that might be signs of osteoarthritis (OA), a degenerative joint disease that can be painful.

**Is your cat showing signs of OA-related pain?**

Think about your cat's activity in the past week. Check all of the signs that you've observed in your cat.

<p><b>JOINT DISEASE</b></p> <p><b>Climbing up stairs:</b> uses bunny-hop, with both back legs hopping at same time, and/or stops for a break</p>	<p><b>JOINT DISEASE</b></p> <p><b>Climbing down stairs:</b> angles body to the side, descends one stair at a time, and/or stops for a break</p>	<p><b>HEALTHY</b> <b>JOINT DISEASE</b></p> <p><b>Chasing moving objects:</b> slows down or takes breaks during play and/or may have thinner frame near the tail</p>
<p><b>HEALTHY</b> <b>JOINT DISEASE</b></p> <p><b>Jumping up:</b> hesitates before jumping up, doesn't clear jumps in one leap, and/or uses arms to pull the legs up</p>	<p><b>JOINT DISEASE</b></p> <p><b>Jumping down:</b> hesitates before jumping down, makes smaller jumps vs one big one and/or reaches down towards the ground instead of leaping</p>	<p><b>HEALTHY</b> <b>JOINT DISEASE</b></p> <p><b>Running:</b> moves at a slower speed and alternates between jogging &amp; walking, and/or back feet angle together</p>

If you checked any of these changes in behavior, your cat may have OA-associated pain.<sup>1</sup> Share these with your veterinarian healthcare team. They will fully evaluate your cat to confirm the diagnosis.

This questionnaire is not a medical diagnostic tool and is not intended to replace discussion with an animal healthcare professional. Discuss medical concerns with your veterinarian.

**Osteoarthritis has physical and emotional effects**



Just as in humans, chronic pain negatively impacts your cat's quality of life, not just physically, but also emotionally. The good news is that by identifying your cat's condition, you and your veterinarian can develop a treatment plan for your cat.

A recent peer-reviewed published study demonstrated the initial validity and reliability of a quality of life assessment for chronic diseases, such as osteoarthritis, in cats.<sup>2</sup> Using these questions, you can help your veterinarian assess and monitor how well your cat's chronic pain management treatment is working.

Think about your cat's behavior in the past week and help us determine a starting point by completing the following table.

Is your cat...	↓ My cat couldn't be less			My cat couldn't be more ↓			
Energetic & Enthusiastic (Vitality)	0	1	2	3	4	5	6
Active & Comfortable (Comfort)	0	1	2	3	4	5	6
Happy & Content (Emotional well-being)	0	1	2	3	4	5	6

**YOUR CAT'S GENERAL BEHAVIOR HISTORY CAN BE HELPFUL**

Additional information that can be helpful to your veterinary team is your cat's behavior.

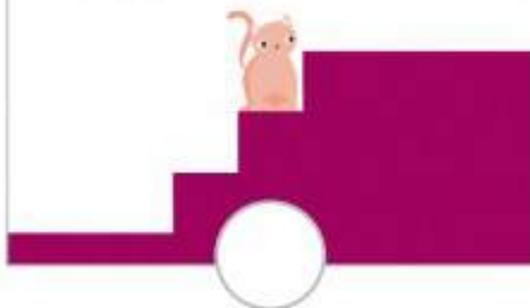
	YES	NO
1. Has your cat's personality and sociability changed?	<input type="radio"/>	<input type="radio"/>
2. Has your cat's urination or defecation habits changed?	<input type="radio"/>	<input type="radio"/>
3. Is your cat hiding more or does your cat seem to be "slowing down"?	<input type="radio"/>	<input type="radio"/>

OA pain can affect cats of any age, and it has been seen in more than 60% of cats that are 6 years or older.<sup>1</sup> If left untreated, the pain can become worse over time. This checklist is designed to help with the recognition of OA pain to help keep your cat happy and active. Your veterinary team will review the results of this checklist with you to identify if your cat might be suffering from OA. This checklist is not a medical diagnostic tool and is not intended to replace discussion with an animal healthcare professional. Discuss medical concerns with your veterinarian.

References: 1. Based on the Musculoskeletal Pain Screening Checklist (MPSC) ©2019 North Carolina State University. 2. Reid J, Nolan A.M., Scott E.M. Measuring pain in dogs and cats using structured behavioural observation. *Vet J.* 2018 June; 236: 72-79. 3. Singanand U et al. Cross-sectional study of the prevalence and clinical features of osteoarthritis in 100 cats. *Vet J.* 2011 Mar;187(3):304-9.

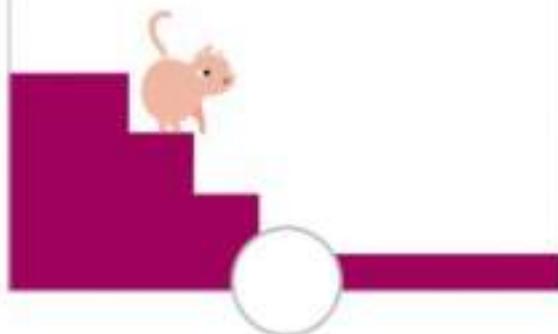
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### JOINT DISEASE



