

Kenneth R. Harkin, DVM, DACVIM (SAIM) Hodes Professor and Head, Section of Medicine



Evaluation of Fortetropin in Geriatric and Senior Dogs With Reduced Mobility

October 11, 2022



College of Veterinary Medicine



Geriatric screening in first opinion practice – results from 45 dogs

M. DAVIES

Journal of Small Animal Practice (2012) **53**, 507–513 DOI: 10.1111/j.1748-5827.2012.01247.x

Prevalence, duration and risk factors for appendicular osteoarthritis in a UK dog population under primary veterinary care

Katharine L. Anderson¹, Dan G. O'Neill², David C. Brodbelt², David B. Church³, Richard L. Meeson³, David Sargan⁴, Jennifer F. Summers², Helen Zulch⁵ & Lisa M. Collins ⁶

SCIENTIFIC REPORTS | (2018) 8:5641 | DOI:10.1038/s41598-018-23940-z

Increased sleeping in 31% Lameness/stiffness in 22% Slowing down in 20%

Reduced range of motion in joints in 24% Pain in 15% Stiffness in 13% Crepitus in 13% Muscle wastage in 11%

Osteoarthritis affects 11.4% of a pet's lifespan Risk for OA at 9-11.9 years is 36X risk vs <3 years Dogs 30-39.9 kg 8X higher risk than dogs <10 kg



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Assessment of methods of evaluating sarcopenia in old dogs

Dana Hutchinson, DVM; James Sutherland-Smith, BVSc; Adrian L. Watson, PhD; AJVR, Vol 73, No. 11, November 2012 Lisa M. Freeman, DVM, PhD

Exceptional longevity and potential determinants of successful ageing in a cohort of 39 Labrador retrievers: results of a prospective longitudinal study

Vicki Jean Adams^{1*}, Penny Watson², Stuart Carmichael³, Stephen Gerry⁴, Johanna Penell⁵ and David Mark Morgan⁶

Adams et al. Acta Vet Scand (2016) 58:29 DOI 10.1186/s13028-016-0206-7 Labrador retrievers 1-5 years and >8 years, all with BCS 5-6/9

Osteoarthritis was an exclusion criteria

- Mean epaxial muscle area was significantly lower in healthy old dogs
- Physical activity alone may also not be the most effective means of managing sarcopenia (anti-catabolic agents,

adequate substrates)

39 Labrador retrievers in 10 year study 11 dogs lived exceptionally long (>15.6 years) After the age of 9, dogs with exceptionally long life spans continuing to gain weight from 9-13 years while others lost weight Lean muscle loss was slower in Exceptional and Long lifespan groups





- 1. Johnson, K.A., et al. Journal of the American Veterinary Medical Association 256.12 (2020): 1335-1341.
- Rychel, JK. Topics in Companion Animal Medicine 25.1 (2010): 20-25
- 3. Dan, G. O., et al. *PLoS One* 9.3 (2014): e90501.

4. Hays, L., et al. American journal of veterinary research 68.1 (2007): 35-41. 5. Impellizeri, J.A., et al. Journal of the American Veterinary Medical Association 216.7 (2000): 1089-1091.

6. Richardson, D.C., et al. Veterinary Clinics of North America: Small Animal Practice 27.4 (1997): 883-911.

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Osteoarthritis

Size – Large breed dogs develop OA compared to small breed dogs [2]. Obesity – Weight-related stress and chronic inflammation [5,6].

Problem(s)

- Loss of lean body mass and osteoarthritis contribute to decreased mobility in geriatric dogs
- 2. Not all pet owners have access to physical rehabilitation centers with experienced personnel

Known(s)

- 1. Fortetropin prevented rise in myostatin and minimized loss of lean body mass in dogs following TPLO surgery (White, Dana A., et al. "Fortetropin inhibits disuse muscle atrophy in dogs after tibial plateau leveling osteotomy." Plos one 15.4 (2020): e0231306.)
- 2. Fortetropin administration resulted in 18% increase in the fractional synthetic rate of muscle protein in geriatric humans (Evans W, et al. Effects of Fortetropin on the rate of muscle protein synthesis in older men and women: a randomized, double-blinded, placebo-controlled study. J Gerontol A Biol Med Sci 2020; doi:10.1093/Gerona/glaa162.)

