Development and validation of the CaOA-QoL-TS instrument

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Background:

- > Osteoarthritis (OA) was diagnosed in 37.3% of dogs presenting for routine preventive care or evaluation of lameness/stiffness, according to a recent study.¹
- > This chronic condition causes pain and mobility impairment in dogs and decreases the quality of life (QoL) of both the dog and owner.^{2,3}
- > There is a need for a standardized approach to assess concepts related to QoL and treatment satisfaction in canine OA to help monitor disease progression in clinical trials and veterinary practice, to assess treatment efficacy and to inform treatment decisions.
- > While numerous QoL instruments have been developed for use in dogs, no existing canine OA-specific instrument comprehensively assessed all three concepts of interest (the QoL of dogs with OA, the impact of canine OA on owner QoL and owner satisfaction with OA treatments).
- > An owner-completed Canine OA QoL, Owner QoL and Treatment Satisfaction (CaOA-QoL-TS) instrument was developed and evaluated.

Results:

Sample characteristics:

- > The demographics of owners varied across location (rural/city) and education level; on average, participants had 9.5 years (range: 0.4-15.5 years) experience caring for a dog with OA.
- > The dogs included in the interview sample (stage 1) and the validation sample (stage 2) had a mean age of 12.7 (2.3 standard deviation [SD]) and 10.3 (3.3 SD) years, respectively. Most dogs were female (≥60% in both samples); there was a wide variety of dog breeds in both stages, including both small (e.g., Chihuahuas) and medium-large dogs (e.g., Labradors).

Qualitative interview results:

- > An updated conceptual model (**Figure 2**) was developed that summarizes the key impacts of canine OA on dog and owner QoL and owner treatment satisfaction identified from the literature and dog owner interviews. Saturation analysis highlighted that no further qualitative interviews were necessary since all important concepts had been identified.
- > All 29 items of the draft CAOA-QoL-TS (v1.0) were understood by \geq 80% of participants and most were considered relevant to \geq 50% of participants.
- > The 7-day recall period was understood and considered appropriate to all participants (N=10/10). All participants demonstrated an understanding of response options (N=10/10), and most considered them appropriate (n=9/10).
- > Ten items were reworded, four removed, and two added, to improve participant understanding and reduce item redundancy, resulting in 26 items that all owners understood and considered relevant. The 26-item version (v2.0) was taken forward to Stage 2 (psychometric analysis).

Figure 2. Conceptual model of the impact of canine OA on dog and owner QoL and treatment satisfaction

