

# 2022 AAHA Pain Management Guidelines for Dogs and Cats\*

Margaret E. Gruen, DVM, MVPH, PhD, DACVB<sup>†</sup>,  
 B. Duncan X. Lascelles, BSc, BVSc, PhD, CertVA, DSAS(ST), DECVS, DACVS, FRCVS<sup>†</sup>,  
 Elizabeth Colleran, DVM, MS, ABVP feline specialty, Alison Gottlieb, BS, CVT, VTS (ECC),  
 Jennifer Johnson, VMD, CVPP, Peter Lotsikas, DVM, DACVS-SA, DACVSMR,  
 Denis Marcellin-Little, DEDV, DACVS, DACVSMR, Bonnie Wright, DVM, DACVAA

## ABSTRACT

These updated guidelines present a practical and logical approach to the assessment and management of acute and chronic pain in canine and feline patients. Recognizing pain is fundamental to successful treatment, and diagnostic guides and algorithms are included for assessment of both acute and chronic pain. Particularly for chronic pain, capturing owner evaluation is important, and pain-assessment instruments for pet owners are described. Expert consensus emphasizes proactive, preemptive pain management rather than a reactive, “damage control” approach. The guidelines discuss treatment options centered on preemptive, multimodal analgesic therapies. There is an extensive variety of pharmacologic and nonpharmacologic therapeutic options for the management of acute and chronic pain in cats and dogs. The guidelines include a tiered decision tree that prioritizes the use of the most efficacious therapeutic modalities for the treatment of acute and chronic pain. (J Am Anim Hosp Assoc 2022; 58:55–76. DOI 10.5326/JAAHA-MS-7292)

## AFFILIATIONS

North Carolina State University, Department of Clinical Sciences (M.E.G.);  
 North Carolina State University, Translational Research in Pain, Department of Clinical Sciences (B.D.X.L.); Chico Hospital for Cats (E.C.); Crown Veterinary Specialist (A.G.); International Veterinary Academy of Pain Management (J.J.); Skylos Sports Medicine (P.L.); University of California, Davis, Department of Surgical and Radiological Sciences (D.M.-L.); MistralVet (B.W.)

## CONTRIBUTING REVIEWERS

Kristin Jankowski, VMD, CCRP, (University of California Veterinary Medical Teaching Hospital, Community Practice); Douglas Stramel, DVM, CVPP, CVMA, (Advanced Care Veterinary Services, Carrollton Texas)

Correspondence: megruen@ncsu.edu (M.E.G.), dxlascel@ncsu.edu (B.D.X.L.)

† M. Gruen and B. Lascelles were co-chairs of the Pain Management Guidelines Task Force.

These guidelines were prepared by a task force of experts convened by the American Animal Hospital Association. This document is intended as a guideline only, not an AAHA standard of care. These guidelines and recommendations should not be construed as dictating an exclusive protocol, course of treatment, or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to each individual practice setting. Evidence-based support for specific recommendations has

been cited whenever possible and appropriate. Other recommendations are based on practical clinical experience and a consensus of expert opinion. Further research is needed to document some of these recommendations. Because each case is different, veterinarians must base their decisions on the best available scientific evidence in conjunction with their own knowledge and experience.

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AI (artificial intelligence); CBPI (Canine Brief Pain Inventory); CMIs (Clinical Metrology Instruments); COAST (Canine OsteoArthritis Staging Tool); COX (cyclooxygenase); CSOM (client-specific outcome measures); FMPI (Feline Musculoskeletal Pain Index); HRA (health risk assessment); HRQoL (health-related quality of life); IA (intra-articular); LOAD (Liverpool Osteoarthritis in Dogs); mAB (monoclonal antibody); MICAT-C (Montreal Instrument for Cat Arthritis Testing - Caretaker); MiPSC (Musculoskeletal Pain Screening Checklist); NGF (nerve growth factor); NSAID (nonsteroidal anti-inflammatory drug); OA (osteoarthritis); PRA (prostaglandin receptor antagonist); SNoRE (Sleep and Nighttime Restlessness Evaluation); TRPV1 (transient receptor potential cation channel subfamily V member 1)

## Introduction

Pain management is central to veterinary clinical practice. Alleviating pain is not only a professional obligation, as reflected in the veterinarian's oath, but a key contributor to successful case outcomes and enhancement of the veterinarian-client-pet relationship. The primary purpose of these guidelines is to help veterinarians and veterinary team members confidently and accurately create a reproducible **pain assessment** in cats and dogs, as well as an **initial therapy plan** with guidance on reassessing and adjusting the plan as needed. As such, these guidelines discuss pain management as a therapeutic continuum consisting of assessment, treatment, reassessment, and plan revision.

Pain management has been recognized as an essential component of compassionate care in canine and feline medicine—increasingly so over the last 20 years. With the approval of safe and effective nonsteroidal anti-inflammatory agents for veterinary use in the 1990s, analgesia became accessible as a therapeutic mainstay in postoperative settings and in cases of chronic pain. Although pain management is now an established component of therapy, the development of new analgesics and nonpharmacologic modalities makes this a still evolving facet of clinical practice. For this reason, these guidelines build on and update 2015 AAHA-AAFP pain management recommendations,<sup>1</sup> with the addition of the following topics of interest:

- A systematic approach to making reproducible pain assessments, including a discussion of available assessment methods and tools.
- Rather than present a randomized list, or buffet, of treatment options, a tiered decision tree based on evaluating acute and chronic pain has been developed to help with *prioritizing the use of the most efficacious therapeutic modalities*.
- The evolution of pain management from a reactive intervention to a proactive, preemptive, and multimodal strategy involving the entire practice team.
- Guidance on how pain management should differentiate between canine and feline patients, with an emphasis on the particular features of feline behavior.

These topics are accompanied by pertinent recent updates on pharmacologic and nonpharmacologic treatment modalities summarized in easy-to-reference tables. Using these resources, clinicians can make informed decisions on developing effective, case-specific treatment plans. Two concepts underlying this approach are preemptive analgesia to minimize pain onset and nociceptive pathology, and a multimodal treatment strategy to offset overreliance on any single drug with the attendant risk of side effects. With respect to chronic pain, most is known about the assessment and treatment of musculoskeletal pain (namely, osteoarthritis [OA]), and the guidelines reflect this. These guidelines are not intended to provide all-inclusive pharmacologic information, or a comprehensive review of feline-friendly handling techniques, nor do they attempt to present a

comprehensive description of specific painful conditions. The guidelines further discuss the benefits of defined pain management roles for each practice team member and how client education plays an important part in ensuring that each patient is able to perform daily activities and maintain quality of life in clinical and home settings.

## An Evolving Philosophy of Pain Management

Pain management in companion animal practice is no longer limited to providing analgesia after fracture repair (i.e., acute pain) or prescribing a nonsteroidal anti-inflammatory drug (NSAID) to an osteoarthritic dog that can no longer climb stairs (i.e., chronic pain). As advocates of our patients whose owners are often unaware of the signs of pain, our thinking must evolve around pain management to include the rapid detection of pain, combined with early multimodal intervention. We must switch our focus from *damage control* pain management to *proactive* pain management. This philosophical shift is particularly relevant to handling chronic pain, in which problems are not quickly resolved and must be managed over the long term. Chronic pain is ubiquitous in companion animals, most commonly as the result of OA, whose reported prevalence appears to be close to 40% in dogs and >50% in cats.<sup>2-4</sup> Chronic pain may also be a consequence of dental, spinal, or cancer pain and other chronic conditions. Managing pain in companion animals must take a collaborative approach, coordinated by owners and a veterinary team who are alert and responsive to changes.

### Proactive and Preemptive Pain Management

It is well accepted that acute surgical pain is most effectively managed *preemptively*.<sup>5,6</sup> In this context, “preemptive” means administering analgesic therapies as early on in the disease process as possible or, in the example of preemptive perioperative analgesia, administering analgesics prior to the start of surgery. This philosophy of management can also be applied to chronic pain—treating earlier in the disease process to prevent the adverse effects of ongoing noxious input.

Preemptive treatment, across both acute and chronic pain, is most effective if a *proactive* approach to pain management is taken. This approach means understanding when pain may be present, taking proactive steps to assess for pain, and educating and engaging the whole veterinary team and owners about pain assessment.

For acute pain, this means having the whole veterinary team educated in how to assess pain in the clinic and putting in place proactive protocols to assess and reassess pain.

In chronic pain conditions, this begins by making owners aware of the risk of chronic disease and its accompanying pain. For example, several dog breeds are at high risk of hip dysplasia, elbow

dysplasia, or patellar luxation, as shown by the statistics of the Orthopedic Foundation for Animals (<https://www.ofa.org/diseases/breed-statistics>). Similarly, the majority of cats  $>10$  years of age show signs of OA pain.

Proactive pain management also includes implementing measures to slow the progression of chronic problems that can be associated with pain. For example, in dogs at risk of OA, growth should be slowed to minimize the expression of faulty genes,<sup>7</sup> body condition should remain within the optimal range,<sup>8</sup> and exercise should be encouraged as it may be protective for hip dysplasia.<sup>9</sup> Dogs should be acclimated to activities that become part of their long-term management such as leash walks or the application of a cold pack.

Owner engagement is key to shifting toward proactive treatment for chronic pain conditions. Musculoskeletal pain (e.g., OA) is very common in dogs and cats, and clients can be engaged in the process of watching their pets for changes in posture, gait, demeanor, and ability to perform daily activities and regularly asked about behavioral changes they observe. Owners can also be educated regarding the high prevalence of chronic pain among pets and the unique postures or behaviors that animals adopt as attempts to alleviate pain. The importance of how pain management is communicated to the owner by an aligned practice team cannot be overemphasized. Early symptoms of chronic disease should be proactively looked for, fully discussed with owners, and managed promptly so that early acute pain does not progress to chronic pain that is more resistant to treatment.