Question(s)

- 1. Would Fortetropin benefit geriatric dogs with reduced mobility?
- Do we have an objective way to measure the effect on mobility?



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LOAD QUESTIONNAIRE

Initial Visit

Mobility					
Generally					For offic
1. How is you	r dog's mobilit	ty in general?			
0	0	0	0	0	
Very good	Good	Fair	Poor	Very poor	
2. How disable	ed is your dog	by his/her lame	ness?		
0	0	0	0	0	
Not at all disabled	Slightly disabled	Moderately disabled	Severely disabled	Extremely disabled	
3. How active	is your dog?				
O	0	O	O	O	
Extremely active	Very active	Moderately active	Slightly active	Not at all active	
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•. what is the	enect of cold,	, damp weather d	in your dog s ia	amenessi	
0		0	0	0	
5. To what deg 'lie down'?	gree does you	r dog show stiffi O Moderate stiffness	Severe stiffness	Extreme stiffness	
At exercise					
6. At exercise	, how active is	your dog?			
0	0	O	O	O	
Extremely active	Very active	Fairly active	Not very active	Not at all active	
7. How interes	sted is your do	og in exercising?			
0	0	0	0	0	
Extremely interested	Very interested	Fairly interested	Not very interested	Not at all interested	
8. How would	you rate your	dog's ability to a	exercise?		
0	0	0	0	0	
Very good	Good	Fair	Poor	Very poor	

No effect	O Mild effect	O Moderate effect	O Severe effect	Extr
. How ofte	n does vour doo	ı rest (stop/sit do	wn) during exe	rcise?
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•What is t	he effect of cold	. damp weather o	on your pet's al	oility t
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No stiffness	Mild stiffness	Moderate stiffness r dog's lameness O Moderate effect	Severe stiffness	Extre ity to Ext

Hercock CA, Pinchbeck G, Giejda A, et al. Validation of a client-based clinical metrology instrument for the evaluation of canine elbow osteoarthritis. J Small Anim Pract 2009; 50(6):266-271 https://assets.ctfassets.net/rp0cdq69asz8/2mKMS10BAUAQUaKMYQGSKw/dbc33dc938e008ce4c32909a7e9b5350/Printable_LOAD_Form.pdf.

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Initial Visit





Kansas State



The LOAD questionnaire

The Liverpool Osteoarthritis in Dogs (LOAD) questionnaire is a 13-item clinical metrology instrument (CMI) used to assess canine articular disorders like OA. Individual question scores are summed to provide an overall "LOAD score" suggestive of the animal's disease presence and severity.

Interpreting LOAD scores

The aggregate LOAD score helps determine the presence and severity of articular disorders like OA.



LOAD score is a recommendation only. Each patient should be carefully evaluated and examined by a registered veterinarian and the diagnosis of OA confirmed. Treatment options - including the benefits and risks of all available modalities - should be carefully considered and discussed with owners ro determine the best course of action.



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6.	At exercise.	, how active is	your dog?			
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Hercock CA, Pinchbeck G, Giejda A, et https://assets.ctfassets.net/rp0cdq69 KANSAS STATE UNIVERSITY College of Veterinary Veterinary Medicine

Initial Visit







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tiffness Severe stiffness	O Extreme stiffness	12.To what degree does yo	our dog show stiffn	ess in the
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cising?		13. What is the effect of yo	ur dog's lameness	on his/he
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Hercock CA, Pinchbeck G, Giejda A, et al. Validation of a client-based clinical metrology instrument Please return the form to a staff member. https://assets.ctfassets.net/rp0cdq69asz8/2mKMS10BAUAQUaKMYQGSKw/dbc33dc938e008ce4c

For office use only

Clicking LOAD Score will tabulate your score once. Reset is not available for this function.

