Current and future treatment of OA worldwide, with an update on the OARSI guidelines

The incidence of osteoarthritis (OA) has been increasing on a global scale. Research is under way to elucidate its causes and pathology; however, no fundamental treatment methods have been established. This roundtable discussion involved leading physicians from the USA, the UK, and Japan, who talked frankly about the current status of and outlook for OA treatment from their respective viewpoints. Their discussion identified similarities and differences between the countries and proved to be a valuable opportunity for building international consensus on OA treatment.

Response to the OARSI guidelines

Kawaguchi: Today we would like to discuss the current status and future of osteoarthritis (OA) treatment in the world. Following last year's release of the OARSI guideline for the management of hip and knee arthritis (**Table**), OARSI have been actively disseminating the information worldwide. George, would you please tell us the response to the OARSI guideline during its first year after publication?

Nuki: I think that it is true to say that the guideline has been widely read and acclaimed. Records show that the guideline has been the article most frequently downloaded from *Osteoarthritis and Cartilage* (*O&C*)[1,2] in the last 12 months. It has also stimulated e-mail correspondence, questions and criticisms. Some of these have been published, with responses in *O&C*. There has also been a lot of interest in translating and adapting the guideline for use in different countries. The first initiative in this regard came from a committee of the French Society of Rheumatology, which has modified and adapted the guideline for use in French-speaking countries. The French document included a verbatim translation of the 25 published OARSI recommendations, as well as a commentary on them indicating where the adapted guidelines differed from the original OARSI publication. I understand that these actions have been very well received in the French rheumatologic community. As you will know, a committee of the Japanese Orthopaedic Association (JOA) is currently working to translate the OARSI guidelines into Japanese and to adapt them for use in Japan. There has also been some interest in translating the guideline into Portuguese for use in Portuguese-speaking countries (Portugal and Brazil).

Abramson: I agree that we have seen a very positive response and enthusiastic endorsement of the guidelines by experts. They are certainly the most up-to-date, comprehensive, and thorough guidelines on OA and other professional organizations are adopting portions of them for their own societies. In particular in the USA the American Academy of Orthopaedic Surgeons (AAOS) and American College of Rheumatology (ACR) are using the principles represented in the OARSI guidelines as the basis of many of their new sets of recommendations. So I think that the guidelines will be used "stand alone" as originally published, modified by national societies, or used as core information for other guidelines that are developed by societies that have slightly different perspectives, for example the surgical perspective. The challenges that we will have to face include not only dissemination of the guidelines, but also, because they are comprehensive, they are presented in great detail, so we want to produce them in a more reader-friendly format especially for primary care physicians and ultimately for patients. Also following their dissemination, we want to judge whether the recommendations are actually being used to provide good-quality care.

Future development of the OARSI guidelines

Kawaguchi: The published guideline was based on a systematic review of the literature up to January 2006; however, since then a large number of studies have been published and new evidence emerging between 2006 and 2008 has been included in the updated version and was presented at the 2008 OARSI congress. Please could you give us a brief summary of the principal changes that have been made to the guideline in light of more recent evidence?

Nuki: Our literature search of articles published between January 2006 and January 2008 revealed that 57 systematic reviews, 200 randomized control trials (RCTs), and 16 economic evaluations have been conducted and these data are currently being systematically reviewed by OARSI. The most important point to stress is that the core modalities of therapy recommended remain unchanged after addition of the recent research evidence. Not surprisingly, however, the effect sizes for pain relief for a number of modalities of treatment did change when the more recent evidence from meta-analyses and RCTs was included. These findings will be presented at the 2008 ACR meeting

1) OARSI recommendations for the management of hip and knee osteoarthritis, Part I: critical appraisal of existing treatment guidelines and systematic review of current research evidence. *Osteoarthritis and Cartilage* 2007, 15: 981-1000.

2) OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis and Cartilage* 2008, 16: 137-162.

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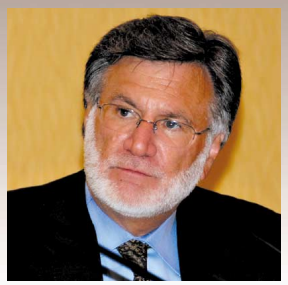
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in San Francisco and subsequently published in *O&C*; a summary is presented in the **Box**.

Kawaguchi: If a further Delphi exercise were to be undertaken, would any of the 25 recommendations in part 2 be changed after adding the new evidence over the last 2 years?