## Coordinated Pain Management

Coordinated pain management extends the responsibility for the development and implementation of the treatment plan to the whole veterinary team. This requires that everyone on the team understands the signs of pain and principles of pain management in order to adopt a common vision for patient care. Ideally, a *case coordinator*, usually a veterinary technician, would be delegated to regularly reach out to a pet owner and make sure that pain is being effectively managed and pets are willing and able to perform daily activities. Communication between the technician and veterinarian is vital. Patients would then be reevaluated regularly (every 3–6 months) with additional evaluations if problems are identified by the case coordinator or owner. To optimize adherence, owners need to understand the reasons for early intervention, and therapy should minimize the financial, physical, emotional, and logistical burden placed on caretakers. The management of chronic pain is a continuing service that the veterinary team offers its clients. The service philosophy generates a strong bond with the owner and protects companion animals from the severe impact of undertreated chronic pain.

## Gentle Handling

It is important to focus on conscious awareness of gentle, or animal-friendly, handling of all patients—but especially the painful patient. As some owners do not appreciate their pet's condition in the absence of a clearly painful response to manipulation, it can be necessary to educate the client on nonverbal or less severe reactions given by the patient (e.g., holding breath, licking of the lips, looking away) versus vocalization. This approach will also allow for a more complete physical examination with the pet's cooperation and will demonstrate to the client that the practice team has a strong awareness of the need to minimize the patient's pain.

For cats, previously published guidelines on feline-friendly handling practices provide a more detailed discussion of this important aspect of pain management.<sup>10</sup> Previsit medications such as trazodone or gabapentin may still be given prior to appointments; although some sedation may be present, these drugs will not produce analgesia to the extent that pain cannot be used as a diagnostic tool, and calmer pets are more compliant with physical and orthopedic examinations.

## Pain Assessment Toolbox

### Guiding Principles of Pain Assessment

In the following sections, we put forward a Pain Assessment Toolbox for use by the veterinary team. In designing the Pain Assessment Toolbox, the advisory panel determined the following guiding principles:

- First, the practice team must consciously create a shared approach to pain management and client communication—particularly for the assessment, interpretation, and explanation of acute and chronic pain.
- Second, the concept of the physical exam must extend beyond handling to include observation of posture, gait, and behavior.
- Third, an emphasis on behavioral observations, including those reported by the owner, will not increase the time needed for exams.
- Finally, across all principles, the assessment of pain is different between cats and dogs, requiring different tools, observations, and communication techniques.

These principles function with the knowledge that the presentation differs between acute and chronic pain, requiring a distinctly different approach for assessment and communication with pet owners. Compared with chronic pain, assessment of acute pain is typically more straightforward for both the veterinarian and the pet owner. In acute pain conditions, the response to palpation and generally recognizable signs are more easily observed. For pet owners, however, there is often a discrepancy between identification of acute and chronic pain. Owners often focus on watching for signs of acute pain rather than the gradual behavioral changes indicative of chronic pain. This discrepancy highlights the importance of the first pain

assessment principle—a shared approach to pain management and client communication. Because owners may be unaware of or underestimate the presence of chronic pain, client education and engagement is critical to both the identification of and appreciation for the need for chronic pain treatment. The practical application of this principle differs for cats and dogs. For cats, many of the important behavioral signs of chronic pain are most detectable in the home, so detection is more effective with owner input. For dogs, a shift in client perception is needed to appreciate the potential for chronic pain to develop even in young dogs and the need for lifelong management.

The second and third pain assessment principles present a shifting mindset regarding the physical examination, extending it beyond the hands-on evaluation to include observations of the spontaneous behaviors of the patient. For the clinician, assessments of visually obvious problems and hands-on palpation remain critical to evaluation of the patient. Yet equally important are the more subtle aspects of patient behavior that may be evaluated as soon as the veterinarian or veterinary technician and animal enter the exam room. These behavioral signs can often be observed while conversing with the client, and with experience and practice, these observations need not add any time to the examination. Under the principle that any extra energy expended by an animal to alter a behavior is done to preserve comfort, changes in how a dog walks or sits or how a cat jumps down from an exam table can provide information that aids our diagnosis.

Our ability to point out these behavioral changes to owners can encourage them to watch for these pain-related behaviors at home. This is especially important for cats, in whom the most common cause of chronic pain—degenerative joint disease/OA—presents primarily as behavioral changes that owners are best positioned to detect.

### Pain Assessment Tools for Cats

Assessment of pain in cats involves a convergence of evidence from physical examination (including observation of behavior), owner input (including standardized questionnaires and video), and imaging as indicated. Several features of a cat's natural behavior influence the behavioral signs seen with pain and discomfort. As mid-level predators, cats display both predatory and prey-type behaviors. Cats may not overtly express pain, but they do exhibit detectable signs. Cats are small and agile and depend on their ability to jump and climb to escape danger. When escape is not possible, cats may use aggression to defend themselves. However, cats do not use aggression as an early defense and typically use elaborate chemocommunication to avoid conflict. Because the ability to escape is critical to a cat's

sense of safety, their access to vertical spaces must be preserved. When cats with painful conditions are unable to access elevated spaces, affective signs such as changes in sociability and mood and reduced tolerance of handling become visible across owner and clinical assessments. **Table 1** summarizes the various pain assessment tools for use with feline patients. **Figure 1** illustrates a logical approach to the diagnosis and monitoring of acute or perioperative pain, and chronic pain, in cats.

### Acute and Perioperative Assessment of Pain in Cats

For assessing acute pain and postoperative comfort in the clinic, response to palpation and clinical metrology instruments should be employed. The use of a standardized scale allows consistent monitoring and response to additional analgesic interventions. The Colorado State University Acute Pain scale, Glasgow short-form pain scale, and UNESP-multi-dimensional pain scale are the most commonly used tools. A Feline Grimace Scale that relies on facial expressions as an indication of pain has been recently introduced.<sup>11</sup> Although initial training is needed, the Feline Grimace Scale can be used by veterinarians and technicians to quickly assess pain without palpation. Owners may also bring videos of their cat's behavior at home for assessment. A version of the Feline Grimace Scale for owners is available as an app and online (<http://www.felinegrimacescale.com>). Conversations with owners should focus on changes that they have seen in the cat's behavior, affect, and activities of daily living; these may reflect more sudden changes occurring over a brief period of time, compared with the progressive changes of chronic pain that occur over a period of months. More information can be found in the ISFM's Guidelines on Acute Pain Management in Cats.

### Chronic Pain Assessment in Cats

#### *Assessment by Owners*

In contrast to acute pain, owner assessment of behavior has a central role in the detection and monitoring of chronic pain in cats. The majority of the standardized clinical metrology instruments in use have been developed for owners to complete. Pain caused by degenerative joint disease is the most common form of chronic pain in cats, and this area has received the most research for instrument development and validation. These instruments ask owners to rate their cat's ability to perform behaviors known to be affected by chronic musculoskeletal pain. They are simple to use and have good reproducibility and generate a score that can be tracked over time. However, a gap exists between owner awareness of the disease process and recognition of behavioral changes in their cat.<sup>12</sup> Because these changes develop gradually over time, owners who are not actively monitoring for these signs may miss them initially. Owner

**TABLE 1****Pain Assessment Methods and Tools for Use in Cats**

TOOL	ACUTE OR CHRONIC PAIN	USER	EASE OF USE	PURPOSE	VALIDITY*
<b>Physical examination</b>	Acute and chronic	Veterinarian	Moderate, requires training	Screening, diagnosing, monitoring	Not formally validated as an assessment of pain
<b>Clinic observation</b>	Acute and chronic	Veterinarian and veterinary technician	Moderate, requires training	Monitoring	Not formally validated as an assessment of pain
<b>Physiological variables (heart rate; respiration; blood pressure)</b>	Acute	Veterinarian and veterinary technician	Simple	Screening, monitoring	Not specific indicators of pain
<b>Wound palpation</b>	Acute	Veterinarian and veterinary technician	Simple	Monitoring	Not formally validated as a stand-alone assessment of pain; forms part of several validated tools
<b>Home videos and photos</b>	Acute and chronic	Owner collects information Veterinarian evaluates	Moderate, requires instructions	Screening, monitoring	Not formally validated as an assessment of pain
<b>Actigraphy (activity monitoring)</b>	Chronic	Clinical Research	Challenging to setup and operate	Monitoring	Valid

(continued)

education and engagement will increase the detection of chronic musculoskeletal pain in cats.<sup>12</sup>

Clinical metrology instruments in regular use can be divided into those used for screening, diagnosis, and monitoring of disease. For screening, a checklist of six behaviors has been developed to help identify cats likely to have chronic musculoskeletal pain.<sup>12</sup> For these six behaviors (running, jumping up, jumping down, going up stairs, going down stairs, and chasing objects), owners are asked if their cat is able to perform them normally or not, with negative responses triggering further evaluation. Several tools have been developed for diagnosis and monitoring, with most support for the Feline Musculoskeletal Pain Index<sup>13–15</sup> and Montreal Cat Arthritis Test (both for diagnosis and monitoring)<sup>16</sup> and Client-Specific Outcome Measures (monitoring only).<sup>17,18</sup> The first two instruments are general questionnaires with standardized behaviors. Owners either rate (using a Likert scale) or indicate “yes” or “no” for a series of behaviors impacted by chronic musculoskeletal pain. The Client-Specific Outcomes Measures instrument is tailored to activities that are impaired in an individual cat. Although these can be highly salient for cat

owners, the selection of appropriate activities and setup for the instrument can be time consuming.

Owners may also provide videos of their cats performing specific behaviors in the home.

This is relatively convenient but requires some client training to capture the whole cat in the frame, the whole behavior sequence, and adequate lighting to make evaluation possible. The six behaviors described above can be documented using video. When done well, video of cat behavior can offer an opportunity to evaluate behaviors rarely seen during the clinical assessment.