**Climbing up stairs:** uses 'bunny-hop', with both back legs hopping at same time, and/or stops for a break

### JOINT DISEASE



**Climbing down stairs:** angles body to the side, descends one stair at a time, and/or stops for a break

### HEALTHY

### JOINT DISEASE



**Chasing moving objects:** slows down or takes breaks during play and/or may have thinner frame near the tail

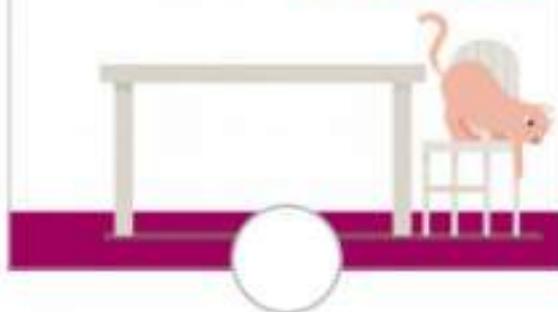
### HEALTHY

### JOINT DISEASE



**Jumping up:** hesitates before jumping up, doesn't clear jumps in one leap, and/or uses arms to pull the legs up

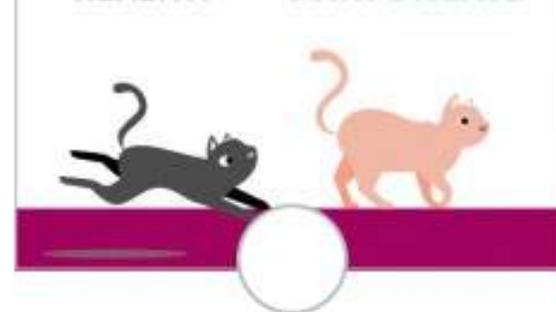
### JOINT DISEASE



**Jumping down:** hesitates before jumping down, makes smaller jumps vs. one big one and/or reaches down towards the ground instead of leaping

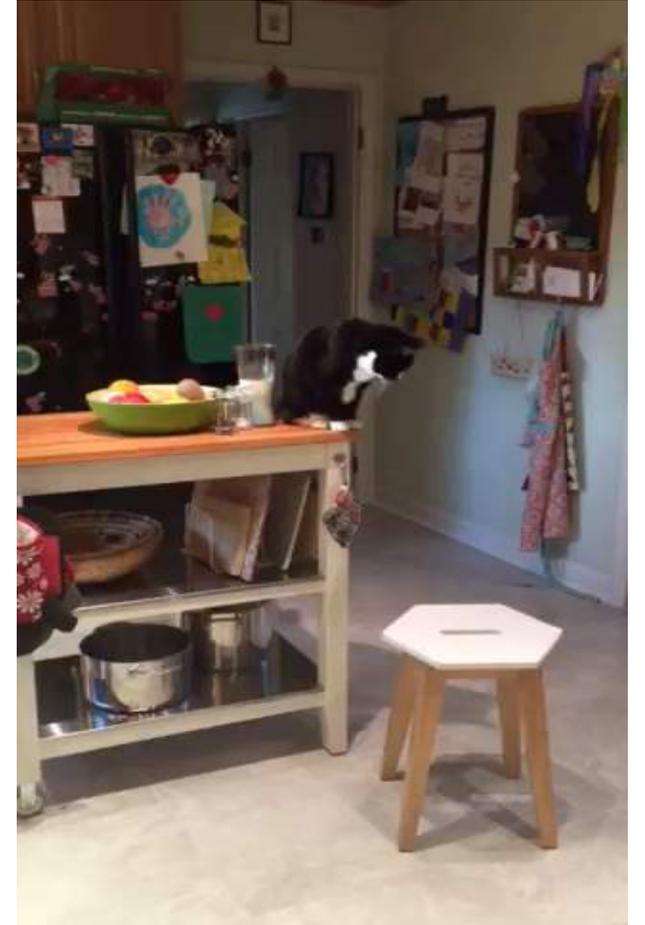
### HEALTHY

### JOINT DISEASE



**Running:** moves at a slower speed and alternates between jogging & walking, and/or back feet angle together

Comparisons are powerful  
(especially for slowly progressing conditions)



What we  
have:

Appreciation for the effects of OA pain on QoL  
for cats

Behaviors we can use to identify and monitor  
OA pain

Owners motivated to provide pain control for  
their cats

What are we missing?

# Treatment and management

PRIMARY GOAL: RESTORE QUALITY OF LIFE



- 1 Lifestyle changes
- 2 Pharmacological intervention
- 3 Nonpharmacological intervention