Nuki: From the analysis of the research evidence 2006-2008 that we have seen to date Rollie Moskowitz, Weiya Zhang, and I do not feel that there is any immediate need to make changes to

Table: OARSI recommendations for the management of knee and hip osteoarthritis
[2] *Osteoarthritis and Cartilage* 2008, 16: 137-162.

Proposition	Levels of evidence	Strength of recommendation (%) (95%CI)
General		
1 Optimal management of OA requires a combination of non-pharmacological and pharmacological modalities.	IV	96 (93-99)
Non-pharmacological modalities of treatment		
2 All patients with hip and knee OA should be given information access and education about the objectives of treatment and the importance of changes in lifestyle, exercise, pacing of activities, weight reduction, and other measures to unload the damaged joint(s). The initial focus should be on self-help and patient-driven treatments rather than on passive therapies delivered by health professionals. Subsequently emphasis should be placed on encouraging adherence to the regimen of non-pharmacological therapy.	Ia (education) IV (adherence)	97 (95-99)
3 The clinical status of patients with hip or knee OA can be improved if patients are contacted regularly by phone.	Ia	66 (57-75)
4 Patients with symptomatic hip and knee OA may benefit from referral to a physical therapist for evaluation and instruction in appropriate exercises to reduce pain and improve functional capacity. This evaluation may result in provision of assistive devices such as canes and walkers, as appropriate.	IV	89 (82-96)
5 Patients with hip and knee OA should be encouraged to undertake, and continue to undertake, regular aerobic, muscle strengthening and range of motion exercises. For patients with symptomatic hip OA, exercises in water can be effective.	Ia (knee) IV (hip) Ib (hip, water-based)	96 (93-99)
6 Patients with hip and knee OA, who are overweight, should be encouraged to lose weight and maintain their weight at a lower level.	Ia	96 (92-100)
7 Walking aids can reduce pain in patients with hip and knee OA. Patients should be given instruction in the optimal use of a cane or crutch in the contralateral hand. Frames or wheeled walkers are often preferable for those with bilateral disease.	IV	90 (84-96)
8 In patients with knee OA and mild/moderate varus or valgus instability, a knee brace can reduce pain, improve stability and diminish the risk of falling.	Ia	76 (69-83)
9 Every patient with hip or knee OA should receive advice concerning appropriate footwear. In patients with knee OA insoles can reduce pain and improve ambulation. Lateral wedged insoles can be of symptomatic benefit for some patients with medial tibio-femoral compartment OA.	IV (footwear) Ia (insole)	77 (66-88)
10 Some thermal modalities may be effective for relieving symptoms in hip and knee OA.	Ia	64 (60-68)
11 TENS can help with short-term pain control in some patients with hip or knee OA.	Ia	58 (45-72)
12 Acupuncture may be of symptomatic benefit in patients with knee OA.	Ia	59 (47-71)