#### **Clinician Assessment of Pain in Cats**

Evaluation of cats in the clinic for chronic pain can be difficult owing to changes in behavior that result from the visit itself; clinical assessment will be affected by the cat’s level of stress. Observation of the cat’s smoothness of movement, hair coat, and posture prior to the hands-on exam can offer important insight into overall comfort. Although a few cats may be convinced to jump up onto a bench or chair, most can be observed jumping down. Offering the cat their

**TABLE 1 (Continued)**

TOOL	ACUTE OR CHRONIC PAIN	USER	EASE OF USE	PURPOSE	VALIDITY*
<b>CLINICAL METROLOGY INSTRUMENTS (CMIS)</b>					
<b>Colorado Acute Pain Scale Feline<sup>a</sup></b>	Acute	Veterinarian and veterinary technician	Simple	Monitoring	Not validated
<b>Glasgow Composite Measure Pain Scale—feline<sup>b</sup></b>	Acute	Veterinarian and veterinary technician	Moderate	Monitoring	Moderately validated
<b>UNESP-Botucatu Multidimensional Composite Pain Scale<sup>c</sup></b>	Acute	Veterinarian and veterinary technician	Moderate	Monitoring	Valid
<b>Feline Grimace Scale<sup>d</sup></b>	Acute	Veterinarian and veterinary technician	Simple	Screening, monitoring	Valid
<b>Musculoskeletal Pain Screening Checklist (MiPSC)<sup>e</sup></b>	Chronic, osteoarthritis	Owner	Simple	Screening	Valid
<b>Feline Musculoskeletal Pain Index (FMPI)<sup>f</sup></b>	Chronic, osteoarthritis	Owner	Simple	Monitoring	Valid
<b>Montreal Instrument for Cat Arthritis Testing—Caretaker (MICAT-C)<sup>g</sup></b>	Chronic, osteoarthritis	Owner	Simple	Monitoring	Moderately validated
<b>Client-specific outcome measures<sup>h</sup></b>	Chronic, osteoarthritis	Owner	Moderate	Monitoring	Moderately validated
<b>Health-related quality of life (HRQoL)<sup>i</sup></b>	Chronic	Owner	Simple	Monitoring	Moderately valid (not specific to pain)

\*Based on an overview of published studies assessing validity

<sup>a</sup> <http://csu-cvmb.colostate.edu/Documents/anesthesia-pain-management-pain-score-feline.pdf>

<sup>b</sup> <https://www.newmetrica.com/acute-pain-measurement/>

<sup>c</sup> <https://bmcvetres.biomedcentral.com/articles/10.1186/1746-6148-9-143/tables/1>

<sup>d</sup> <https://www.felinegrimacescale.com/>

<sup>e</sup> [https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instrument s/](https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instrument-s/)

<sup>f</sup> <https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instrument s/>

<sup>g</sup> <https://ars.els-cdn.com/content/image/1-s2.0-S0168159117303271-mm2c2.pdf>

<sup>h</sup> <https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instrument s/>

<sup>i</sup> <https://www.newmetrica.com/vetmetrica-hrql/>

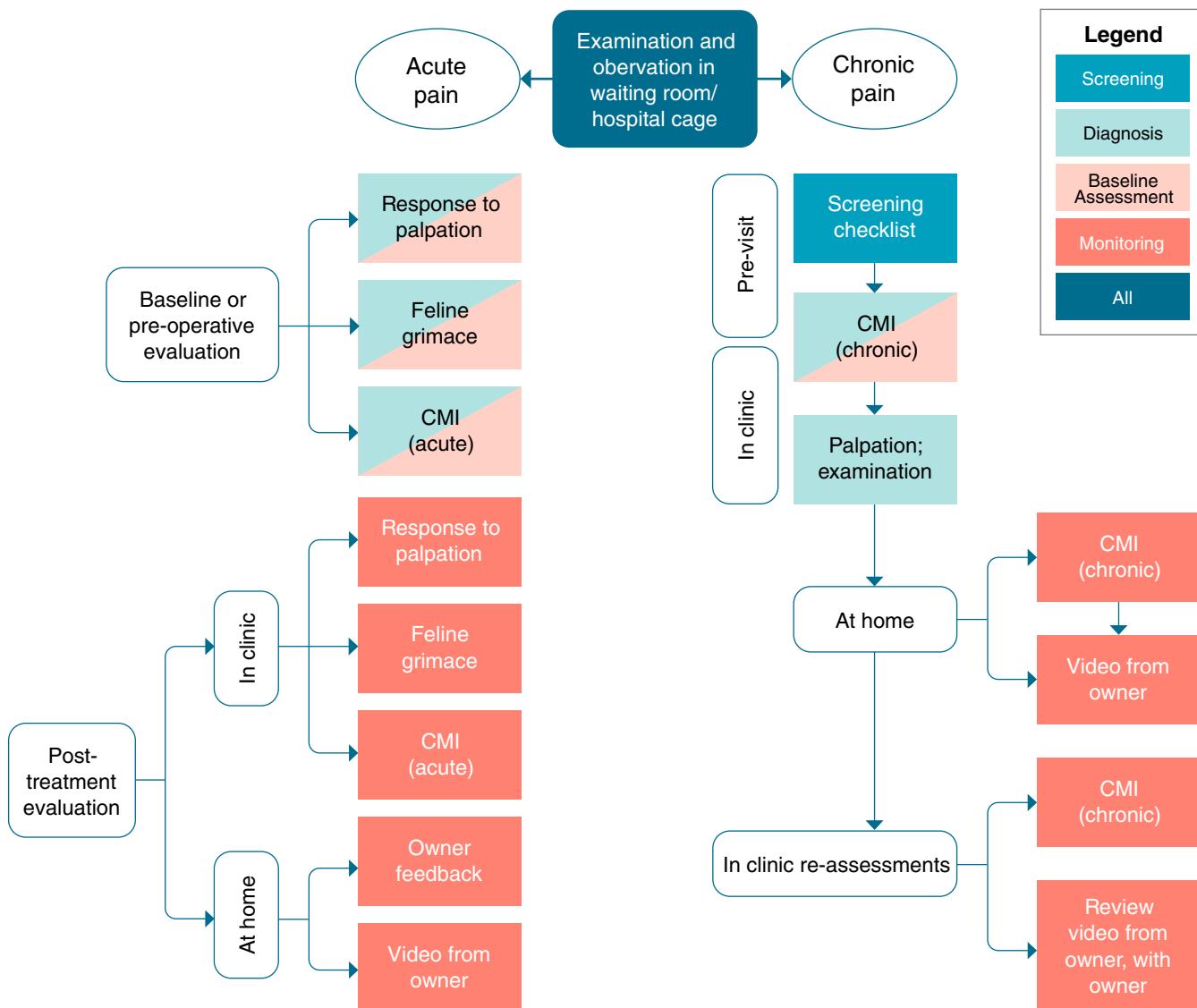
carrier from across the room can also provide an opportunity to watch them as they walk toward the carrier.

During the hands-on exam, cats are evaluated for *changes* in their behavior when an area is palpated or a joint is flexed and extended. Signs include tensing of the area, a change in vocalization (increased or decreased), or an attempt to move away. Imaging of an area where pain is found is important to identify pathology, but it should not substitute for (or replace the findings of) the physical

examination. For example, cats with OA may have painful joints with normal imaging or nonpainful joints with highly abnormal imaging.<sup>19</sup> When evaluating pain, it is important to prioritize the cat's behavior over the radiographic findings.

#### **Chronic Pain Assessment in Research Settings**

Additional tools used in a research setting include wearable activity monitors, weight distribution platforms, pressure walkways, force



## FIGURE 1

**Flow Diagram Outlining Acute and Chronic Pain Assessment in Cats.** This flow diagram outlines a basic approach to the assessment of pain in cats. For assessment of both acute and chronic pain, the core elements are physical examination/palpation and the use of Clinical Metrol-  
ogy Instruments (CMIs) (see Table 1). CMIs that are specific for particular circumstances (e.g., for specific types of surgery or for specific chronic diseases) are being developed, tested, and validated. Future assessment tools in the cat are likely to leverage automated analysis of facial expression and movement, and these may well become core elements assisting with the everyday assessment of pain. At the moment, for chronic pain, all the CMIs designed to assess the impact of pain have been developed for osteoarthritis. Importantly, this flow diagram illustrates two important points: (1) involvement of the owner and (2) follow-up and reassessment.

plates, and kinematic analysis. Activity monitors are often used as objective measures when evaluating therapeutics, but interpretation of findings has been hampered by a lack of understanding of what normal activity in cats is and how to analyze large volumes of high-frequency longitudinal data.

## Summary of Feline Pain Assessment

In cats, assessment of acute pain should rely on a combination of palpation and pain assessment tools, such as the Feline Grimace Scale. Conversely, assessment of chronic pain depends on owner input to a much greater extent. This requires us to collaborate with

owners to identify behaviors associated with chronic pain and to then observe and monitor those behaviors using tools developed for specific conditions and overall quality-of-life tools as they are developed.

Veterinarians need to recognize the power of our observations throughout a clinic visit in the assessment of cats, particularly for chronic musculoskeletal pain, and need to keep in mind that the absence of changes on imaging does not mean an absence of pain.

### Pain Assessment Tools for Dogs

Pain assessment in dogs involves tools that range widely, from functional signs evaluated by owners and physical signs detected by clinicians to physiological signs measured by researchers (Table 2). Assessment methods range from empiric and unvalidated (e.g., “How is your dog climbing stairs?”) to validated (e.g., peak vertical forces measured by force plates). Assessment methods vary widely in labor required, complexity, and cost. Pain assessment is most practically divided into the assessment of acute or perioperative pain and chronic pain (Figure 2).

### Acute and Perioperative Canine Pain Assessment

In the clinic, pain assessment includes appetite, observation of demeanor, behavior, and palpation. Dogs adjust their demeanor, behavior, posture, and movement to minimize pain. Inappetence and calm behavior can represent subtle signs of pain. As with cats, clinical metrology instruments have been developed to capture/measure these behavioral signs, and their incorporation into practice protocols is encouraged. These are for use in the clinic. Findings are converted into a score, such as the Colorado State University Canine Acute Pain Scale or Glasgow short-form Composite Measure Pain scale, which can be tracked over time. No owner-completed assessment tools for acute pain have been developed. Therefore, “at-home” acute pain assessment by the owners should be guided by the veterinary team. Owners know their dogs’ normal behavior. Deviations from that behavior suggest the presence of pain. The review of short videos and photos by the veterinarian can facilitate pain-related conversations.