## Lifestyle changes: Environmental

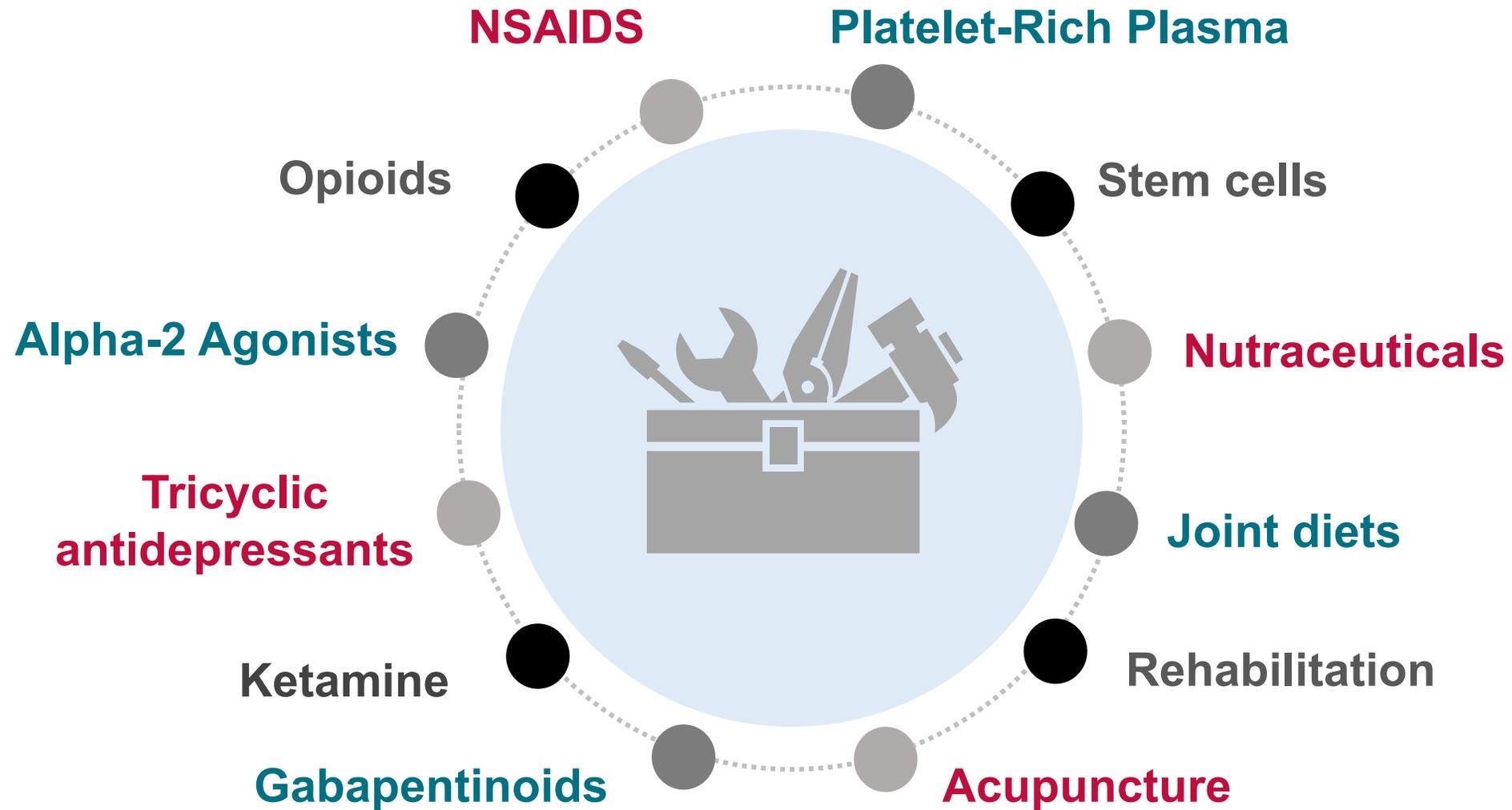
Robertson, S. (2008, November 1). Osteoarthritis in cats: What we now know about recognition and treatment. *Veterinary Medicine*  
Epstein M., et al. 2015 AAHA/AAFP pain management guidelines for dogs and cats. *JFMS*. 2015;17:251–272

# Lifestyle changes: Supportive

- Weight loss
- Controlled exercise
- Grooming



# Current OA intervention toolbox





<b>#Approved therapies</b>	NSAIDs (meloxicam; robenacoxib)  Frunevetmab
<b>*Proven therapies</b>	NSAIDs Diet optimization

## Pharmacologic interventions:

- # None approved in the US
- \* Proven efficacy based on evidence-based veterinary medical literature

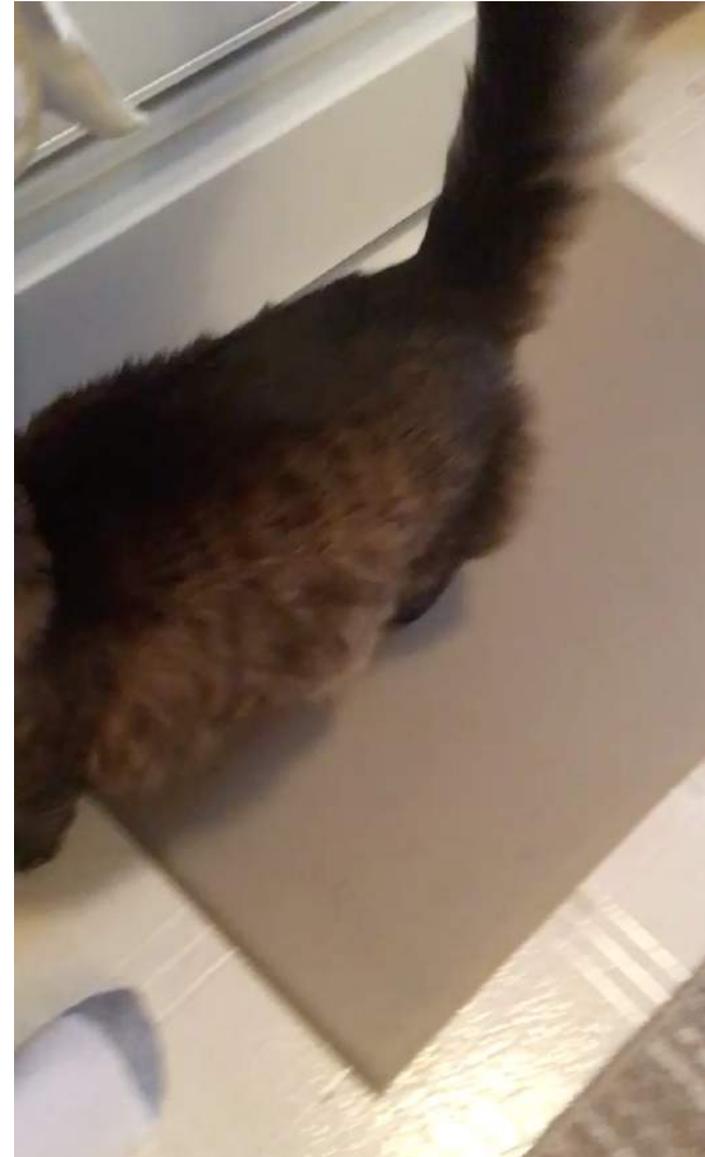
Remember our  
multidisciplinary  
patient...



