

CANADIAN ARTHRITIS NETWORK
WHITE PAPER

**WORKSHOP ON
PAIN AND
ARTHRITIS RESEARCH**

Calgary, Alberta
January 28 – 29, 2006



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**Proceedings of the Canadian Arthritis Network
Pain Workshop
Calgary, AB
January 28-29, 2006**

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INTRODUCTION

In January 2006, the Canadian Arthritis Network (CAN) assembled a group of scientists, clinicians, industry partners and consumers in Calgary, Alberta, to tackle the problem of arthritis pain from multiple perspectives. The guiding principle of this Pain and Arthritis Research Workshop was to assemble like-minded individuals from various backgrounds who are dedicated to elucidating the problem of arthritis pain. CAN's goal by bringing together experts, industry representatives and patients, is to foster future partnerships that would lead to formulating original ideas and developing new therapeutic approaches that will one day provide relief to millions of arthritis patients.

WORKSHOP OBJECTIVES

The Workshop objectives included:

- 1) Developing an understanding of the individual perspectives on pain among workshop participants.
- 2) Identifying the current level of knowledge on the subject of pain among the workshop participants.
- 3) Identifying gaps and weaknesses in current pain research.
- 4) Identifying both short and long term goals for pain research.
- 5) Identifying how CAN should facilitate the achievement of both the short and long term goals in arthritis pain research.

WORKSHOP OUTCOMES AND FUTURE RESEARCH GOALS

The Workshop discussions raised many questions and ideas for future research in pain. It is clear that the origin of pain cannot be disentangled from assessment, treatment, and psychosocial consequences. Pain is recognized as a multi-faceted, bio-psychosocial entity requiring further study in its own right rather than simply as a symptom of another disease; only then will new targets for treatment be discovered. Novel, multidisciplinary approaches are required to adequately address the many types of arthritis pain. In proposing next steps, the workshop participants provided consistent support for:

- 1) Sponsoring additional pain workshops to advance the research agenda.
- 2) Building research capacity specific to arthritis pain research such as funding traineeships and leveraging research funds for interdisciplinary pain studies.
- 3) Involving the multidisciplinary treatment team in future workshops and research.
- 4) Recognizing that well-informed, empowered individuals (patients) are more effective in managing arthritis pain, thus efforts must be made to disseminate knowledge broadly.
- 5) Developing dissemination strategies designed to influence research funding priorities, health professional education and effective patient care.
- 6) Supporting the development of better measures of pain for use in research and practice, from biomarkers and objective indicators of pain through the continuum to psychosocial outcome measures.
- 7) Fostering rigorous and novel research into the origins of pain, assessment/outcome measures, intervention targets, pharmacological and non-pharmacological interventions, and including psychosocial approaches to pain management. Longitudinal studies are important to better understand the long term consequences and burden of arthritis pain as well as intervention effectiveness.

Findings from this initial workshop offer a direction for establishing both immediate and longer term research priorities to work towards the resolution of arthritis pain.

WORKSHOP ON PAIN AND ARTHRITIS: PAIN WORKSHOP COMMITTEE

Chair:

Dr. Jason McDougall, University of Calgary, Calgary

Committee:

Dr. Catherine Backman, University of British Columbia, Vancouver

Ms. Jay Fiddler, Consumer Advisory Council, Vancouver

Dr. Monique Gignac, University Health Network, Toronto

Dr. Gillian Hawker, Women's College Hospital, Toronto

Dr. Jim Henry, McMaster University, Hamilton

Dr. Linda Li, University of British Columbia, Vancouver

Dr. Marc Pouliot, Centre de Recherche en Rhumatologie et Immunologie, Sainte-Foy

November 2006

APPENDIX A: SUMMARY OF THE WORKSHOP SESSIONS

Introduction

The Workshop was designed as multiple, small, break-out sessions. Groups of participants with diverse backgrounds discussed the following questions:

- 1) What is the origin of arthritis pain?
- 2) Is there a better way of measuring and defining joint pain scientifically and clinically?
- 3) What could be useful new targets to treat arthritis pain?
- 4) What alternative, non-pharmacological treatments could be used to effectively treat arthritis pain?
- 5) How can we better manage the psychosocial consequences of chronic joint pain and fatigue?

Each group was assigned the task of answering two of the questions. The ideas and opinions expressed in these small working groups formed the basis of a more in-depth debate involving all of the workshop participants.

Question 1. What is the origin of arthritis pain?

a) Individual perspectives on the question

- There is little evidence of what generates joint pain
- Pain may be generated by increased sensitivity of peripheral nerve terminals
- Pain may be generated by areas in the spinal cord that become “supersensitive”
- Is the psychological component of chronic pain similar in all types of pain?
- There are biological, psychological and social dimensions of pain, so the person who suffers chronic pain must be seen as a whole person, rather than simply someone with diseased joints
- Interestingly, there isn't a strict correlation between structural damage and pain intensity
- Can the sensory nerve fibres be playing a role in aggravating disease progression? Top down from brain to periphery can affect disease progression
- In fibromyalgia there is no identifiable pain pathology, perhaps something can be learned from this with regards to joint pain
- Changes in mechanical loading may induce changes in gene expression that may lead to pain perception
- Pain depends on perspective (i.e. holistic, biological, environmental)
- Joint replacements can reduce pain, but not for everyone. Why is this? What evidence exists that total knee replacement/total hip replacement reduces pain? Is it different for osteoarthritis (OA) vs. rheumatoid arthritis (RA)?