	Impact of Cani	ine Osteo	arthritis on Dog Hea	Ith-Related Q	uality of Life		
Impact on mobility (n=10)	Impact on sleep (n=9)		Impact on toileting (n=8)*		Vocalisations (n=8) ^{LR}		Impact on energy (n=5)
 > Difficulty jumping up/down (n=9)* LR INT > Difficulty getting up/lying down (n=8) LR INT > Limping/gait alteration/lameness (n=7) LR INT > Slow/stiff movements, e.g. on walks (n=7) LR INT > Difficulty climbing stairs (n=4)* LR INT > Reduced ability to run (n=3)* LR INT > Reduced ability to stand (n=1) LR INT 	 > Sleeping more (n=4)* LR INT > Sleeping less (n=3)* INT > Sleeping deeper (n=2) INT Impact on appetite > Lack of enthusiasm for food* 	 Sleeping more (n=4)* LR INT Sleeping less (n=3)* INT Sleeping deeper (n=2) INT Impact on appetite Lack of enthusiasm for food* LR 		 > Difficulty holding position to toilet (n=6)^{LR INT} > Toilets in places they shouldn't (n=5)^{INT} > Walks when toileting (n=3)^{INT} > Incontinence (n=2)*^{INT} 		ng (n=4) ^{INT} need assistance (n=2) ^{INT} onary (n=1) ^{INT} ed (n=1) ^{INT}	 > Reduced desire to play (n=4)* LR IN > Reduced desire to walk (n=2)* LR IN > Less curious (n=1)* LR INT > Lethargic LR > Reluctant LR > No longer pulls on lead LR
 Stopping during walks (n=1) ^{LR INT} Difficulty walking, trotting, galloping ^{LR} 	Impact on temperament/mood (n=5)				Impact on physical appearance (n=4)		
 Difficulty staying upright in moving car ^{LR} Lower mechanical thresholds on joint manipulation ^{LR} 	 > Unsettled/pacing (n=5)^{INT} > Irritable (n=1)* LR INT > Quiet during a flare (n=1)^{LR INT} > Detach withdrawithdra (n=1)^{LR INT} > Aggres 		Iood/depressed IR> Protective/territehensive IR> Confused IRhed, unresponsive,> Lack of confidenrawn IR> Frightened IRssive* IR> Unsociable IR		 > Heavy panting (n=2) ^{LR INT} > Muscle wastage (n=1 ^{LR INT} > Sad eyes ^{LR} > Trembling leg (n=1) ^{LR INT} > Looking awkward ^{LR} > Grooming more (n=1) ^{INT} 		
Emotional wellbeing (n=9)	Impact of Canin Physical functioning (n=8)	e Osteoar	rthritis on Owner He Activities	alth-Related	Quality of Lif 7)	e Enviro	onmental adaptations (n=6) ^{LR}
 > Worried (n=4) ^{LR INT} > Dislikes leaving dog (n=3) ^{INT} > Guilty (n=2) ^{LR INT} > Sad/upset (n=2) ^{LR INT} > Helpless (n=1) ^{LR INT} > Depressed/anxious ^{LR} > Boredom ^{LR} > Reduced enjoyment dog walking ^{LR} > Stressed ^{LR} 	 > Has to lift and carry/support dog's (n=6) ^{LR INT} > Reduced walking distance (n=2) ^{LR IN} > Reduced number of walks (n=2) ^{LR IN} > Reduced pace dog walking ^{LR} > General change in dog walking beh > Weight gain ^{LR} 	weight ^{NT} NT	 > Schedules life around > Restricted in walking l > Limited lifestyle due to (n=2) ^{LR INT} > Walks take longer that > Spends less time with 	treatment (n=3) ^{LR IN} ocation with dog (n o limited time away n previous (n=1) ^{INT} other pets (n=1) ^{INT}	 > Installed stairs/ramp to aid climbing (n=4)^{INT} > Purchased rugs for hard surfaces to reduce slipping (n=3 > Dog's OA contributed to house move with fewer stairs (n=2)^{INT} > Changed furniture to suit dog (n=1)^{LR INT} > New car to suit dog^{LR} 		
Social functioning (n=5)		Sleep	(n=5)		Financial (n=4)		Work (n=1)
 Plans ahead to ensure places/transport is suitable (n=2) ^{LR INT} Works social life around dog's treatment (n=1) ^{INT} Limited time away from dog if left at home (n=1) ^{INT} Sometimes misses social meet ups/events (n=1) ^{LR INT} Avoids going on holiday (n=1) ^{LR INT} 		 Nighttime awakenings (n=3)^{INT} Wakes early to assist dog (n=2)^{INT} Sleeps later to assist dog (n=1)^{INT} 		 Cost of treatment, supplements, physical therapy and environmental adaptations (n=4) ^{LR INT} 		s, physical > Ti aptations = ap > Re > Ch	me off work to attend veterinary opointments (n=1) ^{INT} esigned from work to care for dog ^{LR} nange in work schedule ^{LR}

Objective:

> To generate qualitative and quantitative evidence that the CaOA-QoL-TS is fit-for-purpose (assess canine QoL, owner QoL and owner treatment satisfaction) in the planned context of use (canine OA). This included evidence of content and construct validity and score interpretation thresholds.

Methods:

Stage 1: Developing the draft CaOA-QoL-TS instrument

> A systematic literature review was conducted to develop a conceptual framework that informed the development of a draft 29-item CaOA-QoL-TS instrument (v1.0). The draft instrument assessed three hypothesized domains: Canine QoL (17 items), Owner QoL (8 items), and Treatment Satisfaction (4 items). It had a recall period of 'past 7-days' and used a five-point Likert response scale (Not at all, A little, Somewhat, Quite a bit, A great deal/Very much). Not applicable response options (labelled 'I do not allow or have not seen my dog do this') were included for two items within the Canine OA QoL domain.