### Chronic Pain Assessment in Dogs

#### *Assessment by Owners*

Musculoskeletal pain (e.g., OA) is the most common form of chronic pain in dogs and where most work has been performed to understand how to measure it. Owners can detect the presence of pain in dogs by comparing normal and abnormal behavior, but they may contextualize these signs and delay action for several months.<sup>20,21</sup> Owner responses to open questions—such as “how is he (or she) doing?”—can raise red flags that will warrant more specific

questions. Red flags can also be raised using screening tools. These are not specific for a given condition, although they may be targeted at a specific condition. They allow a conversation focused on possible conditions. Once a condition is highly suspected or confirmed, several questionnaires are used to evaluate chronic pain. Available questionnaires are mostly focused on canine OA. Questions relate to demeanor, mobility, and lifestyle, capturing information in a consistent and repeatable manner. The most widely used questionnaires are the Canine Brief Pain Inventory (CBPI, 11 questions)<sup>22,23</sup> and Liverpool Osteoarthritis in Dogs (LOAD, 23 questions).<sup>24,25</sup> The Sleep and Nighttime Restlessness Evaluation (SNoRE) questionnaire focuses on sleep quality.<sup>26</sup> These questionnaires, which can be downloaded and used at no cost, assume the presence of OA but may also help diagnose other conditions. The client-specific outcome measures (CSOM) assessment is a questionnaire that relies on the veterinarian to define a set of activities that are not being performed normally and that are specific to a pet. These “client-dog dyad-specific” questions are followed over time to assess response to therapy.<sup>27</sup> Client questionnaires have been used to support the regulatory approval of several pain medications for dogs. Although these instruments remain subject to bias, they are validated to varying degrees and provide useful and actionable information. One of their most powerful features is that they standardize the questions that are posed to owners, allowing trends over time to be captured more accurately.

#### *Clinician Assessment of Pain in Dogs*

Observation is a critical part of the veterinarian assessment of chronic pain. Signs of pain can be observed when a patient is resting, standing, moving at a walk or a trot, or doing functional activities such as climbing steps. At rest, awkward limb positions may indicate the presence of joint pain; for example, dogs with elbow joint pain may supinate their forelimbs and flex their carpus. When standing and moving, dogs shift weight away from a painful limb, and such postural abnormalities can be observed in the examination room if the animal is given time to relax. Recently, a staging tool has been proposed for canine OA,<sup>28</sup> which incorporates both owner and veterinarian assessments. The veterinarian assessments include observation of posture and motion as well as results from the hands-on evaluation. A “tucked up” appearance can be an indicator of abdominal pain, and postural straining can be an indicator of lower urinary tract or lower gastrointestinal tract pain. When pain is intermittent or associated with specific activities that are not reproducible in the clinic, pictures or videos collected by the owner and reviewed by the veterinarian provide useful pain-related information.

Palpation is the most widely used clinical method to detect pain in dogs, even if surprisingly few studies have evaluated its sensitivity and specificity.<sup>29</sup>

**TABLE 2**

## Pain Assessment Methods and Tools for Use in Dogs

TOOL	ACUTE OR CHRONIC PAIN	USER	EASE OF USE	PURPOSE	VALIDITY*
<b>Physical examination</b>	Acute and chronic	Veterinarian	Moderate, requires training	Screening, diagnosing, monitoring	Not formally validated as an assessment of pain
<b>Clinic observation</b>	Acute and chronic	Veterinarian and veterinary technician	Moderate, requires training	Monitoring	Not formally validated as an assessment of pain
<b>Physiological variables (heart rate; respiration; blood pressure)</b>	Acute	Veterinarian and veterinary technician	Simple	Screening, monitoring	Not specific indicators of pain
<b>Wound palpation</b>	Acute	Veterinarian and veterinary technician	Simple	Monitoring	Not formally validated as a stand-alone assessment of pain; forms part of several validated tools
<b>Home videos and photos</b>	Acute and chronic	Owner collects information Veterinarian evaluates	Moderate, requires instructions	Screening, monitoring	Not formally validated as an assessment of pain
<b>Force plate and pressure sensitive walkway</b>	Acute and chronic	Clinical research; dedicated assessment center	Challenging and labor intensive	Screening, diagnosing, monitoring	Valid
<b>Actigraphy (activity monitoring)</b>	Acute and chronic	Clinical Research	Challenging to setup and operate	Monitoring	Valid

(continued)

Medical imaging is used to confirm the presence of a suspected problem. Joint pain on palpation and radiographic signs of OA often correlate poorly.<sup>19</sup> Because of that discrepancy, radiographs only confirm the cause of joint pain detected on palpation rather than assume that all radiographic abnormalities represent a source of pain.

### Research and Development of Assessment Tools

The assessment of pain is critical to mechanistic and clinical research to advance our understanding of pain therapy. The subjective clinician or owner-based assessment tools mentioned thus far are most valid when used in the clinical research setting, under blinded, placebo- or active comparator-controlled conditions. In the acute

setting, other measures used include physiological variables (heart rate, blood pressure, cortisol, and c-reactive protein), wound pain sensitivity thresholds,<sup>30</sup> actigraphy to measure activity after surgery,<sup>31</sup> and gait analysis after limb surgery.<sup>32</sup> For chronic joint pain, gait analysis—particularly force plate analysis<sup>33</sup>—is the core feature of the assessment of limb pain in dogs. Other gait analyses are used, including 2-D and 3-D kinematic analysis,<sup>34</sup> pressure-sensitive walkways, and weight distribution platforms.<sup>35,36</sup> Actigraphy (physical activity monitors) is emerging to evaluate the impact of pain on daily activity, and validation efforts are ongoing.<sup>37–40</sup> Clinical research and development of assessment methods drive the development of assessment tools used in clinical practice. A considerable effort is being placed on artificial intelligence (AI) to evaluate images or videos on pain status, particularly acute pain, and future applications may be

**TABLE 2 (Continued)**

TOOL	ACUTE OR CHRONIC PAIN	USER	EASE OF USE	PURPOSE	VALIDITY*
<b>CLINICAL METROLOGY INSTRUMENTS (CMIS)</b>					
<b>Canine osteoarthritis staging tool (COAST)<sup>a</sup></b>	Chronic, osteoarthritis	Owner and veterinarian	Moderate	Screening	Not validated
<b>Colorado Acute Pain Scale Canine<sup>b</sup></b>	Acute	Veterinarian and veterinary technician	Simple	Monitoring	Not validated
<b>Glasgow Short Form scale<sup>c</sup></b>	Acute	Veterinarian and veterinary technician	Moderate	Monitoring	Moderately validated
<b>Liverpool Osteoarthritis in Dogs (LOAD)<sup>d</sup></b>	Chronic, osteoarthritis	Owner	Simple	Monitoring	Valid
<b>Canine Brief Pain Inventory (CBPI)<sup>e</sup></b>	Chronic, osteoarthritis	Owner	Simple	Monitoring	Valid
<b>Helsinki chronic pain index<sup>f</sup></b>	Chronic, osteoarthritis	Owner	Simple	Monitoring	Limited validation
<b>Sleep and nighttime restlessness evaluation (SNoRE)<sup>g</sup></b>	Chronic, osteoarthritis	Owner	Simple	Monitoring	Moderately validated
<b>Client-specific outcome measures (CSOM)<sup>h</sup></b>	Chronic, osteoarthritis	Owner	Moderate	Monitoring	Moderately validated
<b>Health related quality of life (HRQoL)<sup>i</sup></b>	Chronic	Owner	Simple	Monitoring	Valid, not specific to pain

\*Based on an overview of published studies assessing validity.

<sup>a</sup> <https://www.sciencedirect.com/science/article/pii/S1090023318300583?via%3Dihub> and <https://www.galliprantvet.com/us/en/coast-tools>

<sup>b</sup> <http://csu-cvmb.colostate.edu/Documents/anesthesia-pain-management-pain-score-canine.pdf>

<sup>c</sup> <https://www.newmetrica.com/acute-pain-measurement/>

<sup>d</sup> <https://www.galliprantvet.com/us/en/coast-tools>

<sup>e</sup> <https://www.vet.upenn.edu/research/clinical-trials-vcic/our-services/pennchart/cbpi-tool>

<sup>f</sup> <https://www.tassuapu.fi/>

<sup>g</sup> <https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instruments/>

<sup>h</sup> <https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instruments/>