- Response to treatment is not universal, leading to the belief that the origin/cause of arthritis pain must vary across individuals
- Not everyone has pain with injury, so it is imperative to examine beyond the pain associated with tissue injury

b) Group's current knowledge

- Where does pain start: in the joint, brain, etc., and what type of pain is joint pain? Some joint replacement patients still experience pain
- Pain tends to be more intense over time, perhaps due to disease progression, or may be due to neuroplasticity, which yields increasing sensitivity of pain mechanisms over time
- The variable nature of joint pain at different times of the day or on different days is poorly understood
- Belief in the effectiveness of a pain management program is important to its overall success
- There is a lack of knowledge about moderating factors that influence the intensity of joint pain
- There is some evidence of an inflammatory component to OA and further understanding of this particular component may help in understanding the origin of OA pain
- Pain can vary according to activity
- What chemical factors in the periphery cause sensitization of peripheral nerve receptors?
- In animals, the direct injection of glutamate, substance P and some other chemicals can have an effect on joint pain
- There is evidence in humans about the effectiveness of cytokine drugs in pain control
- Multiple tissues are involved in the disease process including the synovium, capsule, bone, cartilage and peripheral and central nervous systems
- The outcome of OA symptoms is a combination of nociceptive, neurogenic and neuropathic pain
- 25 per cent of people with radiographic joint damage do not report pain, which may be postulated as due to psychosocial adjustment
- Severity of pain differs by diagnosis and is not related to the degree of tissue damage indicating differing pain thresholds
- 25 per cent of people with knee pain do not have evidence of OA or joint damage, so maybe damage causing pain is elsewhere in the body (e.g. referred pain phenomenon)
- Do people with single joint versus multi joint arthritis have the same origins of pain?
- What other factors influence pain, for example physical environment (pollution, rural/urban settings), culture, personality traits like stoicism, gender differences, etc.?
- Can pain be caused by environmental and/or genetic factors? For example, RA is an industrial revolution disease without historical evidence of inflammatory arthritis before the 17th century. Why? Also, hip and knee inflammation is rare in China. Maybe there is a geographical correlation in which joint is affected. Lastly, there is evidence of high/low incidence of OA in different joints in different countries.

- Pain is subjective
- Muscular dystrophy patients experience little pain, which begs the question of why some muscular or chronic disabling conditions cause pain and others do not

c) Gaps and weaknesses in current research

- Historically, research priorities for pain have been lacking because pain has been viewed as secondary to another disorder
- It is not known whether joint pain is an inflammatory or a neuropathic pain, or a different type of pain altogether
- It is not known whether the pain of OA begins as a type of nociceptive pain that eventually resolves into a neuropathic pain due to mechanical destabilization of the joint
- Some patients are told that pain comes with joint damage, a potentially demoralizing comment and the result of not recognizing pain as separate from the underlying cause
- There is no explanation for discontinuity between structural damage and pain
- Although bone is known to be well innervated, it remains unclear if the innervation is linked to pain mechanisms
- Assessment tools of pain are not uniform from one health care site to another
- There is a lack of understanding of how the pain experience can be so variable from one person to another
- How much do medications lead to chronic pain?
- OA pain is a multi-factorial, bio-psychosocial disorder
- There is a lack of understanding about the influence of the physical environment on chronic pain or joint disease, including barometric pressure, general weather conditions, pollution, toxic chemicals, geographical region, etc.
- How does culture affect pain perception and the burden of chronic pain?
- What is the causal relationship of pain versus fatigue? In OA, fatigue remains even when pain is treated- does fatigue remain after joint replacement?
- Is there a role for microglia in the spinal cord in the pain of joint disease?
- Do peripherally-released inflammatory mediators cross the blood-brain barrier to alter pain processing mechanisms in the central nervous system?
- What is the relationship between physical activity and pain? Sport and exercise can cause some pain; by persisting with exercise would the pain be worse? Why does movement/exercise relieve pain and stiffness, and how?
- There is a lack of differentiation between pain and stiffness and the ability to move and perform tasks/activities
- What is the mechanism of pain relief? Several suggestions have been offered; is there evidence that they relieve chronic pain? For example, keeping active, manual therapy, cognitive-behavioral therapy, imagery/relaxation, self-hypnosis, etc.