Stage 2: Finalizing and validating the instrument

Following the development of the draft 29-item CaOA-QoL-TS instrument (v1.0), the study included two stages of validation (outlined in **Figure 1**), adhering with best practice guidelines.⁴

Figure 1. Overview of CaOA-QoL-TS instrument development

Stage 1. Qualitative interviews

Draft 29-item CaOA-QoL-TS instrument (v1.0) based on a review of existing literature and assessment of draft items developed by Zoetis

Instrument modified based on owner feedback

ROUND 2: qualitative interviews with owners of dogs with OA (n=5)

Instrument modified based on owner feedback \rightarrow 26-item CaOA-QoL-TS instrument (v2.0)

Stage 2. Psychometric analysis

Administration of 26-item instrument (v2.0) to owners of **OA-treated dogs**

Evaluation of item performance and dimensionality analyses performed

Item reduction \rightarrow 24-item instrument

Evaluation of the instrument's validity and reliability

24-item CaOA-QoL-TS instrument (v3.0) Three domains: Canine QoL (12 items), Owner QoL (7 items) and Treatment Satisfaction (5 items)

- Stage 1: Qualitative interviews: Combined concept elicitation (CE) and cognitive debriefing (CD), semi-structured, telephone interviews were conducted with ten owners of dogs with a presumptive diagnosis of OA in the US (n=5) and UK (n=5).
- > Interviews aimed to assess the conceptual comprehensiveness of the draft instrument (v1.0) and whether the instrument was understood, relevant to canine OA, and captured the concepts most important to owners
- > Interviews were audio-recorded and transcribed verbatim. Transcripts were analyzed using thematic analysis via Atlas.Ti.
- > **Stage 2: Psychometric analysis:** The instruments' psychometric properties were assessed using data collected from a multi-center,

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> Mode of administration (n=7) LR INT

Figure 3. Domain structure of the finalized 24-item CaOA-OoL-TS instrument (v3.0)

Item	Domain
1. In the past 7 days, my dog has been walking slowly	
2. In the past 7 days, my dog has been limping when walking around the house or outside	
3. In the past 7 days, my dog has been slow to get up and/or slow to lie down	
4. In the past 7 days, my dog has had difficulty jumping up and/or jumping down (e.g. onto or off furniture, into or out of a car)	
5. In the past 7 days, my dog has had difficulty climbing up and or down steps or stairs	
6. In the past 7 days, my dog has had difficulty getting into the right position to toilet	Canine
7. In the past 7 days, my dog has appeared stiff in the morning	Quality of Life
8. In the past 7 days, my dog has appeared stiff after activity (e.g. a walk or play)	
9. In the past 7 days, my dog has wanted to go on walks or play	
10. In the past 7 days, my dog has made sounds to show distress (e.g. groans, moans, whimpering)	
11. In the past 7 days, my dog has appeared happy	
12. In the past 7 days, my dog has appeared restless	
13. In the past 7 days, I have felt sad because of my dog's arthritis	
14. In the past 7 days, I have felt worried because of my dog's arthritis	
15. In the past 7 days, I have felt guilty because of my dog's arthritis	
16. In the past 7 days, my dog's arthritis has impacted my social interactions with friends or other dog owners)	Owner Quality of Life
17. In the past 7 days, my dog's arthritis has impacted my exercise activities (e.g walking)	
18. In the past 7 days, my dog's arthritis has impacted my day-to-day activities	

(n=5)^{INT}

cross-sectional, uncontrolled, prospective, longitudinal, phase 4 field study of Librela (bedinvetmab) in the UK. Ninety-three owners of dogs aged \geq 12 months with a presumptive diagnosis of OA completed the CaOA-QoL-TS (v2.0) at six timepoints: day 0 (baseline), day 14 (two weeks after first dose), day 28 (second dose), day 56 (third dose), day 63 (one week following third dose) and day 70 (two weeks following third dose). Owners also completed the VetMetrica Dog⁵ and four QoL global impression items.

> Psychometric analyses were conducted in two phases using SAS version 9.4 and Mplus run in R. Phase 1 determined the item-scale structure of the CaOA-QoL-TS (v2.0) based on item response distributions, inter-item correlations, multi-trait analysis, confirmatory factor analysis, earlier qualitative findings, and the clinical relevance and importance of items. Phase 2 analyses (internal consistency, test-retest reliability, convergent validity, known groups validity, ability to detect change over time, and withingroups meaningful change thresholds) evaluated the psychometric properties of the resulting item-scale structure.

