Development and validation of the FeOA-QoL-TS instrument

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Background:

- Osteoarthritis (OA) is a common condition, particularly amongst older cats. Studies have identified radiographic evidence of OA in approximately 60% and 90% of cats over the age of 6 and 12 years, respectively.[1,2]
- This chronic condition is characterised by cartilage degeneration, resulting in pain and mobility impairment,[3] and has been shown to negatively impact cat QoL (quality of life)[4] and owner QoL.[5,6]
- A standardised process to assess concepts related to QoL and treatment satisfaction in cats with OA is required to help monitor disease progression, demonstrate treatment efficacy and guide treatment decisions in veterinary practice.
- While QoL instruments for use in cats,[7,8] and OA-specific instruments assessing functional impairment in cats exist,[9-11] there are no OA-specific QoL instruments for use in cats that assesses all three concepts of interest (impact of OA on cat QoL, impact of OA on owner QoL, and owner satisfaction with OA treatment).
- To address this gap, an owner-completed feline OA-specific instrument assessing Cat QoL, Owner QoL and Treatment Satisfaction (FeOA-QoL-TS) was developed and evaluated.

Objective:

- To generate qualitative and quantitative evidence that the FeOA-QoL-TS instrument is fit-for-purpose in the planned context of use (assessment of Cat QoL, Owner QoL, Treatment Satisfaction in cats with OA). This included evidence of the instruments content validity and psychometric measurement properties.

Methods:

Developing the initial FeOA-QoL-TS instrument

- A meta-synthesis of published literature was conducted to develop a conceptual model of impaired QoL in cats with OA.[4] A supplementary review of existing literature and interview data was then conducted. These findings informed the development of a 29-item FeOA-QoL-TS instrument (v1_0) which assessed three hypothesised domains: Cat QoL (19 items), Owner QoL (6 items), and Treatment Satisfaction (4 items). The instrument had a recall period of the 'past 7 days' and used a five-point response scale (Not at all, A little, Somewhat, Quite a bit, A great deal/Very much). A not applicable response option ('I have not seen my cat do this') was included for two items within the Cat QoL domain.
- Following development of the 29-item FeOA-QoL-TS (v1_0), the instrument underwent two stages of validation (**outlined in Figure 1**), adhering with best practice guidelines.[12,13]

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

Developing the initial FeOA-QoL-TS

Draft 29-item FeOA-QoL-TS instrument (v1_0) based on a literature review and subsequent supplementary review

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Stage 1: Qualitative interviews with owners of cats with OA in US/UK (N=8)

Round 1 interviews (n=4): 29-item FeOA-QoL-TS (v1_0)

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Round 2 interviews (n=4): 29-item FeOA-QoL-TS (v2_0)

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Instrument modified after each round resulting in 25-item FeOA-QoL-TS (v3_0) for administration in Stage 2

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Stage 2: Psychometric evaluation using data from owners of cats with OA in UK (N=139)

COAs: FeOA-QoL-TS, VetMetrica™ HRQL instrument, 4 QoL global impression items

Schedule: Six timepoints including Day 0, Day 14, Day 28, Day 56, Day 63, Day 70

Phase A: Evaluation of item-scale structure of 25-item FeOA-QoL-TS (v3_0)
Reduction of five items to result in 20-item FeOA-QoL-TS

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Phase B: Evaluation of the psychometric properties of 20-item FeOA-QoL-TS

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20-item FeOA-QoL-TS instrument (v4_0)
includes three domains (Cat QoL [10 items], Owner QoL [6 items], and Treatment Satisfaction [4 items])

Stage 1: Qualitative interviews

- Two rounds of semi-structured combined concept elicitation and cognitive debriefing telephone interviews were conducted with eight owners of cats with a veterinarian-diagnosis of OA in the US (n=4) and UK (n=4).
- Interviews explored owners' understanding of the 29-item FeOA-QoL-TS (v1_0 tested in Round 1; v2_0 tested in Round 2) including the relevance of concepts assessed by the instrument.
- Interviews were audio-recorded and transcribed verbatim. Transcripts were analysed in Atlas.Ti using thematic analysis.