NSAS STATE Initial Visit

For office use only

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g's lameness? 0 ffect

Extreme effect

ng exercise?

itly

0 Very frequently

et's ability to exercise?

ffect

0 Extreme effect

e affected leg after a

0 fness

Extreme stiffness

er ability to exercise?

ffect

0 Extreme effect

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.OAD questionnaire

erpool Osteoarthritis in Dogs questionnaire is a 13-item clinical ogy instrument (CMI) used to assess articular disorders like OA. ual question scores are summed to an overall "LOAD score" suggestive nimal's disease presence and 1.

cores

helps determine the presence and severity of articular



dation only. Each patient should be carefully evaluated and terinarian and the diagnosis of OA confirmed. Treatment fits and risks of all available modalities - should be scussed with owners ro determine the best course of

LOAD Score

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FORTETROPIN® Supplementation

- Randomized, double-blind, placebo-controlled study
- Dogs could not have any disease that could affect 6 month survival
- Dogs had to have lameness, weakness, decreased mobility, decreased voluntary activity, subjective loss of muscle mass, reduced exercise tolerance
- Liverpool Osteoarthritis in Dogs (LOAD) scores (0, 6 and 12 weeks).
 - 23 dogs on Fortetropin Ο
 - 23 dogs on Cheese Powder Ο
- LOAD Score ranges from 0 (normal) to 52 (severe mobility problems)
- Statistical analysis blinded to control, treatment and scoring interpretation
 - Non-parametric *t*-test (Mann-Whitney *U*-test) \bullet
 - Friedman's test for repeated measures over time





Table 1. Distribution of dogs in each treatment group for different senior weight and size classifications and clinical signs reported by owners for each treatment group.

	Weight groups with minimum age for senior designation [number of dogs in each group				Clinical signs reported by owners (number of dogs in each group)				
	(median age in years; range)]					Decreased mobility		Decreased	Muscle
Group	< 9.1 kg (small; 9 y)	9.1 to 22.9 kg (medium; 7 y)	23.0 to 54.5 kg (large; 6 y)	> 54.5 kg (giant; 4 y)	Lameness	and/or weakness	Exercise intolerance	voluntary activity	mass loss
Fortetropin	5 (12 y; 9 to 13.1 y)	6 (12.6 y; 9 to 14.1 y)	11 (10.8 y; 8 to 12 y)	1 (7.4 y)	13	20	12	12	17
Cheese powder	3 (11.8 y; 11.1 to 14 y)	4 (11.9 y; 8 to 12 y)	15 (9.9 y; 7 to 13 y)	1 (9.7 y)	12	20	7	11	17

Hetrick, Katie, Kenneth R. Harkin, and James K. Roush. "Evaluation of Fortetropin in geriatric and senior dogs with reduced mobility." The Canadian veterinary journal= La *revue veterinaire canadienne* 63.10 (2022): 1057-1060.