Proposition	Levels of evidence	Strength of recommendation (%) (95%CI)
Pharmacological modalities of treatment		
13 Acetaminophen (up to 4 g/day) can be an effective initial oral analgesic for treatment of mild to moderate pain in patients with knee or hip OA. In the absence of an adequate response, or in the presence of severe pain and/or inflammation, alternative pharmacologic therapy should be considered based on relative efficacy and safety, as well as concomitant medications and co-morbidities.	Ia (knee) IV (hip)	92 (88-99)
14 In patients with symptomatic hip or knee OA, non-steroidal anti-inflammatory drugs (NSAIDs) should be used at the lowest effective dose but their long-term use should be avoided if possible. In patients with increased GI risk, either a COX-2 selective agent or a non-selective NSAID with co-prescription of a PPI or misoprostol for gastroprotection may be considered, but NSAIDs, including both non-selective and COX-2 selective agents, should be used with caution in patients with CV risk factors.	Ia (knee) Ia (hip)	93 (88-99)
15 Topical NSAIDs and capsaicin can be effective as adjunctives and alternatives to oral analgesic/anti-inflammatory agents in knee OA.	Ia (NSAIDs) Ia (capsaicin)	85 (75-95)
16 IA injections with corticosteroids can be used in the treatment of hip or knee OA, and should be considered particularly when patients have moderate to severe pain not responding satisfactorily to oral analgesic/anti-inflammatory agents and in patients with symptomatic knee OA with effusions or other physical signs of local inflammation.	Ib (hip) Ia (knee)	78 (61-95)
17 Injections of IA hyaluronate may be useful in patients with knee or hip OA. They are characterized by delayed onset, but prolonged duration, of symptomatic benefit when compared to IA injections of corticosteroids.	Ia (knee) Ia (hip)	64 (43-85)
18 Treatment with glucosamine and/or chondroitin sulphate may provide symptomatic benefit in patients with knee OA. If no response is apparent within 6 months treatment should be discontinued.	Ia (glucosamine) Ia (chondroitin)	63 (44-82)
19 In patients with symptomatic knee OA glucosamine sulphate and chondroitin sulphate may have structure-modifying effects while diacerein may have structure-modifying effects in patients with symptomatic OA of the hip.	Ib (knee) Ib (hip)	41 (20-62)
20 The use of weak opioids and narcotic analgesics can be considered for the treatment of refractory pain in patients with hip or knee OA, where other pharmacological agents have been ineffective, or are contraindicated. Stronger opioids should only be used for the management of severe pain in exceptional circumstances. Non-pharmacological therapies should be continued in such patients and surgical treatments should be considered.	Ia (weak opioids) IV (strong opioids) IV (others)	82 (74-90)
Surgical modalities of treatment		
21 Patients with hip or knee OA who are not obtaining adequate pain relief and functional improvement from a combination of non-pharmacological and pharmacological treatment should be considered for joint replacement surgery. Replacement arthroplasties are effective, and cost-effective interventions for patients with significant symptoms, and/or functional limitations associated with a reduced health-related quality of life, despite conservative therapy.	III	96 (94-98)
22 Unicompartmental knee replacement is effective in patients with knee OA restricted to a single compartment.	IIb	76 (64-88)
23 Osteotomy and joint-preserving surgical procedures should be considered in young adults with symptomatic hip OA, especially in the presence of dysplasia. For the young and physically active patient with significant symptoms from unicompartmental knee OA, high tibial osteotomy may offer an alternative intervention that delays the need for joint replacement some 10 years.	IIb	75 (64-86)
24 The role of joint lavage and arthroscopic debridement in knee OA are controversial. Although some studies have demonstrated short-term symptom relief, others suggest that improvement in symptoms could be attributable to a placebo effect.	Ib (lavage) Ib (debridement)	60 (47-82)
25 In patients with OA of the knee, joint fusion can be considered as a salvage procedure when joint replacement has failed.	IV	69 (57-82)

Box: Summary of the principal changes that have been made to the OARSI guideline

- Two guidelines, 57 systematic reviews, 200 RCTs, and 16 economic evaluations published between 31 January 2006 and 31 January 2008 were systematically reviewed.
- OARSI recommendations for a core set of non-pharmacological and pharmacological therapies, which are supported by high-quality systematic reviews and recommendations in all existing guidelines, are not altered by the addition of the recent research evidence.
- While effect sizes for certain treatments (eg NSAIDs) remained stable, the effect sizes for some therapies increased (eg weight reduction and topical NSAIDs), and decreased for others (eg electrotherapy, acetaminophen, glucosamine, and chondroitin sulphate), following inclusion of the additional recent trials.
- Although a meta-analysis of 4 RCTs demonstrated that avocado-soybean unsaponifiable is effective in relieving pain associated with OA, there was considerable heterogeneity in outcomes, suggesting that more trials are required to support a recommendation for this agent.
- Cardiovascular side effects associated with non-selective and COX-2 selective NSAIDs vary from drug to drug but caution should be exercised with the use of all NSAIDs as a class effect cannot be excluded.
- Regular review of well-characterized trials of all modalities of therapy for OA will be required to update the OARSI recommendations and maintain their scientific quality.

any of the recommendations.

Abramson: I should emphasize that the process of the committee was first to look at the evidence and then to try to interpret it in light of each member's expert opinion. One of the challenges in looking at interval publications is that one only sees the new evidence, without having much chance really to scrutinize it, talk about it, understand it, and debate it. We really have to be certain that any new data are consistent with the general consensus. I would like to ask, were the new data fed into the existing meta-analysis along with all the historic data, so that the change in effect size was integrated in terms of all the evidence that has been made available?

Nuki: Yes–cumulative meta-analysis has been undertaken where that was possible with available numeric data.