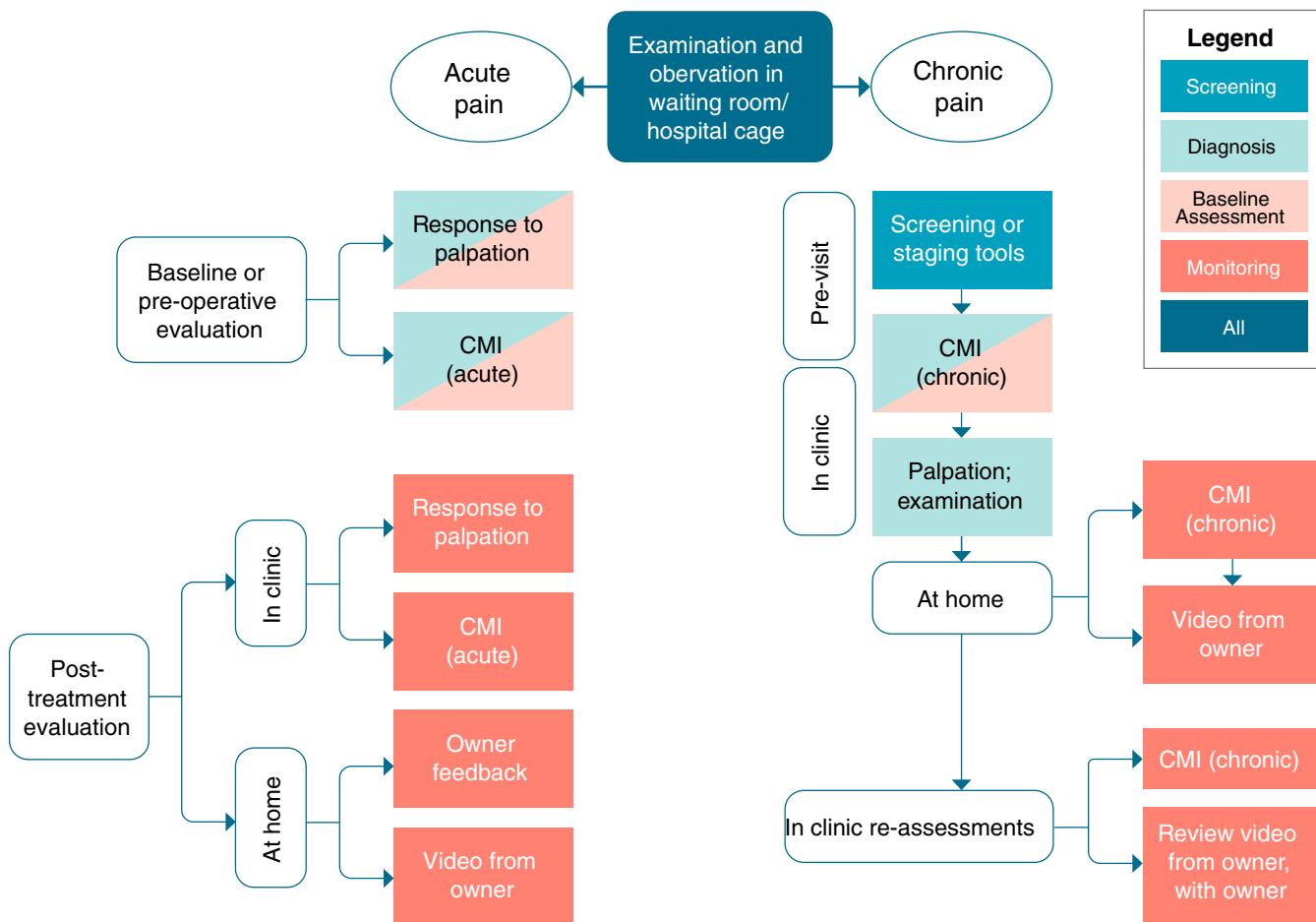
<sup>i</sup> <https://www.newmetrica.com/vetmetrica-hrql/>

developed for use in the clinic setting. AI will also be leveraged to understand and interpret data from wearables, and even implantables, as aids to diagnosis and monitoring.

### Practical Implementation of Assessment Tools

Successful pain management requires veterinarians gaining skills in observation and hands-on pain assessment, involving owners and veterinarians in pain assessment and management, and using all available assessment tools. Veterinary technicians and nurses must

be trained and empowered to use the Glasgow or Colorado scales and to palpate painful regions. Pain scores should be recorded and communicated with veterinarians. Rounds are used to ensure continuity of care and to update pain management. Over the long term, owners can be provided screening checklists such as CBPI or LOAD before or during visits. Survey results are recorded in the medical record and are reviewed at each visit. Palpation of limbs and the spine should be routinely done. Changes over time provide the impetus for changes in pain management.

**FIGURE 2**

Flow Diagram Outlining Acute and Chronic Pain Assessment in Dogs. This flow diagram outlines a basic approach to the assessment of pain in dogs. For assessment of both acute and chronic pain, the core elements are physical examination/palpation and the use of Clinical Metrology Instruments (CMIs) (see Table 2). CMIs that are specific for particular circumstances (e.g., for specific types of surgery or for specific chronic diseases) are being developed, tested, and validated. At the moment, for chronic pain, all the CMIs to assess the impact of pain have been developed for osteoarthritis, although these have been applied to other “limb pain” conditions, such as osteosarcoma. Importantly, this flow diagram illustrates two important points: (1) involvement of the owner and (2) follow-up and reassessment.

## Pain Management Toolbox

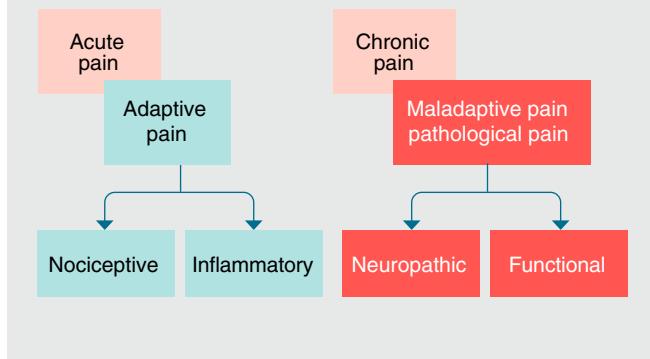
### Guiding Principles for Developing a Therapy Plan

The goal of pain management is to reduce pain to a level where it is well tolerated and does not interfere with daily activities or reduce quality of life. To expect to completely eliminate pain is probably unrealistic. Early intervention, whether in acute or chronic pain, with effective therapies makes pain easier to control. Thus, the recognition of situations that may be associated with pain, the assessment of patients for pain, and proactive treatment are all critically important.

Diagram illustrating descriptors used to refer to different types of pain. Pain is often classified as either acute or chronic. Arbitrarily,

pain of more than 3 months' duration has been considered chronic. However, there is nothing that suddenly changes after 3 months to create “chronic” pain. The mechanistic drivers of pain likely change on a continuum from acute nociceptive through to the pathological pain states. Acute pain is generally associated with tissue damage or the threat of this and serves the vital purpose of rapidly altering the animal's behavior to avoid or minimize damage and to optimize the conditions in which healing can take place. Nociceptive and inflammatory pain are usually considered subtypes of acute or adaptive pain. Pain of a longer duration can result in changes in the pain transmission system at multiple levels. Such changes generally facilitate and amplify pain. These changes result in a progressive

disconnect between the peripheral lesion and the pain being perceived and, as such, are often described as a “maladaptive” or “pathological” pain state. Neuropathic pain (from direct damage to the nervous system) and functional pain (altered functioning of the pain transmission system) are considered subtypes of chronic or maladaptive pain. When considering this classification system, the reader will realize that clinical pain is often a mixture of all these “types” of pain. The longer the pain state has been going on, the more likely there is to be maladaptive pain present and the more difficult pain is to treat.



### Acute Pain of Known Cause (e.g., Perioperative or Diagnosed, Known Trauma)

The mechanisms driving acute and perioperative pain are closer to nociceptive/inflammatory pain than they are to chronic or maladaptive pain (see call-out box 1), so acute/perioperative pain is easier to manage. Exact protocols and approaches can vary, but to be successful, they must be practical and feasible for the individual practice setting. The basic principles of effective perioperative pain management are as follows:

- *Early, preemptive or preventive use of analgesic therapies to optimize preventive therapy.* This refers to the use of analgesic therapies prior to the surgical insult, or as early as possible.<sup>41,42</sup> This approach has been shown to be of benefit in dogs.<sup>5,6</sup>
- *Use of a multimodal approach.* The pain transmission system is complex and has a lot of redundancy, so interrupting the pain pathways using multiple differing approaches is more effective clinically than relying on a single receptor or mechanism.<sup>43</sup>
- *Providing continuous, overlapping analgesia.* An analgesic plan should provide overlapping pain relief and include at least the early “at-home” time period.
- *Matching the provision of analgesia to the degree (dose) of surgery or trauma.* Greater tissue trauma, especially when it includes nerve damage, and more invasive and longer surgeries are generally associated with more pain.<sup>31,44,45</sup>

Effective and frequent assessment of the pain status of patients is critical both for the effective management of the individual patient and for evaluating practice protocols. Patients should be assessed

preoperatively and at regular intervals postoperatively (e.g., hourly or as appropriate for the status of the patient). Follow-up with owners should be at least daily for the first few days and include standard questions. When feasible, review of owner-captured video is useful.

### Chronic Pain

The practice team’s approach to treating chronic pain depends on the underlying cause of pain, duration, and previous treatment. The guiding principles for the effective management of chronic pain are as follows:

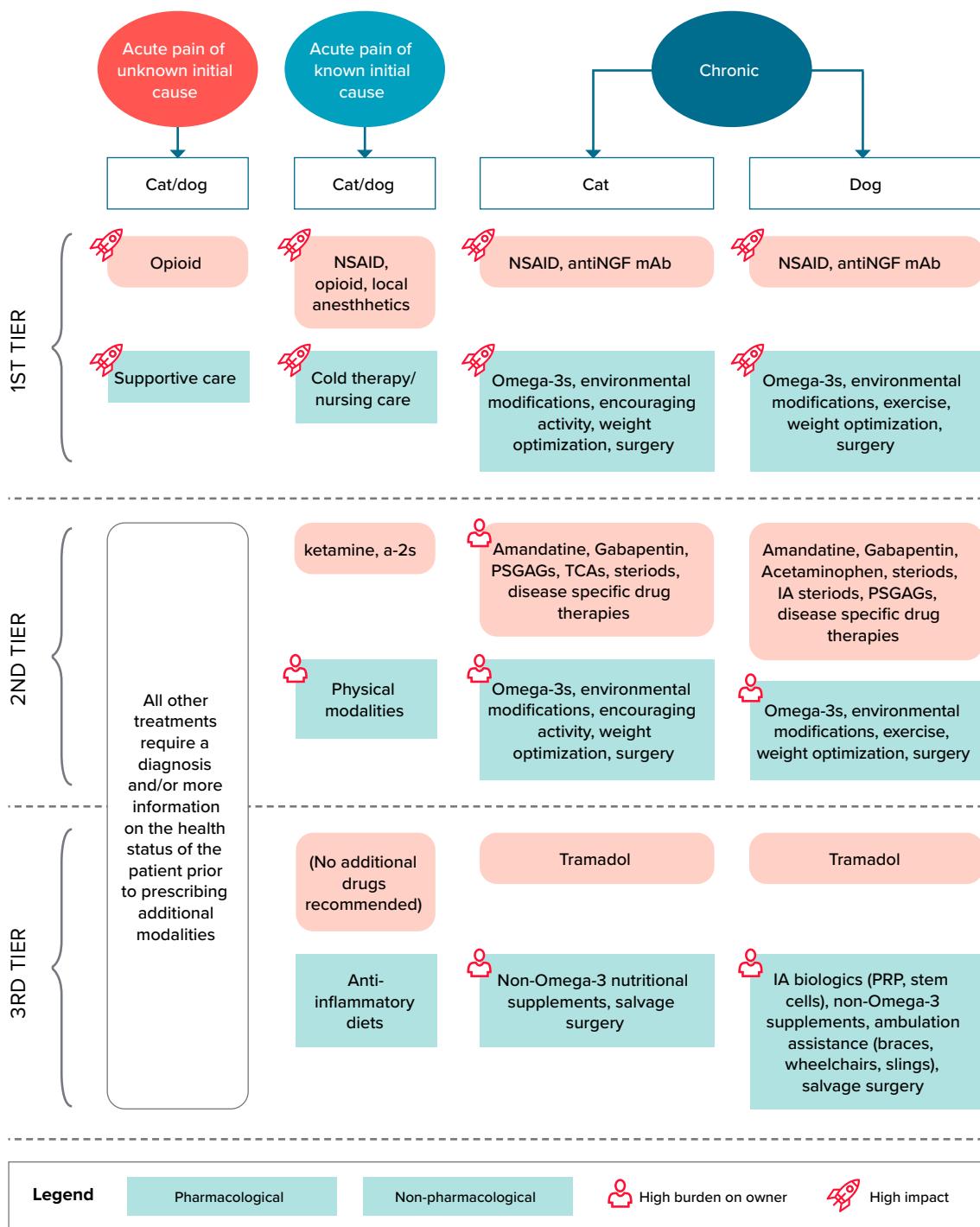
- *Assessment, recognition, and acknowledgment of chronic pain.* The practice team should employ checklists, clinical metrology instruments, and physical examinations to determine if chronic pain is present.
- *Use of a multimodal (combination therapy) approach.* Chronic pain involves multiple and often complex changes in the sensory system.<sup>46</sup> A combination of effective, known analgesics and nondrug therapies, combined with appropriate adjunctive therapies, is optimal.
- *Prioritization of known efficacious therapeutic modalities.*
- *Consider the burden of care on the owner* (e.g., oral medication of cats, multiple visits to the clinic for therapy).
- *Regular reassessment and adaptation of the management regimen.* The pain-sensing (nociceptive) system is bidirectionally plastic; that is, with effective pain management, the nociceptive system can return to normal. This means there is less pain to be managed, and the pain management approach can be reduced and simplified.

### Using a Decision Tree for Pain Management Therapies

Rather than present a list, or buffet, of treatment options, a tiered decision tree (Figure 3) has been provided to help with *prioritizing use of the most efficacious therapeutic modalities*. The tiered or ranked approach is based upon review of evidence-based veterinary medicine, incorporation of pertinent literature from human medicine, practical considerations, and clinical experience of the advisory panel. Tier 1 treatments are those that are considered the mainstay of pain management in the respective categories. As further clinical research is performed and new products are developed, the recommendations in each tier will be adapted. Clinicians may choose to start with tier 2 treatments, especially in combination with tier 1 approaches. Treatments in different tiers can be initiated at the same time, for example, NSAIDs and therapeutic exercise for canine OA pain.

### Acute Pain of Unknown Cause

In cases in which obvious pain is present but a diagnosis or reason for the pain has not yet been determined, effective management of that pain can facilitate management of the patient. Opioids are considered appropriate in that situation.

**FIGURE 3**

*Decision Tree for Prioritizing Pain Management Therapies. This figure outlines a tiered approach to pain management in cats and dogs for acute and chronic pain. Tiers are presented from highest recommendation (most evidence for effectiveness) to lowest, although all therapies presented have some evidence to support their use. Physical modalities include laser therapy, pulsed electromagnetic field therapy, acupuncture, and transcutaneous electrical nerve stimulation. Surgical procedures for chronic pain include top-tier treatments such as dental procedures, removal of painful lesions, joint stabilization and replacement, and amputation; lower-tier (salvage) procedures including arthrodesis, denervation, and excision arthroplasty. Anti-NGF mAB, anti-nerve growth factor monoclonal antibody.*

### Acute Pain of Known Cause (e.g., Perioperative Pain)

An appropriate starting point for every surgery is to plan on using opioids, an NSAID, and local anesthetics, in addition to cold therapy<sup>47</sup> and appropriate nursing care.<sup>48,49</sup> Local anesthetics are the most effective analgesic available in small animal practice, and they should be used in every surgery. Recently, there has been an increase in information available on the practical use of local anesthetics in practice.<sup>50-53</sup> NSAIDs may not be appropriate for every patient, and consideration needs to be given to whether they are provided prior to or after surgery.<sup>54,55</sup> Opioids are very effective for perioperative pain<sup>56</sup> and have proven preemptive benefit.<sup>5</sup> Cold therapy is very effective and can be applied by owners.<sup>47</sup> Nursing care includes appropriate use of bandages (which may mean not using them in cats), care of IV lines and other invasive monitoring, gentle massage and range of motion exercise where appropriate, and ensuring animals are able to sleep. Ketamine and  $\alpha$ 2-adrenoceptor agonists are good analgesic drugs but are in tier 2 to indicate that in general, they should be used after the use of NSAIDs, opioids, and local anesthetics has been considered. There is relatively little in the way of therapeutics with a novel mechanism of action on the horizon for perioperative pain control, but the use of transient receptor potential cation channel subfamily V member 1 (TRPV1) agonists (e.g., capsaicin) holds some promise as a novel approach to augmenting perioperative pain management.<sup>57,58</sup>

Although there is currently limited evidence of efficacy of physical modalities (laser therapy,<sup>59</sup> pulsed electromagnetic field therapy<sup>60</sup>), future work may change recommendations.

Tier 3 contains additional options, including the use of anti-inflammatory diets rich in omega-3 fatty acids prior to and after surgery.<sup>61</sup> The tiered approach should be applied to the preoperative, intraoperative, immediate postoperative, and at-home time periods (Figure 3).

### Chronic Pain

Dozens of treatments have been suggested as being effective for chronic pain, but there is little evidence of efficacy for the majority of these. The tiered approach attempts to provide a ranking and is based primarily on the management of chronic musculoskeletal pain. However, the principles are generally applicable across other chronic pain conditions. Future work will allow disease- or condition-specific recommendations to be made.

In tier 1 are the COX-inhibiting and non-COX-inhibiting (EP4 receptor antagonist) NSAIDs. These are predictably efficacious across the wide range of pain conditions because of the ubiquitous role of prostaglandins in peripheral and central pain processing. Other analgesics, such as the anti-nerve growth factor (NGF) monoclonal

antibodies, are on the horizon and will provide additional first-line choices.<sup>62,63</sup> Nondrug treatment options in tier 1 include omega-3 fatty acids (either supplementing the diet or provided through the use of a therapeutic diet), encouraging activity, environmental modification, weight management, and surgery. Measurable pain relief has been associated with the provision of diets enriched in omega-3 fatty acids.<sup>64,65</sup> Robust data in humans<sup>66,67</sup> and the limited data in companion animals<sup>68</sup> support the analgesic benefits of moderate exercise. Modifying the environment is a very practical way of providing relief from painful activities and facilitating movement. Preserving access to 3-D (vertical) space through building ramps or stairs is especially important for cats, who need access to height to feel safe. Lowering entry to litter boxes for cats, providing easy access to elimination for dogs, and optimizing floor and sleeping surfaces are other important aspects. Surgery is listed in tier 1 because particular surgeries can remove chronically painful lesions (cancer resections, dental procedures, joint stabilizations, and amputations).

In tier 2 are adjunctive drugs—those with little or mixed evidence of analgesic efficacy in various conditions. These are recommended as “adjunctive,” or in addition to tier 1 approaches.

In cases of intolerance or contraindications for NSAID use, steroids (cats and dogs) or acetaminophen (dogs only) can be tried as broad “base” analgesics, despite the lack of data.

Intra-articular (IA) steroids are recommended in tier 2, and various IA biologics (such as platelet-rich plasma and stem cells) in tier 3, based on current data. IA treatments are less practical in cats than in dogs. Some pain conditions in cats (e.g., interstitial cystitis) may benefit from tricyclic antidepressants.<sup>69</sup> Disease-specific drug and other therapeutic therapies (e.g., bisphosphonates and palliative radiation for osteosarcoma pain) should be considered in tier 2 as appropriate for the disease. Therapeutic exercise and physical modalities such as acupuncture, laser therapy, transcutaneous electrical nerve stimulation, and pulsed electromagnetic field therapy may be useful adjuncts to consider, but little work has been performed to evaluate their benefit in chronic pain.

Tramadol is listed in tier 3 given the demonstrated lack of efficacy in dogs<sup>33</sup> and the strong aversion cats have to its taste, despite a potential therapeutic effect.<sup>70,71</sup> The placement of nutritional supplements in tier 3 indicates that there is no evidence to support an analgesic effect of non-omega-3 nutritional supplements.<sup>72</sup> Procedures such as localized surgical denervation should be considered end-stage procedures.

### Pharmacologic Update

The pharmaceutical toolbox continues to grow and improve for companion animals. This section of the guidelines *discusses notable pharmacologic changes and discusses persistent myths by drug class*.