IMPACT OF FORTETROPIN® ON LOAD SCORES IN GERIATRIC DOGS

	Fortetropin	Cheese powder	<i>P</i> -value
Age (y)	11.5 (7.4 to 14.1); 10.9 (1.8) (<i>n</i> = 23)	11 (7.1 to 14); 10.6 (2.3) (n = 23)	0.58
Weight (kg)	24.4 (2.5 to 63.3); 23.4 (14.9) $(n = 23)$	25 (3.3 to 59.8); 23.7 (12.7) $(n = 23)$	0.59
LOAD score, Week 0	21 (10 to 31, 18 to 26); 21.35 (5.7, 30.9) (n = 23)	22.5 (12 to 45, 18 to 30); 23.71(7.9, 62.7) ($n = 23$)	0.425
LOAD score, Week 6	19 (9 to 29, 17 to 24); 19.67 (4.9, 20.5) $(n = 21)$	22 (7 to 43, 16 to 29); 23.69 (9.7, 80.7) (n = 21)	0.521
LOAD score, Week 12	19 (9 to 31, 17 to 23); 19.05 (5.1, 23.9) ($n = 22$)	17 (10 to 45, 15 to 28); 21.04 (9.1, 86.1) ($n = 23$)	0.972
Week 0 versus 6	$P = 0.0352^a \ (n = 21)$	$P = 0.1612 \ (n = 21)$	0.687
Week 0 versus 12	$P = 0.0065^a (n = 22)$	$P = 0.1359 \ (n = 23)$	0.785
Week 6 versus 12	$P = 0.2219 \ (n = 20)$	$P = 0.3129 \ (n = 20)$	0.967
Weeks 0, 6, 12	$P = 0.036^{a} (n = 20)$	$P = 0.106 \ (n = 20)$	
Lower LOAD score [number (%) (median change)]	14 (61%) (-3)	12 (52%) (-8)	
Unchanged LOAD score [number (%)]	5 (22%)	4 (17%)	
Higher LOAD score [number (%) (median change)]	4 (17%) (+2)	7 (30%) (+5)	

Table 2. Age, weight, LOAD mobility scores, statistical comparison of scores and number in each group with lower, unchanged, or higher scores at Week 12 compared to Week zero for dogs receiving Fortetropin or cheese powder.

Values are reported as [(median, range) mean (\pm SD) (number of dogs)] for age, weight, and LOAD score (interquartile range and variance is also listed [(median, range, interquartile range) mean (\pm SD, variance) for LOAD scores]. Number of complete data sets shown for comparisons of weeks. Intergroup comparison (*P*-value) shown in right-hand column. Intragroup comparison (*P*-value) shown in same column with treatment group. Statistically significant difference noted by *. * Statistically significant difference.

Hetrick, Katie, Kenneth R. Harkin, and James K. Roush. "Evaluation of Fortetropin in geriatric and senior dogs with reduced mobility." *The Canadian veterinary journal= La revue veterinaire canadienne* 63.10 (2022): 1057-1060.

SARCOPENIA AND OSTEOARTHRITIS

"Sarcopenia, far from being a pathology of specialistic relevance, is a multidisciplinary and systemic health problem that involves orthopedics as well as geriatrics, internal medicine and nutritionists."

Papalia, R., et al. "Sarcopenia and its relationship with osteoarthritis: risk factor or direct consequence?." *Musculoskeletal* surgery 98.1 (2014): 9-14.

"To minimize sarcopenia, and thus improve patient mobility, treatment by reduction of serum myostatin levels with Fortetropin[®] showed promise compared to a nutritionally similar control. Hetrick et al demonstrate a statistically significant improvement in owner assessed (LOAD) mobility scores after 6 and 12 weeks of treatment compared to a placebo supplement. Based on studies such as this, it is my opinion that use of products that inhibit myostatin levels to reduce sarcopenia, such as Fortetropin[®], should be considered a valuable component of multimodal management for the treatment of canine osteoarthritis."

Michael H. Jaffe, DVM, MS, CCRP, DACVS **Mississippi State University College of Veterinary Medicine**





- Sarcopenia and Osteoarthritis (OA) negatively impact the mobility and quality of life of dogs.
- Fortetropin supplementation showed mild, but statistically significant, improvement of the mobility scores for the treatment group at both week 6 (P = 0.03) and week 12 (P = 0.006) compared to the baseline score. No statistical improvement was noted at any time in the placebo group or between the treatment and placebo group.
- Reducing sarcopenia through Fortetropin supplementation can be a valuable component of a multimodal strategy to treat reduced mobility in geriatric dogs.

CANINE OSTEOARTHRITIS

General Characteristics:

- Progressively painful, multifactorial degenerative joint disease.
- Articular cartilage degradation, loss of proteoglycan and collagen [1].
- Subchondral bone sclerosis [2].
- Periarticular proliferation of new bone [1].
- Chronic inflammation of synovial membranes (synovitis) [2].