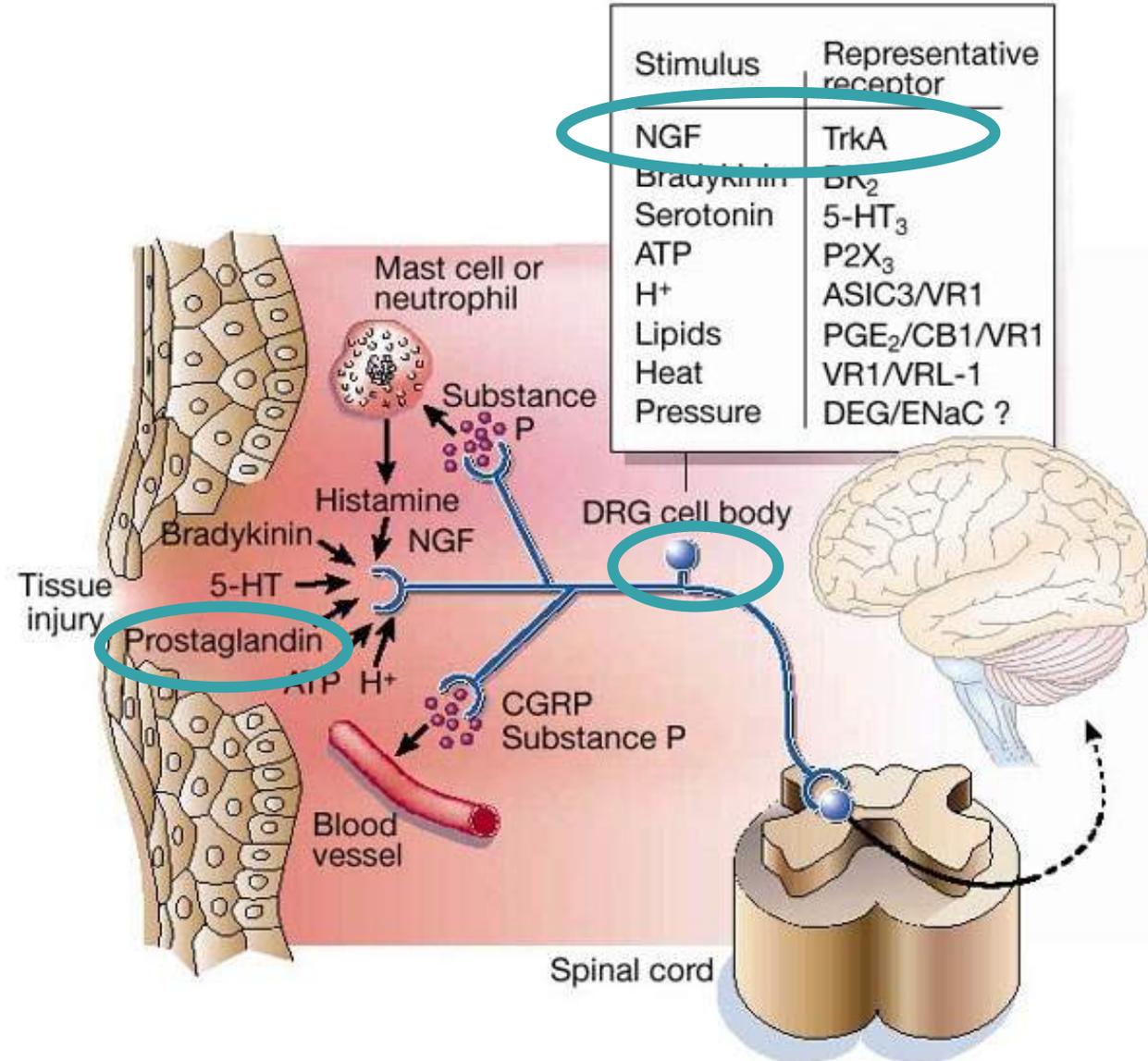
# Balancing treatments and cat-human bond is critical



NO.... MY CAT DOESN'T LIKE BEING GIVEN PILLS EITHER...