Current OA treatment in Japan and the West

Kawaguchi: Although Japan was not one of the participating countries involved in creating the OARSI guideline, the guideline covers almost all treatments that are given in Japan today. However, there are some differences among the conventional OA treatments given in various countries, probably due to different social needs or health insurance systems. In Japan, for example, the majority of OA patients visit orthopedic surgeons or primary care doctors. Some doctors initially recommend non-pharmacological treatments such as exercise, education, and self-management for mild cases, and if the pain does not go away, thereafter we use a combination of pharmacological and non-pharmacological treatments as the guideline recommends. Others start with pharmacological treatment, and the first choice is non-steroidal anti-inflammatory drugs (NSAIDs) or cyclooxygenase-2 (COX-2) inhibitors; acetaminophen is not the first choice in Japan. If the NSAID or COX-2 inhibitor does not work well, many doctors use intra-articular (IA) injection with hyaluronan even when the OA is not so severe. IA hyaluronan is occasionally used as the first choice for moderate cases. Some doctors use IA injections of steroid if there are signs of inflammation or effusion. If this does not solve the problem, surgery is considered. How about the situation of OA treatment in the USA?

Abramson: In the USA, primary care physicians see the majority of cases, and rheumatologists and orthopedic surgeons will only see them if they have inadequate improvement; either the doctor refers them to us or the patient self-identifies a specialist. So by the time we rheumatologists see a patient, he or she usually will already have been on acetaminophen and almost always over-the-counter (OTC) NSAID–most commonly ibuprofen or naproxen. It is interesting however that the first thing that you do in Japan is educate the patient on non-pharmacological means and weight loss. That is not commonly done in the USA. Many people are overweight in the USA, as is well known, so there is a sense that we doctors cannot do much about that. People are offended if we tell them to lose weight; they say, "I know I'm overweight but help my knees." This is why the guidelines are really important on the non-pharmacological aspect, because doctors are not well-trained to prescribe physical exercise and to advise about programs for sustained weight loss. We also undertreat patients pharmacologically, because doctors in the USA are very afraid to use NSAIDs especially in this population. Primary care doctors and cardiologists in particular often discourage elderly patients to take COX-2 inhibitors, and often NSAIDs as well. Therefore there has been a shift to using opioids more than we did 5-10 years ago; increasingly older patients are being treated with oxycodon, hydrocodon, and morphine derivatives. Another difference versus Japan is that in the USA there is a distinction between the orthopedic/rheumatologic community and primary care doctors with regard to IA injections with hyaluronan. Whereas this modality is commonly used by orthopedists, it is uncommon to use it in the non-surgical community. So everything that is done in Japan we do as well, but in a slightly different order.

Nuki: In the UK, a lot of treatment decisions through the National Health Service (NHS) are driven by issues of cost effectiveness. Therefore because of its high cost IA hyaluronan is rather infrequently used except in patients with really advanced disease.

Kawaguchi: So the main difference is that whereas in the USA and European countries acetaminophen and OTC drugs are

used as initial medicine against mild-to-moderate pain in OA patients, in Japan we use selective COX-2 inhibitors or NSAIDs as first choice. Also, in Japan both rheumatologists and primary care physicians use IA hyaluronan even from very early stages of OA, unlike in the USA and Europe. There are discordant findings among the systematic reviews and meta-analyses for the effects of IA hyaluronan. There are reports that hyaluronan is effective against early-stage and not late-stage OA, therefore some Japanese doctors point out that in western countries use of hyaluronate is too late.

Abramson: In the USA orthopedic surgeons will more commonly use hyaluronan to treat disease at earlier stages, whereas rheumatologists and primary care doctors do not so much. Indeed, in general practice many doctors nowadays do not do any injections or other invasive treatments because of the medical malpractice environment. Doctors do not get paid extra to give an injection; if somebody comes in and I want to give him or her an injection, I keep stores of cortisone on my shelf, since it is inexpensive. But I cannot keep an inventory of hyaluronan because the cost is high. Patients must be given a prescription and then asked to bring the medication to my office. If hyaluronan were cheaper and it was on my shelf, I would use it even in early-stage disease.

Nuki: In the UK IA hyaluronan is not recommended for the treatment of OA by the National Institute of Health and Clinical Excellence (NICE) largely because of a perceived lack of cost effectiveness, as judged by the cost/quality-adjusted life year (QALY).

Abramson: I think the reason why people use hyaluronan in the USA is that although meta-analyses of the available studies have shown only modest effect sizes in populations, anecdotally we have all seen individual patients who have remarkably good responses. Therefore basically there is a responder population and the question is how do we identify those people? It is not simply a question of early versus late disease because some people with late disease have had remarkably quick and sustained responses.

Issues in pharmacologic treatment

Kawaguchi: How about COX-2 inhibitors and their associated side effects? The guideline recommends using a COX-2 selective or specific inhibitor especially in patients with increased gastrointestinal (GI) risk, and specifies that NSAIDs should be used with caution in those with history of cardiovascular events. The statement by the American Heart Association (AHA), for example, advocates very strict restrictions on the use of not only COX-2 inhibitors but also the entire class of NSAIDs.