Stage 2: Psychometric evaluation

- The psychometric properties of the 25-item FeOA-QoL-TS (v3_0) were evaluated using data collected from a multi-centre, uncontrolled, prospective, longitudinal, phase 4 field study of Frunevetmab (Solensia®) in the UK. The instrument was administered to owners of cats aged ≥12 months with veterinarian diagnosed OA (N=139) at six timepoints (over 70 days) on a smartphone device.
- Psychometric analyses were conducted in two phases. Phase A determined the item-scale structure of the FeOA-QoL-TS (v3_0) based on item response distributions, inter-item correlations, multi-trait analysis, confirmatory factor analysis (CFA), earlier qualitative findings, and the clinical relevance and importance of items. Phase B analyses evaluated the psychometric properties of the resulting item-scale structure, via internal consistency reliability, test-retest reliability, construct validity (convergent validity and known groups comparisons), ability to detect change over time, and meaningful change thresholds. Analyses were conducted using SAS version 9.4[14] and Mplus version 7.3.1 run in R version 4.2.2.[15]

Results:

Sample characteristics:

- Stage 1 (N=8): More owners were female (n=6/8), highly educated (n=7/8) and, on average, had owned one or more cats for 35.8 years (range: 14-55 years). All cats were senior (>10 years[16]) with a mean age of 15.2 years (2.0 standard deviation [SD]). More cats were male (n=7/8) and of mixed breed (n=5/8).
- Stage 2 (N=139): There was an approximately even split of female (n=70; 50.4%) and male cats. On average, the sample comprised of senior cats with a mean age of 13.6 years (3.2 SD), who weighed 4.5kg. Owner demographics were not collected.

Qualitative interview results:

- The conceptual model developed following the literature review to summarise the key impacts of cat OA on cat and owner QoL and owner treatment satisfaction was updated to include interview findings (**Figure 2**). Saturation analysis indicated that saturation was largely achieved and that further interviews were not needed to obtain further insights.
- Across both rounds all 29 FeOA-QoL-TS (v1_0 Round 1; v2_0 Round 2) items were understood by 87.5% of participants, and over half of the items were relevant to ≥50%. All participants understood the recall period (100%). The response options were understood and considered appropriate by 50% in Round 1, increasing to 100% in Round 2 following modifications.
- Based on interview findings, 16 items were reworded, nine removed, and five added. The resulting 25-item FeOA-QoL-TS (v3_0) was taken forward for psychometric evaluation (Stage 2).

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

Impact of Feline Osteoarthritis on Cat Quality of Life

Impact on mobility (n=7) [LR INT]
- Difficulty jumping up/down (n=6) [LR INT]
- Slowness/stiffness (n=6) [LR INT]
- Difficulty walking (n=5) [LR INT]
- Difficulties climbing up (n=5) [LR INT]
- Difficulties getting into lying down position (n=5) [LR INT]
- Difficulties climbing down (n=4) [LR INT]
- Difficulties getting up from lying down (n=4) [INT]
- Difficulties stretching (n=3) [LR INT]
- Lameness or change in gait (n=3) [LR INT]
- Difficulties jumping down (n=2) [LR INT]
- Difficulty claw sharpening/scratching [LR]

Impact on physical appearance (n=7) [LR INT]
- Change in grooming habits (n=5) [LR INT]
  - Grooming less (n=4) [LR INT]
  - Grooming more (n=1) [INT]
- Weight loss (n=3) [INT]
- Weakness (n=2) [INT]
- Change in muscle structure (n=2) [INT]
- Postural appearance (n=1) [LR INT]
- Coat changes (n=1) [LR INT]
- Long claws [LR]
- Shivering [LR]
- Unsteadiness [LR]

Impact on temperament (n=5) [LR INT]
- Aggressive/irritable (n=3) [LR INT]
- Less interaction (n=2) [LR INT]
- Depressed/unhappy (n=1) [LR INT]
- Lethargic (n=1) [LR INT]
- Stressed (n=1) [INT]
- More interaction (n=1) [INT]
- Discomfort [LR]
- Intolerance of others [LR]
- Fearfulness [LR]
- Disinterested [LR]
- Reduced enjoyment in usual activities [LR]
- Confusion [LR]
- Withdrawn [LR]