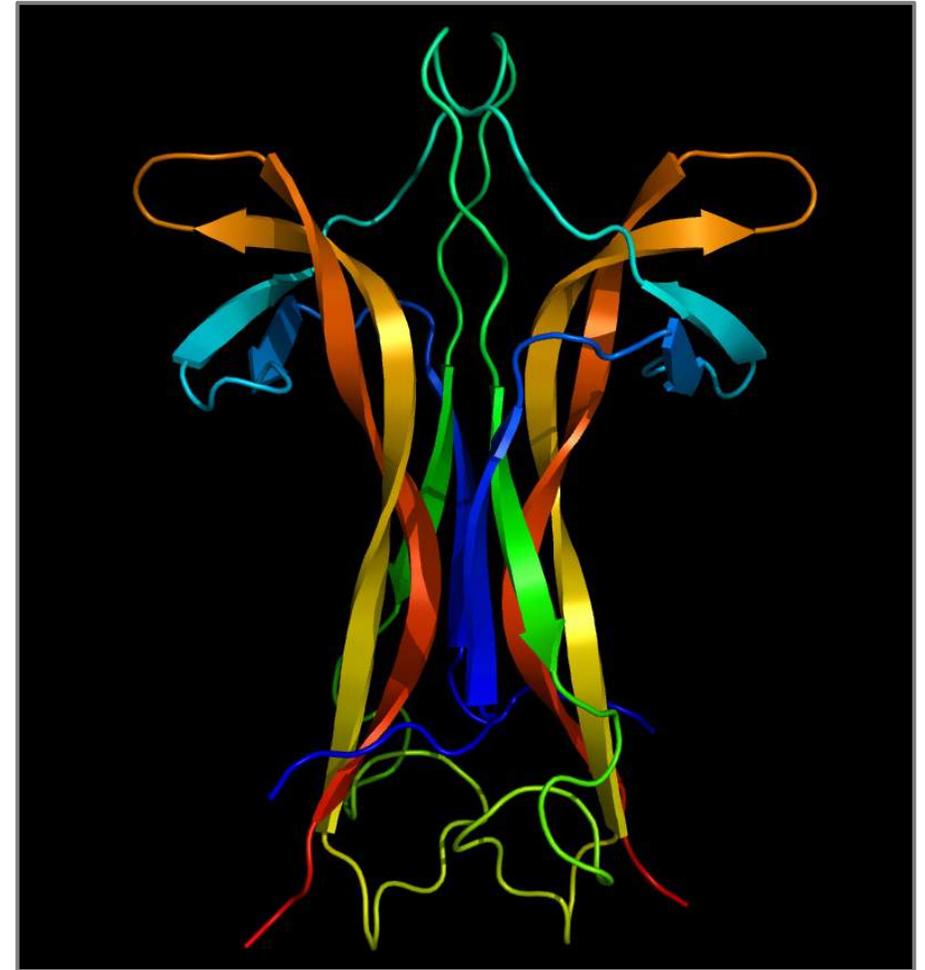


# Many target opportunities in the periphery



# Nerve Growth Factor (NGF)

- During development: aids the normal development of the nervous system
- In the adult: primary role is pro-nociceptive



*Target NGF dimer*

# NGF plays an important role in OA pain



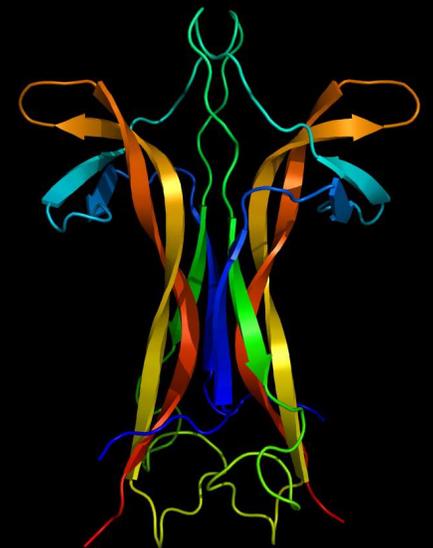
OPEN ACCESS

REVIEW

## Anti-nerve growth factor monoclonal antibodies for the control of pain in dogs and cats

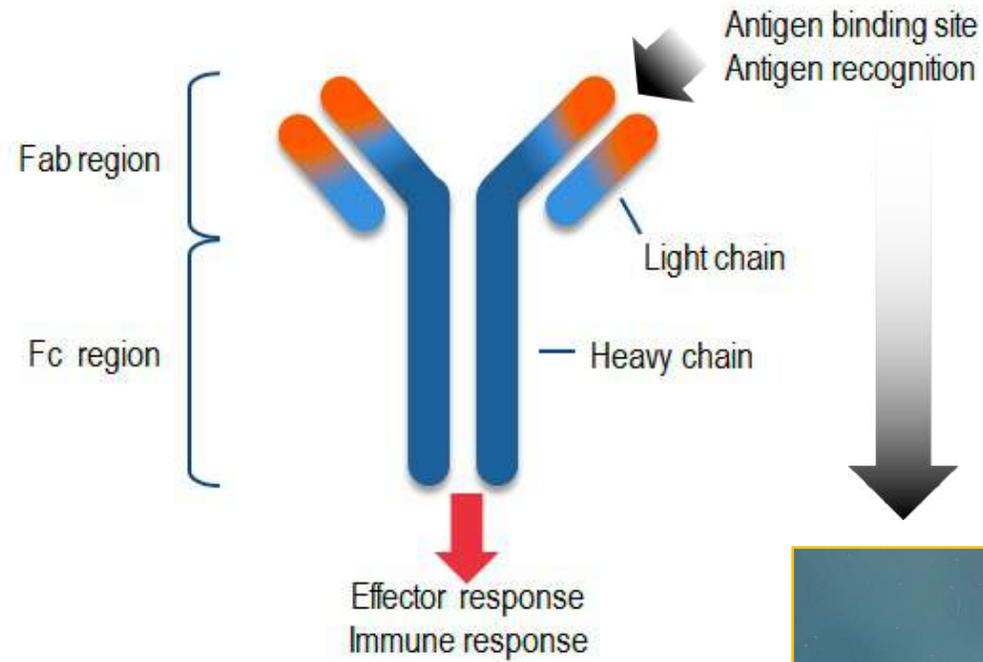
Masataka Enomoto,<sup>1</sup> Patrick W Mantyh,<sup>2</sup> Joanna Murrell,<sup>3</sup> John F Innes,<sup>4</sup> B Duncan X Lascelles<sup>1,5,6,7</sup>