Abramson: The AHA statement is probably the greatest misuse of a professional organization's title that I have witnessed in the public arena. They gave, in essence, a series of recommendations that purported to be evidence-based but actually were not only opinion-based but, in some instances, also incorrect. Their recommendations included using aspirin as first choice, which we stopped doing since the mid-1990s because of GI and other toxicity. For aspirin to be effective against OA requires doses >1-2 g/day, which confer substantial GI risk, Furthermore, according to AHA the preferred NSAID are the non-acetylated salicylates, which they claim are safer. However, certainly for cardiovascular events, this is not evidence-based. They misused the organization's name and reputation to call these guidelines scientific. It is very clear and it has been very clear from the beginning that there are no differences between selective and nonselective COX-2 inhibitors with respect to cardiovascular risk. Perhaps naproxen might be considered safer than some other drugs on the market; however, that is based on studies using 1000 mg daily, which may not reflect common usage, certainly for OTC use. In contrast, the non-specific COX inhibitor, ibuprofen, may have a higher cardiovascular risk than some COX-2 specific drugs, particularly when used concomitantly with aspirin. It is a complex field. Most NSAIDs appear to confer an elevated relative risk of cardiovascular disease, somewhere between 1.2 and 1.7-fold. The risk is probably dose-dependent. That is why the OARSI recommendations note that there is no single first-line drug. The biggest shift in treatment in the last 5 years has seen people trying to avoid side effects by periodically going on then off NSAIDs and, as a consequence, there is a treatment gap and probable pain gap–but that is the tradeoff.

Nuki: It is also perhaps worth remembering that cardiovascular risks may be different in Japan when compared with Europe and the USA. As far as I know there are no data as yet on the cardiovascular risks of NSAIDs in Japanese patients, and it is possible that Japanese physicians are worrying themselves unnecessarily because of concerns about cardiovascular risks associated with the use of NSAIDs in western Europe and the USA.

Abramson: There are some very good data showing that there are different polymorphisms of COX-1 and COX-2 that make inhibitors more or less effective in some people. Down the line, we may be able to stratify risk in populations by looking at polymorphisms of COX-1 and COX-2 and seeing whether these align with risk for cardiovascular disease.

Nuki: How are views evolving on appropriate prophylaxis against peptic ulceration and GI haemorrhage? Should one be using a proton pump inhibitor (PPI) together with selective COX-2 inhibitors?

Abramson: According to data on people with a history of GI bleeding, the most effective treatment in these individuals does appear to be the combination of a COX-2 drug and a PPI.

The role of supplements in OA treatment

Kawaguchi: Many Japanese physicians and orthopedic surgeons are very interested in supplements such as glucosamine and chondroitin sulfate. Even though many of such supplements are neither regarded as medicines nor covered by the social insurance in Japan, they sell very well. In the guideline, are there any updated points on glucosamine and chondroitin sulfate after adding new evidence from the last 2 years?

Nuki: Yes. Before the guidelines were published sensitivity analyses were undertaken to examine the effect of adding interim data for effect size for pain relief from two large multicenter trials conducted in Europe (GUIDE) and the USA (GAIT). The effect sizes for both glucosamine and chondroitin sulfate diminished and the addition of the GAIT data suggested that treatment with chondroitin sulphate did not have significant efficacy for relief of pain in patients with knee OA. Cumulative meta-analysis is currently being undertaken following publication of further RCTs.

Abramson: In the USA there are groups of physicians who are very strongly against the data purportedly showing that these supplements are effective. However, in some people there is a response, and meta-analyses indicate that there is some response. Therefore we leave it to the patient to determine whether they want to try supplements. The most guidance that we do in the

USA is we choose one or two brands that have some credibility, then we tell people to try them for 3-4 months and not to stay on them after that if they do not notice appreciable effects.

The role of combination treatment

Kawaguchi: Are there any plans for OARSI to make a guideline for combination therapies?

Nuki: The OARSI guidelines for the treatment of hip and knee OA strongly recommend using a combination of pharmacological and non-pharmacological treatments. There is no clinical trial evidence to support the recommendation, which is based on expert opinion and common sense alone. This is certainly an area which could benefit from some further clinical research.