### ***Pharmacological Agents in the Treatment of Acute or Perioperative Pain***

Although most opioids are in common use in veterinary species, they do not generally carry species-specific licenses in the United States. Simbadol is a recent exception. It is a buprenorphine formulation licensed for use in cats as an every-24-hour subcutaneous injection.<sup>73,74</sup> Recent studies also support its use in dogs,<sup>73-75</sup> although it is not licensed for canine use. The 24-hour duration of action helps in providing pain relief to animals that are discharged into the home environment. A persistent myth surrounding opioid use in cats is the belief that they create excessive hyperactivity or dysphoria at clinical doses in cats. They do not, unless very high doses are administered.<sup>76</sup> A justified belief is that hyperthermia can be potentiated with opioids in cats, but this can be managed with monitoring and environmental modification.<sup>77</sup>

Newer drugs of the NSAID class include the expanded perioperative approval of robenacoxib in dogs and cats. Robenacoxib was initially released for 3 days of perioperative use in cats using oral tablets, and since 2015, the injectable solution is now also approved.<sup>78</sup> Robenacoxib is now also licensed for perioperative use in dogs.<sup>79,80</sup>

Local anesthetic techniques have hit a new renaissance, with the promotion of their use in the dental college, increased availability of detailed descriptions of how to effectively use them,<sup>52,81</sup> and the development of more advanced methods to ensure reliable placement, such as nerve-location devices and ultrasound.<sup>50,51</sup> A newly available long-acting bupivacaine has added further momentum.<sup>82,83</sup> The recently available long-acting preparation of bupivacaine is a liposome-encapsulated formulation, Nocita. When injected into the wound at the end of surgery, this agent can provide local analgesia that lasts up to 3 days. It is labeled for orthopedic surgery in dogs and onychectomy in cats. Opioids have been shown to have varying levels of independent sodium-channel blockage and to augment local blocks, with buprenorphine being a potent sodium-channel channel antagonist.<sup>84,85</sup> Dexmedetomidine has also been shown to prolong local anesthetic blockade, likely from pharmacologic synergy as well as local vasoconstriction.<sup>86</sup> Our knowledge of the efficacy of local anesthetic drugs other than lidocaine and bupivacaine has recently expanded. Ropivacaine is pharmacologically similar to bupivacaine but with an increased safety profile in humans, and it was recently shown to be similar in efficacy to bupivacaine.<sup>87</sup> Recent data have also confirmed previous work<sup>88</sup> demonstrating the efficacy of intraperitoneal local anesthetic instillation with or without local tissue infiltration.<sup>87,89-91</sup>

$\alpha$ 2-Agonists have a variety of perioperative roles, including adrenergic-based analgesia, mitigation of vasodilation, reduced sympathetic outflow, and augmentation of sedation. Over the last 10 years, no new drugs in this class have emerged, but different uses

and formulations of existing  $\alpha$ 2-agonists have. Intraoperative micro-infusions are being used to provide additional analgesia and improve respiratory and hemodynamic function.<sup>92</sup>

Tramadol was once a reflexively used oral analgesic in dogs, but it has been seriously deemphasized in the last decade. Oral tramadol has not been shown to be effective postoperatively in dogs.<sup>93</sup> Studies of IV tramadol have shown some mixed efficacy for surgical pain in dogs.<sup>94-96</sup> Injectable tramadol has shown perioperative efficacy in the cat<sup>97</sup>; however, an IV form of tramadol is not available in the United States.

Gabapentin use has become widespread and common, although without supporting data, especially in chronic pain conditions (as described in the next section). It has not been shown to be effective for acute pain in dogs.<sup>98,99</sup>

The NK receptor system is bound by substance P and was studied for years as a possible target for analgesia. Although these studies failed, the NK receptor antagonists have been found to be excellent antiemetics. Maropitant has become very popular in veterinary medicine as an antiemetic but also to provide some visceral analgesia. Studies showing analgesia are limited and weak,<sup>100</sup> but the antiemetic qualities of maropitant are well established.

### ***Pharmacological Agents in the Treatment of Chronic Pain***

Long-term use of oral opioids is not recommended for chronic pain control. There are concerns about the potential for human abuse of these drugs, and dogs have demonstrated repeatedly poor uptake of opioids via the oral route because of pronounced enterohepatic recirculation and elimination. No opioid-type drug shows reasonable, repeatable drug levels after oral administration; opioids combined with acetaminophen also provide inadequate analgesia for chronic pain.<sup>101</sup>

There are several NSAIDs approved for use for chronic pain in dogs. Although renal, hepatic, and gastrointestinal toxicity can be associated with their use, the true incidence is likely low (and unknown).<sup>102</sup> Studies of long-term use of NSAIDs in dogs do not show increased organ-based toxicity with longer treatment but do show a positive trend toward increased efficacy.<sup>103</sup> Since 2016, grapiprant has been approved in the United States for managing chronic pain in dogs. Grapiprant is the first “pirrant” NSAID, that is, NSAIDs that block prostaglandin receptors. Grapiprant blocks the EP4 receptor, leaving the production of prostaglandins unaltered. It has been shown to be efficacious for canine OA pain<sup>104</sup> and to have a favorable safety profile. Grapiprant decreased the clinical signs of OA safely and effectively in a study of 131 dogs.<sup>104</sup>

No NSAID is approved for long-term use in cats in the United States, although both meloxicam and robenacoxib are approved for long-term control of musculoskeletal pain in the United Kingdom,

elsewhere in Europe, and in other parts of the world. Recent studies have confirmed the efficacy of both drugs for treating OA pain in cats.<sup>14,18</sup> Large studies of the clinical safety of robenacoxib have been published and demonstrate its safety in older cats, even those with chronic kidney disease.<sup>105</sup> A recent review emphasized that fears over the long-term use of NSAIDs in cats, including those with chronic kidney disease, are not fully justified.<sup>106</sup>

NGF has been shown to be an important driver of pain in OA.<sup>107</sup> Studies have shown good pain relief with anti-NGF monoclonal antibodies in dogs<sup>108,109</sup> and cats.<sup>62,63</sup> The first anti-NGF monoclonal antibodies have been approved in the United Kingdom, elsewhere in Europe, and in other countries. Anti-NGF monoclonal antibody treatment was recently approved in the United States for use in cats.

Amantadine is the oral counterpart to ketamine. More than 10 years ago, amantadine was shown to be useful in combination with NSAIDs for the treatment of chronic OA pain,<sup>110</sup> although no new data are available. Although once-daily doses were used in that study, pharmacokinetic studies in greyhounds suggest that twice-daily doses may be more appropriate,<sup>111</sup> but this has not yet been evaluated in efficacy studies. There is a perception that amantadine should be dosed as a 3-week rescue protocol. However, this assertion is merely a result of the duration of administration in the original study.<sup>110</sup>

Gabapentin has become the “new tramadol,” with widespread usage. While some practitioners report benefits anecdotally in both species and for a variety of pain conditions, virtually no supporting data are available at this time. It has not been evaluated for analgesic efficacy in chronic pain in dogs. Limited data indicate some efficacy in cats with OA pain,<sup>112</sup> although sedation was noted, and indeed, treated cats moved less (as measured by activity monitor output). There is evidence to support its use as a behavioral modifier or stress reducer in cats when given several hours prior to hospital visits.<sup>113</sup> This application may help with chronic pain control in cats by facilitating veterinary visits and evaluations.

The endocannabinoid system is intrinsically integrated with the more traditionally studied systems (opioidergic, serotonergic, noradrenergic), and the scientific feasibility of benefits on pain sensation and other homeostatic systems is undeniable. However, the data required for evidence-guided prescriptions of cannabinoid compounds in veterinary medicine are lacking. Some efficacy studies have been performed, with both mixed<sup>114</sup> and negative<sup>115</sup> results. The field is complicated by the lack of regulation and quality control from a regulatory body such as the FDA.

There are few data on the efficacy of acetaminophen, but it was recently shown to be inferior to carprofen for OA when combined with hydrocodone.<sup>116</sup>

IA and intralesional injections of analgesics can be useful when the pain, particularly chronic, is localized to one or two limited areas

or in patients intolerant of effective systemic treatments. There is emerging evidence for the efficacy of IA treatments (such as corticosteroids, hyaluronic acid, and orthobiologics [including platelet-rich plasma and stem cell therapy] in dogs),<sup>117,118</sup> although most studies are small and results have been mixed. Options continue to be expanded, and most recently, a radioisotope of Tin-117m has been developed and found safe in normal elbow joints.<sup>119</sup> Other effective options, such as the TRPV1 agonists (capsaicin and resiniferatoxin), appear to be on the horizon.<sup>120,121</sup>

## Nonpharmacologic Modalities for Pain Management

Although pharmacological agents are often necessary to assist with managing discomfort, nonpharmacological modalities are critically important in the management of chronic pain and maintaining the body in an active state. Thus, it is advisable for veterinarians to be prepared with substantiated options.

### Weight Optimization

Adipose tissue secretes a mixture of cytokines that circulate throughout the body, contributing to the pathology of many diseases, including OA, other inflammatory conditions, and the pain-associated hypersensitization process. Studies in human medicine have linked obesity with increased progression of OA in weight-bearing joints as well as non-weight-bearing joints, meaning these cytokines play an important role in the degradation process. Longitudinal cohort studies in the veterinary literature strongly support maintenance of a lean body condition score (caloric restriction over the lifetime of the dog) for decreasing the rate of OA progression and extending life span.<sup>122,123</sup> With respect to pain, obesity is most often linked to OA pain, but, increasingly, it is becoming apparent that an obese state contributes to other pain conditions, such as neuropathic pain.<sup>124</sup>

### Dietary Modulation

As described above, caloric restriction assists in preventing obesity, and this has a positive effect on helping prevent painful disease, such as OA, and likely helps decrease pain associated with other conditions. Beyond calories, there has long been an interest in “nutritional supplements” for the management of pain, especially OA or degenerative joint disease. The most comprehensive review on the efficacy of nutraceuticals to alleviate the clinical signs of OA concluded that the strength of evidence was low for all nutraceuticals except for omega-3 fatty acid in dogs.<sup>125</sup>

### Exercise and Rehabilitation Therapy

The profound health benefits of movement and exercise are well established in human medicine, including the benefits of exercise in reducing and controlling pain.<sup>66,67,126</sup> The strength of these data in

humans suggests that the same is highly likely to be true for cats and dogs, although clinical study evidence is sparse. However, daily walking has been associated with a decrease in the severity of lameness in dogs with hip dysplasia.<sup>68</sup> Whereas the terms physiotherapy and physical therapy refer to the treatment of humans, the most appropriate terminology in veterinary medicine is rehabilitation therapy. Rehabilitation therapy broadly encompasses the use of varied manual techniques (joint mobilization, passive range of motion, stretching, massage, and myofascial release, to name a few), treatment modalities (therapeutic ultrasound, photobiomodulation-laser therapy, extracorporeal shock wave therapy, neuromuscular electrical stimulation, and thermal modification of tissue), and therapeutic exercises including hydrotherapy.