- The holistic approach to investigating the origin of pain should be appropriately studied – including all forms of relief (drugs, self management, rehabilitation, alternative approaches and traditional healing)
- Which tissues are involved in pain?
- Clinically, no one drug works well, so poly-pharmacology should be considered– i.e. complex, multiple mechanisms need multiple approaches using a variety of drugs
- Pharmacological research needs a tissue target; knowing it will help a specific population
- There is a need to stratify populations to determine what works for whom based on their origin of pain

d) Short and long term goals for future research

- Pain needs to be seen as a disorder unto itself, divorced from an underlying cause
- Greater understanding of the origin of pain is needed as this may lead to the development of novel drugs or other therapeutic approaches to joint pain, increasing the effectiveness of treatment
- The placebo effect suggests differences in pain perception and needs to be explored for possible novel approaches to pain management
- Besides the medical approach to pain management, there are coping strategies that help to improve quality of life and functional state, and research and knowledge translation on these strategies are needed
- Early-stage joint pain may differ from joint pain at later stages. There is a need to begin to understand the nature of the pain at these different stages, as the approaches to pain management may be different for each
- There is a need to understand:
 - changes that are occurring in peripheral sensory fibres, in the spinal cord and in brain structures in animal models of joint disease
 - differences in inflammatory joint disease vs. OA models to compare the differences and similarities of the respective types of pain
 - the possible role of adhesion molecules in the etiology of joint pain
 - the role of peripheral nerve endings in pain from the joint
 - the relationship to joint pain of the cysts that appear in subchondral bone diseased OA joints
 - the role of the fat pad in the cause of pain in healthy progression vs. disease progression of the joint
- There is a need to determine whether the pain in animal models of joint disease is due to sensitization of peripheral nerve terminals, to recruitment of additional nerve fibres or to a change in phenotype of these fibres
- Some evidence exists that cytokines are involved in the pain of joint disease, but it needs to be determined whether these cytokines are producing the pain at a peripheral site of action or in the spinal cord

- There is a need to define the different roles of detection vs. perception of pain, and to develop methods to address both
- There is a need to know:
 - if structural changes in subchondral bone lead to joint pain; in some cases drilling holes in subchondral bone has reduced the severity of the pain
 - how much do changes in mechanical loading lead to structural changes and could these, in turn, lead to pain?
 - whether changes in the circulation or the microcirculation are a source of pain
 - whether the pain arises from soft tissue that is damaged by structural changes in bone
 - how to translate data from animal models to innovative approaches to the management of joint pain in humans
 - if the right measurements of pain in animal models are being used
 - the possible role of the joint capsule, which has been largely ignored in animal studies, but may yield important information regarding pain from the diseased joint
- Information is needed about nociceptive characteristics in the joint, responses to specific inflammation-related cytokines in animals and the effects of peripherally-released cytokines on central pain mechanisms
- There is a need to relate joint pain to subchondral bone changes and new imaging findings to the clinical experience and to structural changes
- There is conflicting evidence regarding exercise; we need to define what is meant by exercise, to understand which types of exercise are beneficial and which are harmful
- We need to identify the genes that are related to joint disease and to joint pain
- We need to identify the specific types of nerve fibres innervating the various components of the joint and how these may undergo changes in the diseased joint
- Longitudinal studies should be conducted to follow people's experience of pain and response to pain treatment
- Investigate genetic predisposition and biologic markers
- What are the common mechanisms across types of arthritis and across people (genetic expression)
- What are the commonalities and differences at various stages of disease?
- There is a lack of information about pain in the elderly; not much is known about its origin, or even how to measure this pain

e) How does CAN facilitate achieving the short and long term goals in arthritis pain research?

- The European Chapters of the International Association for the Study of Pain have asked the European Parliament to pass legislation declaring pain a disease. CAN should endorse this concept and take a leadership role in disseminating this view of pain.
- Build capacity in the field of joint pain through specifically-directed traineeships (for all levels of students).

- Foster translation and uptake of knowledge by all healthcare providers that the chronic pain patient has a complexity of symptoms and that a simplistic approach that treats single clinical entities does not constitute maximally effective treatment of the patient.
- It has been proven that quality of life and functional measurements are improved when chronic pain sufferers participate in the management of their pain. Research is needed to define how best to achieve an optimal level of patient involvement and to develop the tools with which to equip the patient.
- It has been suggested that the first biomarker of OA is pain. Early, longitudinal, multidisciplinary studies are needed to trace the time course of development of various different factors in the progression of joint disease to determine the earliest biomarker. The patient and/or the specialist need to be taught to recognize the implications of the first signs of pain. If the earliest pain is more amenable to treatment, and if the earliest pain can evolve into neuropathic pain that is much more refractory to treatment, how do we translate the concept that the earliest pain should be treated by a pain specialist to avoid development into these more refractory types of pain?
- Identify risk factors for joint disease and develop methods to treat at the earliest stages, possibly before the onset of clinical signs.
- Organize additional discussion platforms where the various stakeholders are brought together to address issues related to the pain of joint disease.
- Continue workshops focused on topics to brainstorm directions that include multiple perspectives (researcher, industry, consumers); for example, each of the five questions outlined in this paper could be a workshop.
- Prioritize topics and research questions generated at this workshop, organize them into key themes and work towards consensus on the most important topics.
- Bring stakeholders together to determine their tolerance to various treatments and their limitations.
- Avoid redundancy with other organizations and identify which area is lacking with short and long term opportunities to make progress in the care and management of pain.
- Train researchers and influence educational programs to encourage better treatment.