> There were statistically significant differences in both the mean change of Canine QoL (p<0.001) and Owner QoL (p<0.003) scores between improved, no change and worsening groups defined by global impression of QoL items, providing evidence of the CaOA-QoL-TS (v3.0) instrument's **ability to detect change**. This was supported by larger effect sizes for improved (\geq 1.28) compared to stable (\leq 0.70) group mean change scores over time (Day 0 to Day 56 of the field study).

> Analyses were conducted to determine within-group **meaningful change** thresholds, which indicated that a change of -0.9 and -1.0 in the Canine and Owner QoL domain scores, respectively, would be considered meaningful.

19. In the past 7 days, my dog's arthritis has impacted my sleep	
20. I find it easy to fit my dog's most recently prescribed arthritis treatment into my daily life	
21. I am satisfied with how often my dog receives his/her most recently prescribed arthritis treatment	
22. I am satisfied with the way my dog is given his/her most recently prescribed arthritis treatment	Treatment Satisfaction
23. My dog's most recently prescribed arthritis treatment is worth the financial cost	
24. I am satisfied with my dog's most recently prescribed arthritis treatment	

Conclusions:

> Treatment efficacy (n=7) LR INT

Psychometric analysis results*:

Satisfaction), as hypothesized.

mean residual=0.099).

INT: Reported in concept elicitation interviews with owners of dogs with OA

(n=): Number of owners reporting concept in concept elicitation interview

* Key canine guality of life indicator - as reported by owners in concept elicitation interviews

Inter-item correlations suggested that the 26 items (v2.0) clustered

into three distinct domains (Canine QoL, Owner QoL and Treatment

Confirmatory factor analysis supported deletion of two items (one

item from Canine domain ['my dog has been sleeping well'] and one

item from Owner domain ['had to lift/carry my dog']) and calculation

Satisfaction), with acceptable model fit (comparative fit index=0.966;

root mean square error of approximation=0.071; standardized root

The resulting 24-item CaOA-QoL-TS (v3.0) demonstrated strong internal

consistency. Internal reliability of the domains of Canine QoL, Owner

≥0.70 (Cronbach's alpha=0.90, 0.91, and 0.86, respectively).

(ICC>0.90) for the Canine QoL domain score.

reported among owners with worse QoL.

QoL, and Treatment Satisfaction were well above the priori threshold of

The 24-item instrument (v3.0) demonstrated good to excellent **test-**

retest reliability. Test-retest reliability was good (ICC>0.75) for the

Owner QoL and Treatment Satisfaction domain scores and excellent

Convergent validity of v3.0 was supported by moderate (≥0.30, <0.50)

to strong correlations (≥ 0.50) between the instrument domain scores

-0.52]) and concurrent QoL instruments (VetMetrica[™] Dog⁵ and global

and owner] over the past 7 days and change in QoL since treatment).

Known-groups validity of v3.0 was demonstrated by a statistically

domain scores when grouped by owner global impression of QoL

significant difference in both mean Canine QoL and Owner QoL

(p<0.001), with higher domain scores (indicative of lower QoL)

impression items. The global items assessed owner-rated QoL [of the dog

(Canine QoL [range:-0.48 to-0.68] and Owner QoL [range: 0.31 to

of three domain scores (Canine QoL, Owner QoL and Treatment

LR: Reported in literature review

- The study highlights the significant impact of canine OA on the QoL of both the dog and their owners.
- This study provides evidence that the 24-item CaOA-QoL-TS instrument (v3.0) has strong content and construct validity and reliability to assess canine QoL, owner QoL and treatment satisfaction in Canine OA.
- > The instrument can either be administered in its entirety or each domain can be used as an independent tool to inform veterinary decision making, support stakeholder communications in the field of pain management, and/or to support study endpoints in future clinical research in canine OA.

*The Treatment Satisfaction domain was not assessed for convergent validity, known-groups validity, ability to detect change over time, and within-group meaningful change thresholds due to a lack of available anchors.

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