Impact on energy (n=4) [LR INT]
- Moving around less (n=4) [LR INT]
- Reduced playfulness (n=3) [LR INT]
- Reduced time hunting [LR]
- Less alert [LR]

Vocalisations (n=4) [LR INT]
- When touched (n=2) [LR INT]
- To signify they need assistance (n=2) [INT]
- To signify distress (n=1) [INT]

Impact on sleep (n=4) [LR INT]
- Sleeping more (n=4) [LR INT]

Impact on roaming behaviour (n=3) [LR INT]
- Going to usual places less (n=3) [LR INT]
- Reduced time spent outside (n=2) [LR INT]
- Reduced exploration [LR]

Impact on toileting (n=3) [LR INT]
- Difficulties using the litter box (n=3) [INT]
- Difficulties with bowel movement due to posture (n=1) [INT]

Impact on feeding habits (n=2) [LR INT]
- Decreased appetite (n=1) [LR INT]
- Fussier (n=1) [INT]

Impact of Feline Osteoarthritis on Owner Quality of Life

Emotional wellbeing (n=6) [LR INT]
- Sad/depression (n=5) [LR INT]
- Worried/anxiety (n=4) [LR INT]
- Stressed (n=2) [LR INT]
- Guilt [LR]
- Reduced sense of control [LR]
- Annoyance [LR]

Financial (n=6) [LR INT]
- Treatment costs (n=4) [INT]
- Buying supplements/different foods (n=2) [LR INT]
- Vet costs (n=1) [INT]

Activities of daily living (n=5) [LR INT]
- Increased cat maintenance (n=5) [LR INT]
  - Unable to let other people care for cat (n=3) [INT]
  - Help to groom cat (n=2) [INT]
  - Increased focus on cat (n=2) [LR INT]
  - Cleaning up after cat (n=1) [LR INT]
- Increased time at vets (n=1) [INT]
  - Difficulty travelling to vets [LR]
- Interaction with cat (n=1) [LR INT]
  - Unable to groom cat (n=1) [INT]
  - Reduced interaction with cat (including ability to pet and play with the cat) [LR]
  - Difficulties feeding cat [LR]
- Limited time away from home (n=1) [INT]
- Routine changes/time for self [LR]

Social functioning (n=5) [INT]
- Unable to take vacations (n=5) [INT]
- Negative impact on relationships (n=3) [INT]
- Reduced social activities (n=1) [INT]

Physical functioning (n=3) [INT]
- Cat requiring help to access areas (n=3) [INT]

Sleep (n=3) [INT]
- Reduced amount of sleep (n=3) [INT]
- Difficulty falling asleep (n=1) [INT]

Environmental adaptations (n=2) [INT]
- Provided heated beds (n=1) [INT]
- Changed litterbox (n=1) [INT]
- Built stairs (n=1) [INT]

Treatment Satisfaction in Owners of Cats Treated for Feline Osteoarthritis

- Treatment efficacy (n=8) [LR INT]
- Cost of treatment (n=8) [LR INT]
- Mode of administration (n=8) [LR INT]
- Frequency of administration (n=6) [LR INT]
- Ease of fitting treatment into daily life (n=4) [INT]
- Treatment options (n=1) [LR INT]
- Communication of treatment information [LR]

LR: Reported in literature review
INT: Reported in concept elicitation interviews with owners of cats with OA
(n=): Number of owners reporting concept in concept elicitation interview

Psychometric analysis results:

Phase A: Item scale structure of the 25-item FeOA-QoL-TS (v3_0)

- **Item response distributions** demonstrated that participants endorsed a good spread of response options across the response scale for most items across Cat QoL and Owner QoL domains at Baseline. Treatment Satisfaction item responses were skewed but this was expected due to efficacy of Frunevetmab.
- **Inter-item correlations** suggested that items generally clustered into three domains (Cat QoL, Owner QoL and Treatment Satisfaction). There was however some evidence of item redundancy as four item pairs ('Jumping up/down', 'climbing up/down', 'sad/worried', 'ability to leave home/fitting treatment into daily life') were very strongly correlated (r≥0.90), which informed later item reduction.
- **CFA** supported the deletion of five items (Cat QoL: 'difficulty jumping down', 'difficulty climbing up', 'distressed when touched/held'; Owner QoL: 'clean up after cat'; Treatment Satisfaction: 'fitting treatment into daily life') due to item redundancy, poor psychometric performance and qualitative findings/relevance. CFA confirmed a three-domain score structure (Cat QoL, Owner QoL and Treatment Satisfaction) with acceptable model fit (comparative fit index=0.977; root mean square error of approximation=0.077; weighted root mean square residual=0.988).