Question 2. Is there a better way of measuring and defining joint pain scientifically and clinically?

a) Individual perspectives on the question

- Current clinical assessment of pain is too subjective
- Patients must be provided with descriptors for ownership and use
- Presently, the answer to questions largely depends on the context of measurement – i.e. clinic vs. trial vs. observational studies

- There is a need to move away from the perspective of a homogenous population of patients. There are many subgroups that need to be identified and characterized
- There is a need to correlate physiological and imaging data with subjective measurements
- Longitudinal studies are required
- Encourage the use of existing pain assessment tools using valid and reliable measures, and promote the standardization of these assessment approaches in arthritis clinical settings

b) Group's current knowledge

- There are tools to measure pain, but there is not a high degree of confidence in them and a lack of clarity regarding which are the best to use in different situations
- There is an international initiative underway that is aimed at developing new measures of pain in OA
- There is considerable knowledge regarding animal models of pain, but a dearth of knowledge regarding whether this translates in humans and how this happens
- New methods for testing pain in animals need to be developed that include consideration of
 - placement pressure
 - vocalization
 - imaging soft tissue
 - novel methods of brain imaging to indirectly correlate with other, i.e. direct, measurements
- Measure blood flow in the joint, in the brain, and in the subchondral bone; do these correlate with pain level? Subchondral bone blood flow relates to the hypothesis that pain arises due to an increase in intra-osseous pressure

c) Gaps and weaknesses in current research

- Most current clinical pain assessments are subjective and don't account for what is important to people with arthritis. Patient input is vital, as currently the clinician/researcher decides what to measure without consideration of the patient's opinion on what affects him/her the most
- People are different and they feel things differently, so it is difficult to obtain any objective measurement
- Pain measurements don't usually measure quality of life, level of activity, or consider the context of the person's life
- There appears to be a lack of integration of pain specialists and a missing pain curriculum to train arthritis health professionals
- Chronic pain and acute pain are two different experiences involving different sensations, different mechanisms and different outcomes
- Need innovative testing paradigms
- Need to explore vocalization as a measure of pain in animals

d) Short and long term goals for future research

- Define subgroups within disease populations (using tissue banks, histopathology, genetics, clinical characteristics, etc.) which should improve classification by diagnosis, prognosis and response to interventions, while also taking into account racial/ethnic variability and culture
- Standardize data collection criteria for clinical studies/practice to develop and test “objective” measures of pain, although the nature of such measurements has yet to be identified. Options include functional MRI, evoked potentials and muscle hypersensitivity
- Determine how well side effects are assessed and the downside of various therapeutic interventions to balance assessment of efficacy (pain relief)
- Develop the following:
 - imaging approaches to diagnose earlier and match imaging measurements with development of pain
 - assessment tools for different cultural groups as their pain reports differ
 - early biomarkers that predict impending development of pain
- Understand the basis of differences in pain threshold between genders and children vs. adults

e) How does CAN facilitate achieving the short and long term goals in arthritis pain research?

- Support research to define subgroups within disease populations
- Support longitudinal studies of pain
- Encourage assessment of pain using valid and reliable measures in the arthritis clinic setting and emphasize the need for repeat assessments using the same tools over a follow-up period
- Prepare a RFA that supports multidisciplinary research on pain measurement
- Bring stakeholders together to determine tolerance to various treatments and their limitations

Question 3. What could be useful new targets to treat arthritis pain?**a) Individual perspectives on the question**

- Separate RA & OA because with different aetiologies, they will have different targets
- Divide pain into chronic and acute phases and examine the difference in pain perception and threshold between these pain states
- The perception of pain changes with time since the sufferer is better able to cope with it
- Case Study Patient 1: began with NSAIDs, then Celebrex, was monitored for cardiovascular complications, tried massage and exercise and noted that the basal pain

was okay, but became progressively worse during flare-ups, some pain relief was experienced by meditation, hypnosis etc., the best treatment: taking control of one's own life, including lots of exercise and a good diet

- Case Study Patient 2: In the 1980s tried alternative medicines, but had no observable improvement, tried Bextra and loved it, Robacox worked too, but Celebrex didn't work, fatigue was a huge problem as living with pain is tiring, can't sleep well, the pain is worse with inactivity, support groups very helpful as they teach other coping mechanisms and interaction with others who are in the same or worse situation is comforting, glucosamine treatment seemed to improve stiffness of joints, ultrasound treatment improved muscle systems, hypnosis and acupuncture worked temporarily (if you stop regular treatments, no pain relief), chiropractic approaches were not effective and hurt a lot of people, best treatment was the use of opiates
- Fatigue would likely be improved if pain was alleviated
- What about non-neuronal cell involvement in pain perception? (Glia in spine and brain contribute to pain perception)
- Input from consumers is pivotal to identify what symptoms or outcomes to target for therapeutic intervention. There is a need to identify the symptoms and to take into account the full spectrum of symptoms, likely need to include fatigue and mood as being central issues

b) Group's current knowledge

- RA is a systemic disease with severe inflammation of the synovial membrane (cardiovascular and renal complications occur in addition to joint pain).
- OA is not usually complicated by cardiovascular or renal problems, may only involve one joint (although contralateral joints might be affected by gait or compensation, but not by the disease itself). Inflammation is mild and generally secondary.
- Treatment for OA pain: opiates, Celebrex
- Known treatments: viscosupplements (e.g. hyaluronic acid), peptide antagonists for intra-articular injection are in clinical trials, NSAIDs, COX-2 inhibitors, opiates, alternative therapies (e.g. massage), intra-articular saline seems to work (temporarily) for pain relief
- There are multiple pathways and mechanisms that are known. There are many effective therapies but none in all subgroups of patients.
- People with arthritis and their physicians have misperceptions regarding the risks and benefits (tolerance, safety, etc.) of pain medications. A large placebo treatment response exists in people with arthritis (~30 per cent) and it is not properly appreciated. Most importantly, communications between patients and their caregivers is not believed to be effective as visits are too short and infrequent.