Risk Factors

- Age $\ge 90\%$ of dogs that are 5+ years of age [1].
- Size Large breed dogs develop OA compared to small breed dogs [3].
- Breed OA is more prevalent in certain pure breeds (Labrador Retrievers, Border Collies) relative to other pure breeds and mixed breeds [4].
- Sex OA is more prevalent in males relative to females [5].
- Obesity Long-term stress on joints leads to loss of articular cartilage
 [6] and obesity is associated with elevated inflammation [7].
- 1. Johnson, K.A., et al. *Journal of the American Veterinary Medical Association* 256.12 (2020): 1335-1341.
- 2. Shorter, E, et al. *Current rheumatology reports* 21.8 (2019): 40.
- 3. Rychel, JK. Topics in Companion Animal Medicine 25.1 (2010): 20-25
- 4. Dan, G. O., et al. *PLoS One* 9.3 (2014): e90501.

Normal

Synovium –

Synovial fluid -----

Cartilage ——

Capsule ——

Subchondral bone

https://www.zoetisus.com/products/pages/rimadyldvm/osteoarthritis_iframe.aspx

5. Hays, L., et al. America
 6. Impellizeri, J.A., et al.
 1089-1091.
 7. Richardson, D.C., et al
 883-911.

Osteoarthritis involves all components of the joint



5. Hays, L., et al. *American journal of veterinary research* 68.1 (2007): 35-41.
6. Impellizeri, J.A., et al. *Journal of the American Veterinary Medical Association* 216.7 (2000):

7. Richardson, D.C., et al. Veterinary Clinics of North America: Small Animal Practice 27.4 (1997):

DIAGNOSIS OF CANINE OSTEOARTHRITIS

- **Physical Examination**
 - Evidence of Lethargy, Cracking Joints, Visible Pain, Stiffness, Muscle Wasting. •
 - Goniometry Range of Motion (ROM) Measurements [1]. •
 - **Clinical Metrology Instruments** \bullet
 - Liverpool Osteoarthritis in Dogs (LOAD) Questionnaire [2]. Ο
 - Canine Brief Pain Inventory (CBPI) Questionnaire [3]. Ο
 - Helsinki Chronic Pain Index (HCPI) Questionnaire [4]. Ο
- Blood Tests Sedimentation Rate, C-Reactive Protein, Antinuclear Antibody (ANA) and Rheumatoid Factor [5].
- Radiography Most radiographic signs of joint disease are non-specific [6]. Signs include:
 - **Increased Synovial Volume.** •
 - **Compressed Intrapatellar Fat Pad.** •
 - Altered Thickness of the Joint Space.
 - **Decreased Subchondral Bone Opacity.** •

Kinematic Gait Analysis [7].

1. Jaegger, Gayle, Denis J. Marcellin-Little, and David Levine. "Reliability of goniometry in Labrador Retrievers." American journal of veterinary research 63.7 (2002): 979-986

- 2. Hercock CA, Pinchbeck G, Giejda A, et al. Validation of a client-based clinical metrology instrument for the evaluation of canine elbow osteoarthritis. J Small Anim Pract 2009; 50(6):266-271
- 3. Brown, Dorothy Cimino, et al. "Ability of the canine brief pain inventory to detect response to treatment in dogs with osteoarthritis." Journal of the American Veterinary Medical Association 233.8 (2008): 1278-1283.
- 4. Hielm-Björkman, Anna K., Hannu Rita, and Riitta-Mari Tulamo. "Psychometric testing of the Helsinki chronic pain index by completion of a questionnaire in Finnish by owners of dogs with chronic signs of pain caused by osteoarthritis." American journal of veterinary research 70.6 (2009): 727-734. 5. Bland, Stephanie D. "Canine osteoarthritis and treatments: a review." Veterinary Science Development (2015).
- 6. Allan, Graeme, and Sarah Davies. "Radiographic signs of joint disease in dogs and cats." Textbook of veterinary diagnostic radiology (2018): 403 etic measurements of gait for osteoarthritis research in dogs and cats." The Canadian Veterin