*Vet Rec. 2019 Jan 5;184(1):23. (Open Access: doi: 10.1136/vr.104590)*

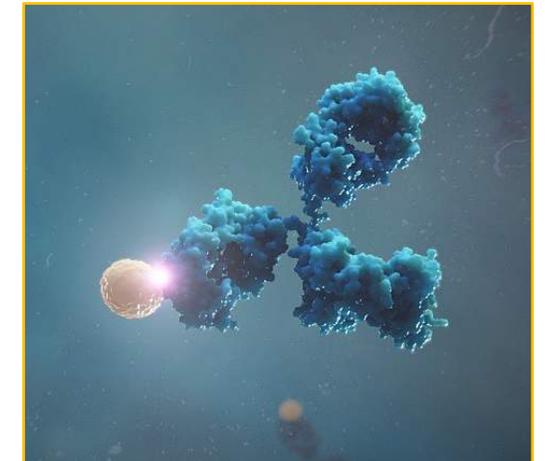


# Anti-NGF Strategies

- Removing free NGF (Anti-NGF mAb)
- Preventing NGF from binding to TrkA
- Prevent TrkA activation

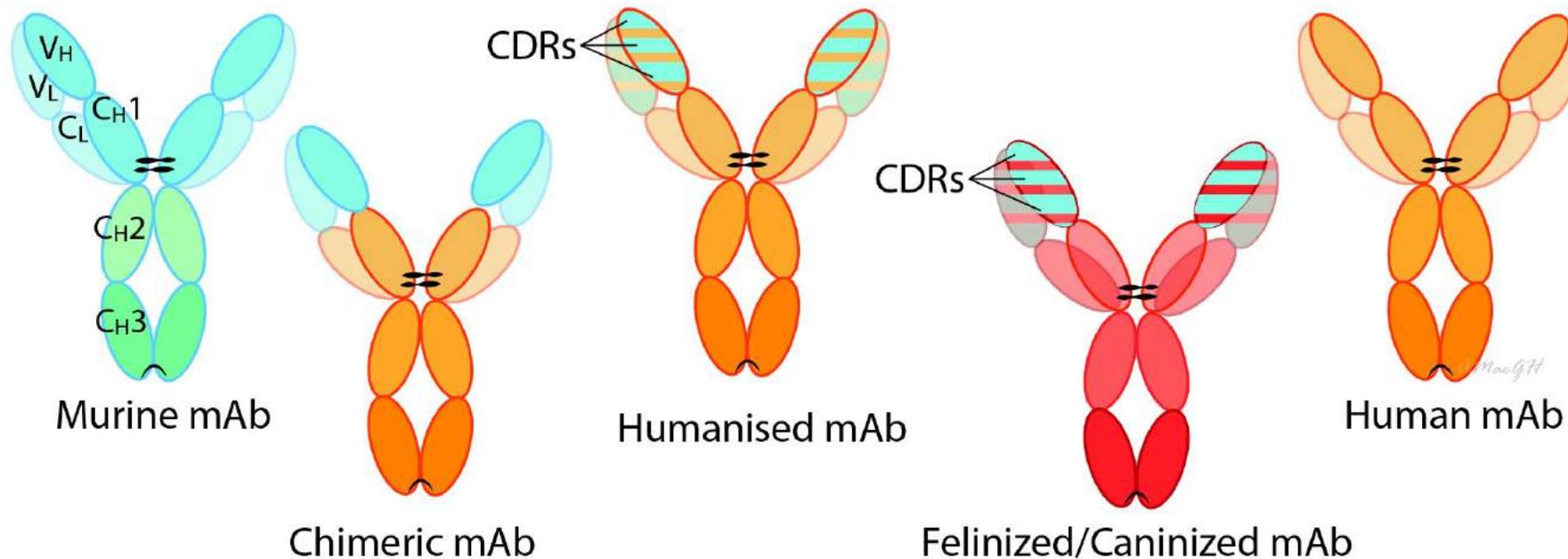


■ Constant region  
■ Variable region



# Benefits of Monoclonal Antibodies (mAb)

- Long duration of action (long half-life)
- Injectable
- Low risk of toxicity
- Highly specific; not cross BBB



# Feline anti-NGF mAb

## Proof-of-concept study<sup>1</sup>

- 34 cats (single site)
  - 23 frunevetmab; 11 placebo
- 1 injection (SQ)
  - 7 weeks additional follow-up
- Activity monitors and owner questionnaires

## Pilot field study<sup>2</sup>

- 126 cats (multi-site)
  - 85 frunevetmab; 41 placebo
- 2 injections (SQ or IV)
  - 4 weeks apart
- Activity monitors and owner questionnaires

Both studies showed a positive effect of frunevetmab for treatment of chronic pain in cats



<sup>1</sup> Gruen, M. E., et al. *Journal of veterinary internal medicine* 30.4 (2016): 1138-1148.