c) Gaps and weaknesses in current research

- What are the consequences of removing bone in joint replacement? How true is it that patients do not experience pain after joint replacement?
- Could there be a chemical reason for fatigue? Is it stress-related? Though poor sleep could contribute, it's more than just a "bad night's sleep"
- Why aren't MMP inhibitors tested?
- Why do OA drugs target the knee? What about other joints (fingers, hip, shoulder, etc.)
- What about Botox therapy?
- How significant are clinical outcomes? How effective is pain relief and are proper measurements being utilized?
- What about the models we are currently using in academia and industry?
- What about effects on oedema and blood vessels?
- What about the effects of ultrasound or shock-wave therapy? Does shock-wave therapy mechanically stimulate tissues to activate endogenous opioid release?
- Effects of anti-depressants on pain: could we use these in combination therapies with other treatments, being aware that there are dangers to using anti-anxiety or anti-depressant drugs – namely suicide, etc.
- Effective tools are lacking to preemptively identify "responders" to various pain therapies and there is a lack of learning from patients' responses to various therapies.
- Many routine medications lack known mechanisms of action and there is no full understanding of pain's origin and peripheral versus central pain.
- The development of new targets is hindered by the lack of precise measures.
- The role of combination therapies is not considered (i.e. pain therapies plus a disease-modifying agent)

d) Short and long term goals for future research

- Examine the following:
 - the involvement of glial cells in pain perception
 - chondroprotective agents (in addition to glucosamine & hyaluronic acid)
 - pain sensation and the pathology of the disease
 - the feasibility of local therapies (as OA is mainly a local disease)
- What about preventing local excitability changes of nerves, which may in turn affect central excitability?
- What about looking into therapies for other joints that are not as easy to access as the knee, such as the shoulder, hip, etc.?
- Stop cell death in spinal cord (spinal cell death occurs as a result of chronic stimulation of nerves in OA; could inhibitory interneurons be dying?)
- Patient #2 described opiates as the best therapy. Can better, non-addictive opiates be developed? Currently, addictive effects can't be avoided (i.e. the property allowing

morphine's good effects also confers a bad side effect). What about local administration of opiates? Could this diminish negative side effects?

- What about tapping into the endogenous cannabinoid system? What is its interaction with the endogenous opioid system? How does pain alter the set points of the endogenous opioid/cannabinoid system? Why is the endogenous painkiller system failing?
- What about stress and emotional effects (glucocorticoids, etc) and how do they affect the immune system, inflammatory response, or perception of pain?
- What about the balance of pro- and anti-inflammatory factors in chronic conditions?
- What about factors that normally affect central neural processes? Could they have peripheral effects?
- What about the effects of diet? What is the omega-3 versus omega-6 fatty acid balance and how could these affect inflammatory responses? Dietary factors seem very important and these effects are not currently explained, but it seems that there is a great potential here for improvement of OA
- Are the current pain drugs disease-modifying?
- Develop and test new measures of pain
- Develop and validate animal models for various new targets
- Explore the role for biologics in OA
- Improve the safety of COX-2 inhibitors
- Find targets for fatigue and sleep

e) How does CAN facilitate achieving the short and long term goals in arthritis pain research?

- Continue facilitating pain workshops (e.g. bi-annually)
- Involve all stakeholders to address a specific question on pain
- Improve/facilitate contractual agreements between industry, basic scientists and clinicians
- Provide financial support for testing of new targets
- Maintain a databank of consumers willing to participate in studies of new targets and indicate the level of risk to which they are willing to be exposed
- Promote research on arthritic pain

Question 4: What alternative, non-pharmacological treatments could be used to effectively treat arthritis pain?

a) Individual perspectives on the question

- More research in this area is required
- Industry's involvement in this area is encouraged although their current focus seems only drug related, rather than being sensitive to the needs of the patient and which populations benefit from which medications

- Would be beneficial to have government involved as industry is subject to government regulation as well
- Culture/ethnicity should be considered
- Study the combined use of treatments (mainstream, alternative therapy and pharmacology), for example, how was arthritis treated before pharmacological treatments, as in First Nations groups?
- Interdisciplinary partnerships based on mutual interest need to be developed
- Natural treatment regulation is needed by the Marketed Health Products Directorate and Therapeutic Products Directorate, (for example Devils claw – used by many and regulated)
- Non-pharmacological view is also required – not just the pill but a holistic approach to treatment and one that includes alternative therapies in clinical trials (for example with a spirituality component such as at the Alex Seniors Community Health Centre where spiritual leaders participate in the overall treatment plan, massage, etc). Some non-pharmacological options have only weak evidence of efficacy but patients are using them so further study is required. Also consider diet, acupuncture, chiropractic and exercise treatments.
- An individual intervention may not work as well as a multi-disciplinary approach, which could push the effect size even higher
- Obesity drug studies are not acceptable for the formulary without a full plan. A mindset change of the government is required about arthritis drugs to use a similar model.
- Adolescents stop taking drugs due to their side effects and then fail to inform their physicians
- 70-80 per cent of patients use treatments without consulting their physicians, which can lead to problems
- Cost is an issue for patients. Some patients are spending considerable amounts for herbal remedies even though they are unsure of the quality of these products
- A universal language is required for everyone
- There is a lack of knowledge about the safety of these products, for example, whether negative drug interactions occur