Abramson: Whereas there are very few data comparing the efficacy of pharmacological versus non-pharmacological therapies given alone, we know that people with OA are generally out of condition and possibly overweight and feel better when they exercise: their quality of life improves. I think it is imperative that, even if you are only spending a short time to see someone in the office, to do more than simply limit your treatment to drug therapy. The great value of the OARSI guidelines is to encourage doctors to spend time with people thinking about their quality of life, exercise, and non-pharmacological modalities. Another important consideration is that safety issues of combination medical regimens really need to be looked at carefully.

Growing expectations for the development of disease-modifying drugs for OA

Kawaguchi: As acknowledged in the OARSI guideline, unfortunately the core set of treatments all have small or modest effect size. This implies that we still do not have a definite effective therapeutic for the treatment for OA. What do you think is the most plausible candidate for a breakthrough disease-modifying drug for OA?

Abramson: From the industry point of view there is a lot more optimism for new pain treatments, because the time for their development is only several years, and studies require a 12-week outcome for signs and symptoms as opposed to 2 years for disease-modifying drugs. On the other hand there is less optimism for bringing new drugs to market. Several years ago, I would have tried to answer that question by thinking of new molecules, new pathways of signal transduction, metalloproteinase inhibitors. But now I think that if anyone is going to take a chance on OA structure modification, it is companies that have existing drugs where there is some reason to think that they might be disease-modifying. When you want to launch a brand new drug there is a risk that the regulatory authorities will ask you to study it in 10,000 people for safety. Therefore it is more attractive to take candidate drugs that are on the market with known safety profiles and develop them for OA. We are currently seeing that with calcitonin. Also I might predict that somebody soon will make a tumor necrosis factor (TNF) blocker. The evidence is fairly strong that cytokines are driving OA and not only in cartilage but also in bone and synovium. Therefore an anti-cytokine drug that works in all three tissue compartments, and that is already on the market, seems the most likely candidate for future therapy-based on the observation that drug companies have stalled new drug development because of cost.

Nuki: Yes, two of the major companies that had large research programs specifically directed towards looking for potential disease-modifying drugs have terminated this approach to discovery in the last 2 years so as to focus on improving pharmacological treatments for pain in OA. However, some industry-based research directed towards development of a disease-modifying osteoarthritis drug (DMOAD) is continuing. Some of the most exciting recent work has shown that in mechanically induced animal models of OA one can prevent progression of joint damage by inhibition of aggrecanases.

Abramson: Although aggrecanase inhibitors certainly work in animal models, I wonder whether blocking events in cartilage alone will protect against the bony changes and mechanisms that overwhelm the progression. For example, in the animal models I do not know how established the bony lesions are. Do aggrecanase inhibitors protect against those, or merely keep the cartilage intact?

Kawaguchi: ADAMTS5 (aggrecanase-2) knockout mice, which were protected from cartilage damage after induction of OA by surgical instability, are also reported to show minor changes in the subchondral bone structure, in contrast to the control wild-type mice, in which substantial bone thickening was found. These findings suggest links between cartilage damage and subchondral bone changes during OA progression, although which is the cause or the consequence remains controversial. I believe that mouse models will give us good hints for establishing therapeutic targets for OA because the molecular regulation of cartilage metabolism is identical in mice and humans, as evidenced by the similarity of skeletal phenotypes produced by mutations of several critical genes, whereas it is not so, for example, for osteoclast and osteopetrosis studies.

Conclusion: improving OA treatment

Kawaguchi: Finally, Steve and George, last year's newsletter on the roundtable discussion was a trigger for dissemination of the guideline in Japan, and I am sure that this year's newsletter will do so even more. Do you have any message to Japanese clinicians about OA treatment or research?

Abramson: Currently, we are really not serving our patients well. We need better pain medicines and we need to pay more attention to the patients' quality of life. I think that for anybody who has got OA the key thing for a doctor to do is give him or her 15 minutes and to ask "what is your life like?" We need to do a better job. That is why the guidelines are important, to hold doctors accountable and say, "are you doing this, are you doing this?"

Nuki: My message would be the same for Japanese physicians as it is for European and North American physicians. They really should take each individual OA patient more seriously. The guidelines have identified a large number of potentially effective treatments. Now we need to encourage physicians and other health care professionals to take a more holistic approach to their patients, and to offer them both pharmacologic and non-pharmacologic therapies. We also need audits to examine what therapies are currently being offered to patients with OA in different countries and in different treatment settings; and we need to develop optimum standards of care.

Kawaguchi: Thank you very much. This has been a wonderful roundtable discussion with two expert professionals from whom I have learned a lot.