<sup>2</sup> Gruen ME, Myers JAE, Lascelles BDX. *Frontiers in veterinary science* 8 (2021).

Tamara Grubb, DVM, PhD, DACVAA



## KEY POINTS

- Owners should be educated that cats experience pain from OA, which impacts health, QOL, and behavior. Behavioral and QOL scores and mobility animations such as those available through Zoetis can be useful tools on educating owners how to recognize OA-associated pain (see **Education & Diagnostic Tools**, next page).
- Using pain-specific questionnaires and performing feline-friendly, OA pain-specific examinations can help expedite a diagnosis of pain (see **Education & Diagnostic Tools**, next page).
- Feline OA patients should be treated with the drugs and techniques currently available, but clinicians should stay abreast of future data and new treatment options as they emerge.

ZOETIS PETCARE

## clinicalnotes™

## Feline Osteoarthritis Pain: Tools for Clinicians & Pet Owners

Osteoarthritis (OA), a form of degenerative joint disease (DJD), is the most common cause of chronic pain in mammals, including cats. More than 90% of adult cats may have radiographic evidence of OA, with the presence/severity of disease expected to increase by >10% each year.<sup>1</sup>

Pain can be classified as either adaptive (physiologic) or maladaptive (pathologic). Adaptive pain facilitates tissue protection and healing, whereas maladaptive pain negatively impacts health, quality of life (QOL), and behavior, which can impact the human-animal bond, potentially leading to surrender or euthanasia of the pet.<sup>2</sup> OA is a nonhealing disease, with OA-associated pain having no protective benefit; thus, OA causes maladaptive pain that, without treatment, progressively worsens as peripheral and central sensitization and neuropathic pain develop.<sup>1</sup>

Although OA is not curable, if identified and treated early, the progression of the intensity of OA pain can be slowed, providing a prolonged period of controllable pain and good QOL (likely a normal lifespan). Because OA is more common in geriatric cats,<sup>1,3</sup> OA screening should begin when cats reach 7 to 10 years of age.

### Recognizing OA-Associated Pain

OA-associated pain may not be obvious—to owners and to veterinary teams.<sup>4</sup> Because cats are evolutionarily both predators and prey, their natural instinct is to hide any vulnerability that could increase predation, including pain. Tools such as checklists, animations, and videos can help owners and veterinary teams accurately recognize and assess pain associated with OA in cats.

### Tools for Owners

Although the expected prevalence of OA is similar between dogs and cats, cat owners may be less likely than dog owners to identify pain in their pet.<sup>4</sup> However, educating owners on the prevalence of OA-associated pain and available treatment options may make owners more likely to bring their cat to the clinic.<sup>5</sup>

Owner education starts with an understanding of feline behavior and mobility. Owners should understand that the clinical signs of OA-associated pain are rarely what is expected but the impact of pain (ie, pain-mediated changes in behavior, activity, and mobility) can still be identified. Behavior and activity changes related to urination/defecation, grooming, and social interactions (with humans and/or other pets) are often indicators of pain and, if not due to pain, could be due to other conditions that may require medical attention. Cats are largely sedentary, making