b) Group's current knowledge

- Double dosing
- Knowledge on drug interactions will never be complete but progress has been made
- There is a question of whether or not physicians should supply patients with information when they are “prescribed” natural medications? It sometimes happens that these off the shelf products lack information
- Knowledge is lacking about precise dosage, validity, and safety of natural products
- National Health Products Directorate (NHPD, part of Health Canada) regulates natural health products for sale in Canada

- Naturopaths provide services under the Drugless Practitioners Act (DPA), but are not regulated by the Regulated Health Professional Act (RHPA) like all other primary healthcare professionals (RHPA assures educational, training and practice standards)
- There is no common language; for example, what is a non-pharmacological drug? Is glucosamine included? Complimentary and Alternative Medicine (CAM) is not taught in regular medical schools; there is not even a standard for CAM
- Some consumers feel that physicians can be resistant to them deciding on their own treatment, when they are simply trying to take ownership of their own health
- Knowledge is lacking about safety and about physical and emotional interventions
- There are no systematic exercise trials, but guidelines around exercise are being developed. There is a lack of synchronicity between exercise and medications – pain is stopping exercise
- A cultural change is required; for example, consumers need to understand that the injection is not the goal, rather the goal is to facilitate function. This is also true from a system level standpoint, e.g. with cuts to physiotherapy
- A multi-disciplinary approach to pain is needed as it seems better to combine approaches; for example a physical therapist and a rheumatologist working together
- A very high percentage of arthritis pain sufferers seek out alternative therapies: occupational therapy, hypnosis, yoga/meditation (e.g. 'glanding' to target specific organs to release endorphins, etc.), group therapy (sharing fears, effective approaches and asserting the knowledge that you are not alone), aromatherapy, describing pain in a non-emotional way (thinking of pain as a shape or a form), music therapy, laughter, having a pet, saltwater, cold/hot pools, mixtures of herbs and spices, or snakes, tree bark, etc. to relieve pain (India and China)
- Maybe joint laxity or changes in synovial fluid are responsible for joint pain or stiffness once you start moving

c) Gaps and weaknesses in current research

- The best model for treatment and for access to treatment is unknown
- Knowledge is lacking about exercise: what works and how do patients access resources (groups, pools, supervised programs, etc.)?
- Ineffective knowledge translation is a problem: for example research findings do not reach the consumer
- The best time to intervene is unknown
- There is no trust between alternative/complementary and traditional medicine. Alternative/complementary medicine is approached by attempts to refute the results rather than show how it works, a more open mind is required
- There is a lack of research on proliferation therapy (e.g. regeneration injection therapy – injecting solutions into the joints to induce brief inflammation and thus the growth factors – which reconstructs the cartilage)

- Proper evaluation is needed (e.g. prolotherapy?)
- The outcomes currently measured are poor and should include other important outcomes, such as how the patient feels
- There is a lack of study about counter-indications between CAM and traditional medications
- There is a lack of consideration of emotional aspects of illness and the power of hope, etc., to transform the way we feel
- How does industry approach/standardize non-pharmacology and CAM? Does there need to be a new approach?
- There needs to be a qualitative approach that better understands the patients' experiences
- There are a huge number of interventions available
- The quality of research is poor, as is the quality of reporting
- Improvements are required to conduct these trials and how results are published
- Need to undertake prevention to understand what is preventative (e.g. is diet important?)
- Comparative trials are required to evaluate efficacy and cost-effectiveness
- There is a need to know what therapies/remedies work
- Assessment: we need to look at other things, such as function and quality of life; if people can participate in their lives then although pain may not be reduced it could become less important
- Focus on outcomes other than pain
- Observational studies
- How does diet play a role in altering pain states?
- The lack of clear regulation for alternative medicines and approaches is of grave concern
- The effectiveness of alternative therapies, in conjunction with pharmacological approaches, should be examined as there lacks robust science behind these therapies
- How can we tap into the body's natural pain-killing system (e.g. yoga, meditation)?
- What types and levels of exercise are helpful (mild or moderate)? Physiotherapists need to better advise individuals on their personal requirements
- Massage therapy (e.g. depth of pressure varies with each individual)

d) Short and long term goals for future research

Short term:

- Determine the current status of the evidence via a systematic review in both academic settings and in practice (community-based)
- CAN should provide research funding of a broad research program and facilitate information gathering and dissemination
- Political backing – we need to study this at the government level and it requires support from government (for example, the Canadian Institutes of Health Research (CIHR))
- Patient involvement