Phase B: Psychometric properties of the resulting 20-item FeOA-QoL-TS (v4_0)

- Strong **internal consistency** and **test re-test reliability** were demonstrated; reliability coefficients were well above the a priori thresholds of ≥0.70 for all three domain scores (Cat QoL: Cronbach's alpha [α] = 0.88; Coefficient omega [ω]= 0.90; Owner QoL: α = 0.84; ω= 0.85; and Treatment Satisfaction: α = 0.84; ω = 0.84). Intraclass correlation coefficient (ICC) was >0.75 for all three domain scores.
- **Convergent validity** was supported by strong correlations (≥0.50) between the Cat QoL domain scores and other QoL instruments (VetMetrica™ Feline HRQL[17] and global impression items; range: -0.66 to -0.80); as well as Owner QoL domain scores and other QoL instruments (range: -0.62 to -0.72).
- **Known groups comparisons** demonstrated significant differences in mean Cat QoL and Owner QoL domain scores between groups defined by global impression item responses (p<0.001), with large effect sizes between groups reporting worse QoL versus better QoL (Cat QoL:-1.07,-2.49; Owner QoL:-1.09,-2.36).
- Statistically significant differences were observed in the mean change between improved, stable, and worsened groups when defined according to global impression items, for the Cat QoL (p<0.001) and Owner QoL (p<0.001) domain scores. Effect sizes were larger for improved (Cat QoL: ≥1.26; Owner QoL: ≥1.22) compared to stable groups (Cat QoL: ≤0.30; Owner QoL: ≤0.82), providing evidence of the instruments **ability to detect improvement** in cat and owner QoL over time (Day 0 to Day 56).
- Analyses of **within-group meaningful change** indicated that an improvement of -1.0 and -0.9 for the Cat and Owner QoL domain scores, respectively, would be considered meaningful.

Figure 3. Domain structure of the finalised 20-item FeOA-QoL-TS instrument (item concepts only)

FeOA-QoL-TS Item	Domain
1. 'Difficulty walking'	Cat Quality of Life
2. 'Moving slowly'	
3. 'Difficulty jumping up'	
4. 'Difficulty climbing down steps or stairs'	
5. 'Difficulty lying down/getting up from lying down'	
6. 'Difficulty stretching'	
7. 'Difficulty toileting'	
8. 'Appeared happy'	
9. 'Been active'	
10. 'Difficulty grooming'	
11. 'Difficulty picking up/petting cat'	Owner Quality of Life
12. 'Had to help cat get to places'	
13. 'Felt sad'	
14. 'Felt worried'	
15. 'Impacted my ability to leave home'	
16. 'Impacted my sleep'	
17. 'Satisfied with how often cat receives treatment'	Treatment Satisfaction
18. 'Satisfied with the way cat is given treatment'	
19. 'Treatment worth financial cost'	
20. 'Overall satisfaction with treatment'	

Conclusions:

- The study highlighted the significant impact of OA on cat QoL and owner QoL, as demonstrated by the number of identified concepts in the updated conceptual model (Figure 2).
- The findings provide evidence that the final, validated 20-item FeOA-QoL-TS instrument (v4_0) has strong content validity, reliability, and construct validity, and is therefore fit-for-purpose to assess Cat QoL, Owner QoL and Treatment Satisfaction in cats with OA. The item concepts included within the final instrument are presented in Figure 3 (full instrument available through licensing with Zoetis).
- Depending on user objectives, the instrument can be administered either in its entirety or using each domain independently to inform veterinary decision making, support stakeholder communications in pain management, and/or support study endpoints in future clinical research in cats with OA.

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