Brought to you by Zoetis

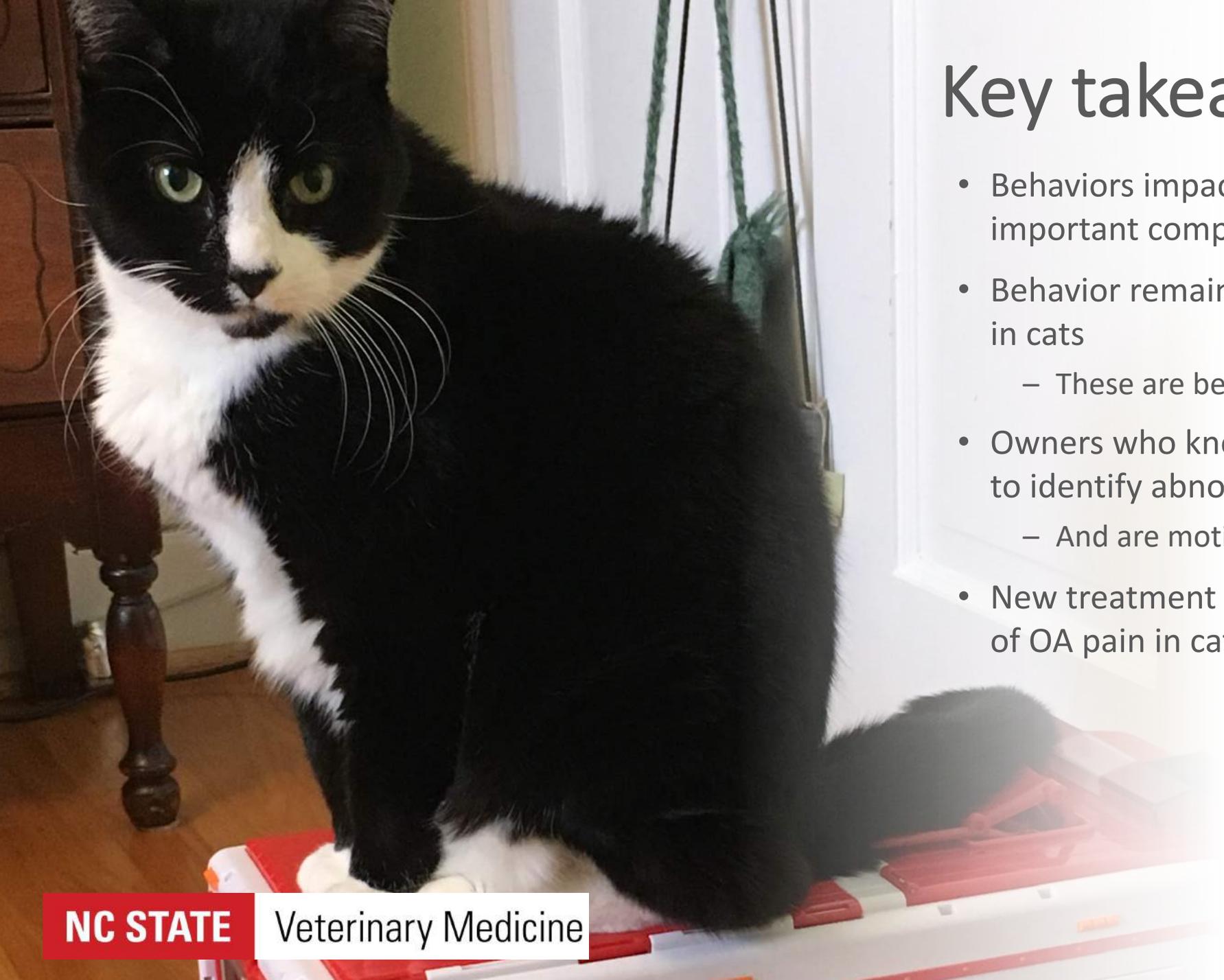
## TABLE

### COMMON MEDICATIONS USED TO TREAT CHRONIC PAIN IN CATS: ADVANTAGES, DISADVANTAGES, & DOSAGES

Drug & Class	Dose, Frequency, & Route	Advantages	Disadvantages	Notes
Robenacoxib (NSAID)	1-2.4 mg/kg PO every 24 hours*	Class is effective against OA-associated pain	Oral administration, which may be difficult for owners Adverse effects are possible with NSAIDs, which can frequently be an owner concern	Approved outside the United States for treatment of chronic pain in cats No limit on duration of therapy
Meloxicam (NSAID)	0.1 mg/kg PO first day, then 0.05 mg/kg every 24 hours thereafter*	Class is effective against OA-associated pain	Oral administration, which may be difficult for owners Adverse effects are possible with NSAIDs, which can frequently be an owner concern	Approved outside the United States for treatment of chronic pain in cats No limit on duration of therapy Doses as low as 0.01-0.03 mg/kg every 24 hours may be effective <sup>17</sup>
Gabapentin	3-20 mg/kg PO every 8-12 hours	Minimal adverse effects One study has indicated efficacy for treatment of OA-associated pain in cats <sup>18</sup>	Oral twice- to three-times-daily administration Can cause sedation Often a controlled drug	Proven effective for calming prior to transport to the clinic, which may decrease pain, as pain causes anxiety and anxiety exacerbates pain
Amantadine (NMDA-receptor antagonist)	3-5 mg/kg PO every 12 hours	Minimal adverse effects Potential for significant pain relief due to monoamine oxidase inhibition	Oral twice-daily administration Efficacy can be difficult to determine	Dosing is based on one canine study and may be inadequate Neither pharmacokinetics nor pharmacodynamics have been studied in cats
Ketamine (NMDA-receptor antagonist)	4-10 µg/kg/min IV following a loading dose of 0.5 mg/kg	Minimal adverse effects Potential for significant pain relief due to monoamine oxidase inhibition	Patient must be hospitalized for infusion Repeat infusions may be necessary	Proven effective in other species, particularly in patients with pain of central sensitization Most effective dose and infusion duration are unknown and are likely highly individual
Amitriptyline (tricyclic antidepressant)	3-4 mg/kg PO every 12 hours	Minimal adverse effects	Oral twice-daily administration Cats typically do not like the taste	Serotonin-reuptake inhibition may provide analgesia through the descending inhibitory limb of the pain pathway
Tramadol (opioid)	1-2 mg/kg PO every 12 hours	Two studies indicate efficacy for treatment of OA-associated pain in cats <sup>19,20</sup>	Cats typically do not like the taste Oral twice- to three-times-daily administration Can cause sedation or dysphoria Controlled drug	Adverse effects like dysphoria, sedation, and diarrhea are common at the effective dose <sup>19</sup>
Buprenorphine (opioid)	0.02-0.05 mg/kg oral transmucosal every 8-12 hours	Opioid-level pain relief	Potential adverse effects Oral twice- to three-times-daily administration Controlled drug Opioids are not ideal for treatment of chronic pain	Oral transmucosal absorption is fairly low, potentially leading to the need for higher doses

\*Dosage used outside the United States





# Key takeaways

- Behaviors impacted by chronic pain are important components of quality of life for cats
- Behavior remains the best way to assess pain in cats
  - These are best assessed in the home
- Owners who know what to watch for are able to identify abnormal behavior
  - And are motivated to treat their cats
- New treatment options offer promise for relief of OA pain in cats





Questions?