- Develop a common language (sometimes called companion, or PPP) through CAN bringing together a multi-disciplinary group to talk about what this encompasses, whether it means a consensus meeting and/or a position paper
- Summarize the evidence; doing so will demonstrate the gaps, weaknesses, and required areas of focus
- CAN should hold a request for applications (RFA) and partner with other organizations such as CIHR and the pharmaceutical industry to support health systems research
- A reliable source needs to develop outreach tools and information for exercise guidelines, etc.
- CAN should provide research findings in lay language to enable knowledge translation and exchange
- Facilitate research use for care and advocacy
- Recognize that findings will have different uses between different cultural groups
- Increase the amount of qualitative research being done, for example, use existing health surveys to generate more information about health seeking behaviour
- Pain management to be a core interdisciplinary component of the medical and allied health professions school curriculum

Long term:

- Health systems research should be supported
- Develop approaches that aren't too specific – each age group or mobility group would have different access.
- Develop better knowledge translation and exchange strategies, for example, working in collaboration with funding agencies and interest groups (consumers and healthcare professionals) to ensure knowledge is disseminated to receptor groups
- Provide support and facilitate the education of pain for inter-disciplinary teaching in all health care. Fund the development of teaching materials and programs to ensure pain is part of the medical and allied health education curriculum.
- Use the CAN Annual Scientific Conference to invite international speakers to educate CAN researchers and consumers on what has worked
- Work to change the regulatory process, enabling more industry involvement with government representation present
- Develop a database of what alternative therapies people are using/have used
- Study how weather (cold or humidity) affects OA pain; maybe a change in synovial fluid is responsible (synovial fluid viscosity)

e) How does CAN facilitate achieving the short and long term goals in arthritis pain research?

- Seek out new individuals (clinicians, researchers, industry reps) who are not CAN members
- Encourage and advocate for self-help groups

- Alternative/non-pharmacological treatments to pain relief:
 - request and maintain a database detailing alternative approaches to pain relief experienced by patients
 - educate patients about some of the potential hazards of non-pharmacological treatments
 - demand increased scientific rigour regarding these therapies

Question 5: How can we better manage the psychosocial consequences of chronic joint pain and fatigue?

a) Individual perspectives on the question

- Chronic pain has different consequences for individuals at different points in their lives
- Pain is a very personal, individualized experience. How can treatment of individuals be improved in the current system?
- Psychosocial issues begin at the onset of illness and need to be addressed from the beginning. They are often left unaddressed due to lack of time (on the part of health care providers)
- Short term immediate issues include anger, stress and dealing with the real pain. There are also long term consequences, such as significant depression
- There is a societal responsibility for pain and pain management, due to the socioeconomic impact of pain and the provision of health care services, yet the responsibility is often left to the individual
- Knowledge translation about chronic pain and how to manage it effectively is a huge issue. Effort should be expended on getting the best information to those who need it. Education (as currently conceived) may not be the best method; researchers need to more effectively translate knowledge into the hands of the consumer, the public and health care providers
- Consumers receive conflicting information from different sources and require a consistent message based on knowledge of the disease and its progression; they want to be provided with an idea of what to expect. How can knowledge be translated broadly beyond relying on computers? What are some better mechanisms?
- How effective are psychosocial interventions for managing pain? How can this information be shared with the public and the health care community? Physicians do not have resources to deal with psychosocial issues, and availability of services is poor
- Why are there no immediate responses to arthritis as opposed to other life-altering diseases such as cancer? There is a real disconnect as arthritis is seen as a chronic problem rather than a disease that kills
- What can be done for people in extreme pain waiting for surgery? If alternative ways to manage pain are offered, it would likely discourage individuals from taking unnecessary medication while waiting for surgery as their health declines

- Consumers need to know more about the research around the origin of pain and fatigue as these are both very real
- There needs to be an adjustment of work and day schedules to deal with pain and fatigue. Changing lifestyle is easy to say and hard to do
- Resources are required for patients and health professionals to facilitate adjustment
- There needs to be methods to facilitate communication with teachers, coaches and parents so that children living with pain get the necessary support to enable schooling and activities
- Ethnic and culturally sensitive services are lacking for patients

b) Group's current knowledge

- Arthritis is life-altering and long term
- Arthritis pain has psychosocial consequences and is a burden to individuals, families and society through the cost of treatment, lost employment, decreased productivity, decreased enjoyment and quality of life, etc. Awareness of arthritis pain, psychosocial issues/problems and interventions is low
- Psychosocial issues are partly addressed in current outcomes and outcome measures (e.g., psychosocial factors may be part of quality of life measures) but this is likely inadequate. There are some data on psychosocial outcomes of arthritis pain interventions, but more can be gathered
- The psychosocial consequences of chronic joint pain and fatigue include: poor sleep, anxiety, short attention span, depression, poor peer relations, poor self esteem, lost productivity, diminished (impaired, reduced?) sexuality, poor body image, grieving, loss of sense of being "normal", sense of guilt, work stress, and negative economic impact
- Psychosocial support and psychologists' interventions can be helpful in dealing with the consequences of depression, anxiety, and pain perception
- From a patient's perspective, the current treatments aimed at breaking the psychophysical cycle of pain are poor
- There is uncertainty about the current social support models for arthritis related disability
- The economic impact of modified duties is not well-known
- There is a huge problem with getting help and the provincial jurisdiction for health is just part of the explanation for this. Lack of awareness (patients and providers), lack of local resources, and other factors contribute to the disparity
- Good descriptions exist of how pain stops, reduces or changes people's ability to do what they need and want to do, such as participating in work, play, school, social relationships, etc.
- Some exemplary, interdisciplinary clinical programs are known, but there is a lack of access for the majority of people who need care (for their chronic pain)
- Peer support is effective for pain and fatigue and social science has chronicled this in literature