Although there is a dearth of controlled prospective clinical trials in the veterinary literature, the advisory panel believes that rehabilitation therapy should be considered part of a comprehensive wellness plan for patients who are affected by acute or chronic pain.

“Therapeutic exercise” usually refers to specific exercise targeting particular goals, such as restoring range of motion in arthritic joints, building muscle following surgery or prolonged immobility, or retraining the proprioceptive system after neurological injury. Creative planning between an owner and a trained rehabilitation specialist can often yield at-home alternatives to buying specific animal fitness equipment.

### ***Cold Therapy***

Cold therapy has a long history as an analgesic modality for acute pain. Applying cold therapy to skin decreases temperature up to a depth of 2–4 cm, resulting in decreased activation of tissue nociceptors and slowed conduction velocity along peripheral axons.<sup>127</sup> Cold therapy also decreases edema formation via vasoconstriction, decreased delivery of inflammatory mediators to injured tissues, and decreased neurogenic inflammation as a result of decreased neuronal activity in sensory nerves. The practical application of cold therapy to patients was recently reviewed, and its use in acute and chronic pain conditions was discussed.<sup>47</sup>

Several studies in veterinary medicine have demonstrated that cryotherapy or cold compression therapy applied with the first 72 hours following stifle stabilization surgery resulted in decreased pain, decreased lameness, and increased joint range of motion.<sup>128</sup>

### ***Environmental Modification***

Environmental modification is the adjustment of environmental surroundings to positively influence comfort. In the hospital environment, this can be as simple as separating cats from dogs, placing pets in appropriately sized cages or runs, providing cage pads in addition to bedding, and having hiding places for cats. Reducing noise can

decrease stimulation and secretion of cortisol, which can reduce patient stress.<sup>129</sup>

At home, environmental modification can also be used to preserve access to preferred areas. Owners can provide injured, arthritic, or neurologic pets with secure footing (carpet runners) or with ramps or steps to areas that would otherwise be inaccessible. Animals in discomfort often feel vulnerable and prefer to rest in areas of the house that are quieter or more protected, such as a behind a couch or under a bed. Cat doors or baby gates can be used to provide “restricted access” areas in the home and allow pets to rest more comfortably. Placing these areas at a manageable distance from food or litter boxes may encourage mobility and exercise, particularly for cats.

### ***Acupuncture***

There is not an abundance of evidence-guided studies supporting the use of acupuncture. However, a 1997 National Institutes of Health Consensus Statement indicated promising results for the use of acupuncture in humans postoperatively, for treating chemotherapy nausea and vomiting, and in cases of postoperative dental pain. In the veterinary literature, acupuncture has been reported to be helpful as an adjunct treatment for postoperative pain following ovariohysterectomy in cats<sup>130</sup> and dogs and for managing intervertebral disc disease, but it was not found to be beneficial for the treatment of pain associated with OA in dogs.<sup>131</sup> Further work is needed to fully define the role of acupuncture in pain control.

### ***Feline-Specific Factors in Pain Management***

Cats living today have essentially the same brains and behavioral repertoire as their wild ancestors; they have just learned how to form social attachments to people when kept in confinement with them.<sup>132</sup> Cats benefit from safe and predictable environments that permit their perception of control to exceed their perception of threat. Such environments include the people to whom cats are bonded. Cats respond to human communication and emotional cues, particularly when expressed by their owners. Significant differences in feline threat response system activity have been found when attending to human “happiness” or “anger” emotional signals.

For these reasons, effective chronic pain management plans include consideration of the human-cat bond as well as the effectiveness of medical interventions. Research in other species has shown that positive environments and emotions decrease pain behaviors and that negative ones have the opposite effect.<sup>133</sup> Thus, the treatment plan must minimize negative interactions with owners and caregivers, such as unpleasant-tasting medications or unskilled handling for administration.

The benefits of any treatment should be weighed against the potential costs to the cat's comfort, including any treatments that require restraint or repeated trips to the veterinarian. For example, whereas therapeutic laser treatments may be a tolerable and effective form of therapy, the necessity for repeated transportation for treatment may limit their effectiveness for many cats. For medications, alternative formulations like compounded liquids, very small tablets, or preferred flavors may help reduce the difficulty of administration. The value of treatments that cause anxiety, fear, or frustration when administered must always be weighed against their negative consequences on the human-cat bond.

Conversely, humans initiating and maintaining contact with cats in their homes in ways that result in positive emotional states can reduce pain-related behaviors and improve animal welfare. Predictable interactions with humans reduce the cat's perception of threat. And the ability to choose likely permits cats to increase their perception of control.<sup>134</sup> Choice in the timing and duration of play sessions and activities such as petting, grooming, or training, combined with high-value treats, should ideally be planned for predictable times of the day and can reduce pain-related behavior.<sup>135</sup>

A cat's perception of threat also can be reduced by increasing opportunities to express feline-specific behaviors, such as exploration and play, by providing stimulating feeding strategies, and by reducing or eliminating conflict. Humans are part of this, whereas unrelated cats are not. Cats also rely more than humans do on smell, hearing, and touch to experience the world. For example, cats commonly use scent to mate, mark territory, bond, and communicate. Thus, odors preferred by cats, such as catnip, silvervine, or a pheromone, can add to enrichment. Additionally, cat-specific music has been shown to reduce blood pressure in cats,<sup>136</sup> and preferred bedding materials, fabrics, and scratching surface textures can enhance tactile experiences. Effective chronic pain treatment plans should always include environment and emotional enrichment as integral components.

## Roles and Responsibilities for the Practice Team

Every member of the practice team has a potential role in implementing a culture that supports pain management strategies for canine and feline patients. It is extremely important that each staff member understands their respective role and responsibilities in the practice's integrated approach to pain management. In order to accomplish this, team members should be given role-specific instructions and training for applying an appropriate pain management plan individualized for each patient. Delegation of each role will vary based on a particular practice's needs. Important roles for team members are as follows:

- Providing pain-related continuing education for the team.
- Attending pain-related continuing education.
- Developing hospital-specific materials from the AAHA toolbox.
- Holding consistent meetings/communication across the team to discuss pain management assessment and protocols.
- Scheduling pain-related appointments.
- Implementing specific, consistent discharges in relation to pain management plans.
- Communicating low-stress handling with owners and use of antianxiolytic medications prescribed by veterinarian.
- Conducting pain clinics.
- Implementing an acute pain scale and providing in-house education on its use.
- Facilitating pain-related medication, diet, and therapeutic refills.
- Evaluating patients for any pain postures or signs noted upon arrival, at check-in, or during history taking.

## Client Education, Instructions, and Follow-up

With each pain management plan, it is important that the client be given specific instructions, both verbally and in writing, including when the next assessment is recommended. Where owners play a critical role, such as in the provision of cold therapy following surgery or in weight management and exercise for chronic joint pain, they should be given clear instructions and guidance in the medium best suited to them (e.g., digital versus paper). As treatment progresses and pain control improves, modifications to instructions should be made clearly and in full consultation with the owner. It is important that owners be made aware of potential adverse drug effects and of the action to take if these are seen. Especially for cats, technicians should provide a hands-on demonstration on how to administer medications and handle the pet at home.

Compliance will improve if the pet owner understands the treatment schedule, a demonstration is given, video links are provided, and technicians actively engage in follow-up at regular intervals. Clients should be encouraged to address their concerns about the pet's condition and treatment plan via email, phone, or follow-up consultations. Finally, providing pet owners with quality, accessible online or in-person education will foster client goodwill and improve compliance and patient care as owners are welcomed as part of the management team.

### Top 5 messages for effective pain management

1. Be proactive: train and prepare the whole veterinary team to understand and appreciate the procedures and diseases that can be associated with pain and to proactively manage diseases early in their course.
2. Use the tools and recommendations available to facilitate and assist with the assessment of pain.
3. Engage the owner as a team member in both the recognition and management of pain.

4. Practice preemptive, multimodal management based on a tiered approach to both pharmacological and non-pharmacological treatments.
5. Reevaluate patients on a regular basis, and adjust treatment plans accordingly.

## Summary

It is helpful to view pain management as a continuum of care, a sequence consisting of assessment, treatment, reassessment, and plan modification. Using tools and approaches known to be valid measures, clinicians can diagnose acute and chronic pain and the patient's response to treatment with a high degree of assurance. The broad assortment of pharmacologic and nonpharmacologic modalities for treating pain gives veterinarians considerable flexibility in developing a patient-specific treatment plan. In using these therapeutic tools, preemptive analgesia and, whenever appropriate, multimodal therapy are two underlying principles of effective and judicious pain management.

The client plays an important role in pain management by providing relevant patient history, participating in assessment and reassessment of the patient, and adhering to treatment recommendations, including administering treatment and management recommendations in the home environment. Practices that implement an integrated approach to pain management ensure that all healthcare team members and their clients understand their respective roles in preventing and controlling pain in their patients and pets. This shared responsibility ensures that effective pain management will be a central feature of compassionate care for every patient. ■

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