c) Gaps and weaknesses in current research

- There is a lack of longitudinal studies. Natural history/illness trajectory studies that include analysis of long term effect and the long term benefits of intervention are needed
- Better, more adequate measures of psychosocial impact are required for both research and use in clinical practice. The feasibility of measures varies for research compared to practice settings (for example, short, widely applicable measures are required in practice)
- Inter-professional education and models of care need to be developed and evaluated. There is a perceived need to research the effectiveness of these programs
- There is a need for innovative methodologies to study the problem and understand the cause (i.e. move beyond the biomedical model: e.g., the question “how can I be like other children” is more important than which drugs are available)
- More training opportunities for health professionals are required to learn about pain and its management, or to infiltrate the pain agenda into existing programs for health professionals and researchers
- Where do psychosocial issues fit in the causal pathway between diagnosis and societal outcomes? Do psychosocial problems lead to disability or does disability lead to psychosocial problems? There is a poor association between psychosocial factors and the physical manifestations, plus there is poor communication about the importance of psychosocial care. This leads to difficulties in accessing psychosocial care. This type of care is usually poorly funded and has a long wait time
- There is weak legislation to support people in dealing with psychosocial stress and mandating employers to provide flexible working conditions
- Arthritis has not been taken seriously by the general public
- Cognitive biofeedback therapy and mind/body therapies work, but their mechanism is unknown
- There is a gap between research and policy, family education, relationship management and physical intimacy
- Management of psychosocial consequences is poorly studied, including:
 - timing of treatment and how much to give to which group
 - who should provide the treatment? Coaches vs. health care providers vs. lay community health workers, peer support vs. facilitators in the reserve
 - do outcomes reflect the reality?
- Problems in practice:
 - physicians don’t usually ask about anxiety and depression
 - system issues, for example in some provinces such as Alberta, physicians can only bill for one issue each visit so patients are treated by their body parts
- A strategy is lacking to enable care for the homeless population with arthritis and provide access to care

- 21 per cent of children with chronic pain go to school. How do we teach children to communicate with teachers, coaches and parents so that they can get the special assistance they need to enable schooling and associated activities?

d) Short and long term goals for future research

- Add psychosocial outcomes to clinical trials
- Develop appropriate outcomes to capture effectiveness
- Expand and improve psychosocial outcome measures as many psychosocial domains have not been adequately addressed
- Promote innovative methodology to include consumers/clients, clinicians, researchers (from basic health services, economists and behavioral scientists). Listen more closely to what each group thinks is relevant to measures and treat accordingly. Incorporate multiple methods into study design including, but not limited to, longitudinal, qualitative, and experimental
- Conduct epidemiological studies on impact of arthritis pain on psychosocial aspects and link to costs for the individual and society (lost jobs, lost taxes, etc.)
- How does pain interact with other symptoms? Is its definition too simplistic? Pain intensity must be measured more than on a 1-10 scale
- Does measuring pain and the implications of pain influence treatment decisions? If so, in what ways?
- Move research measures into one that is clinically feasible and captures the pain experience
- Rather than pain, measure “Are you doing what you need and want to do in life?”
- Study changes in pain and outcomes over time, in children, families and adults
- How do we teach people to advocate for change, to improve the study of chronic pain, as well as the treatment/management of pain? Advocate to policy makers, educators, corporate sponsors, etc.
- Develop and evaluate strategies to prevent the psychosocial consequences of pain that affect adults and children
- Develop a media campaign to increase visibility of the psychosocial impact of arthritis and the scope of the impact, to:
 - change the perception that arthritis is an old person’s disease
 - inform the public that young people and children with arthritis have different issues from adults with arthritis
- Develop strategies to educate general practitioners and other health professionals, also include teachers, exercise therapists and personal trainers

e) How does CAN facilitate achieving the short and long term goals in arthritis pain research?

- Summarize all research goals from this workshop, align into themes, determine what resonates across the areas and participants, and set priorities.
- Work towards a centralized source of quality information available to all (public, including patients, researchers and health care providers).
- Fund or leverage funds for novel pain research.
- Facilitate the formation of teams to obtain research funds.
- Sponsor and deliver a knowledge translation plan (for example, develop factual “one-pagers” for broad distribution).
- Facilitate the development of a media campaign by holding a competition in college and university business and MBA programs, and as part of the campaign include a myth buster portion
- Partner with industry to raise the profile of arthritis
- Develop position papers for government and policymakers
- Invite key people like general practitioners, psychologists, psychiatrists and social workers to future CAN meetings to give their perspectives
- Facilitate the development of a youth initiative during arthritis awareness month (September)

APPENDIX B – FURTHER READING

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