Elevance Health

Moderator: Stephen Boren, M.D.
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Coordinator: Welcome, everyone, and thank you for standing by. I would like to advise you that today's call is being recorded. If you have any objections, you may disconnect at this time. All participants will be in a listen-only mode for the duration of today's call.

I would now like to turn the conference over to Dr. Stephen Boren. Thank you so much. You may begin.

Stephen Boren: Thank you very much. Hi. My name is Dr. Steve Boren. I am one of the medical directors here at National Government Services. And I really appreciate all our speakers coming and giving - reviewing articles and giving their opinions. Like Medicaid and a lot of private insurance companies, the physicians don't have any voice in any decisions that are made. We give physicians a voice, we do listen, we might not always agree, but at least we listen, which is to me as a physician very important.

So, again, I'm very glad that we have these speakers. They've all been chosen because of the expertise in this area.

But what's going to happen is I will read their 10 questions, I will read, and ask the lead subject matter expert for his or her response, and then I will ask the other subject experts that - experts if they have anything to add on. This would last roughly about seven minutes for each question. Thank you very much.

Stephanie, do we have the next slide? Okay. Thank you. It's a little small. Fortunately, for me, I have one bigger Word document.

Okay. The first question is to Dr. Blumstein, and before I ask Dr. Blumstein to speak, I will ask him, you know, to introduce himself and to acknowledge any possible conflicts. But the first question for him would be, how confident are you that there's adequate public evidence that intra-articular hyaluronan shoulder injections for osteoarthritis improves health outcomes, symptom status, and functional abilities? Are you ready, Dr. Blumstein?

Howard Blumstein: Yes. Thank you, Dr. Boren. So, my name is Howard Blumstein, I'm a rheumatologist in practice in Long Island, in an 11-person group. I've been practicing for almost 18 years. I'm the managing partner for my practice. I've also served on various committees, including right now at the American College of Rheumatology. And I was formerly the State Society President for the New York State Rheumatology Society. And I have no conflicts of interest related to this topic.

So, my answer was, so, was I rated it a four. So I do feel there is adequate clinical evidence that hyaluronans improve health outcomes, ameliorates symptoms, and improve functions in patients with osteoarthritis of the glenohumeral joint. While there are certainly other effective modalities that may be affected for short-term relief, differentiation appears particularly evident past the four to six-week mark. And also would likely carry a lower risk compared with some of the other alternatives.

In terms of supporting literature, I'll briefly review, you know, the bibliography that we were presented with. And I'm going to focus on just a few of those details of some of the papers.

So, the McKee trial, just looked at a single dose, hyaluronan, and it was looking at shoulder pain on movement over six months study period, and did achieve its primary outcome, along with statistically significant improvements in shoulder pain at night, as well as patient global assessment.

Weil's paper was a smaller trial looking at 27 patients. And they were - each patient received three weeks of high molecular weight hyaluronate. And

again, achieved the desired or the expected outcome with statistical significance. And additionally, there was improved pain both on the visual analog scale and the WOMAC score, range of motion, stiffness, and physical functioning score.

In Oduoza's paper, they looked at a younger population. So these were individuals that were 55 or less than 55. Importantly, again, in the patients that had moderate to severe glenohumeral joint osteoarthritis, there was significant improvement in their desired - their outcome measure with the Oxford Shoulder Score, and persisted up to 12 weeks after the injection, with improvement lasting up to 26 weeks in the more severe cases.

Importantly, they did note that the patients that had very mild OA did not see these statistically significant changes. So had a predilection for improvement in the more severe cases.

Di Giacoma's study looked at 78 patients. And this was a study looking at physiotherapy compared with physiotherapy plus HA. And patients that received the HA treatment plus physiotherapy, it has more significant improvement, and again, statistically significant - statistical significance was achieved.

Blaine study was a little bit better in terms of the number of patients. So they had 660 patients. They had a variety of conditions though. So, some had glenohumeral osteoarthritis, which is my question's focus, some had frozen shoulders, some had rotator cuff tear. All have failed conventional therapy. And this was a double-blinded randomized study, so they either received five injections of the study agent, three injections, followed by two injections of a phosphate buffered saline solution, or five injections of the saline solution.

Their main outcome was 13 weeks improvement of shoulder pain on movement. It did not achieve statistical significance at 13 weeks. However, importantly, in most of the active arms, so, in week seven, the five injection hyaluronic group did achieve significant differences. At week 17, both the

three and five-injection groups achieved statistical significant. And week 26, there was improvement in the three-injection series.

So when you look at the stratified population, especially with patients that had osteoarthritis, they did see a treatment effect. And in cases of patients that did not have osteoarthritis, they did not see a significant difference in either regimen, whether it was three or five injections.

Finally, Zhangs' paper, which was a med analysis, again they did see improvements in treatment arms in all of the studies that they looked at. However, and importantly, there was an effect in control groups as well. And this is probably the point that I would gather from all of these studies, that studying pain is very hard.

So, placebo responses, you know, I think that this is borne out in many rheumatologic literature, don't always indicate that a treatment has been effective. Pain in general is a complex and subjective and heterogeneous experience. There's also very, you know, reliable variations, natural fluctuations that we have in symptoms. That impacts on the interpretability of any intervention, because a placebo response will be compounded by the natural history of the condition.

Additionally, I think that one has to consider the motivation of the participants in these studies. So, in the case of a patient that has end-state osteoarthritis to the shoulder, they're looking at this treatment or possibly surgery. So, most of these individuals are going to be particularly motivated to feel better no matter what is done.

And finally, I think, you know, there is some, indeed, some body of literature talking about the intensity of placebo response based on the aggressiveness or invasiveness of that intervention. So I think, where it is a pill, we may not see the same impact, but you start sticking needles in patients, then there's a higher likelihood that people would feel better. But that doesn't, I think, negate the positive impacts.

So that's my answer to the first question.

Stephen Boren: Well, thank you very much. It's really appreciated. Does anyone else have any comments to make about this?

Okay. Thank you very much.

Now, to the second question, which is also for Dr. Blumstein. How confident are you that there's adequate published evidence that intra-articular hyaluronate shoulder injection for osteoarthritis improves health outcomes, symptom status, and functional abilities that's effective and well-tolerated in the treatment of osteoarthritis and persistent shoulder pain that is refractory to other non-standard, non-operative interventions?

Howard Blumstein: So, for this, I rated it a five. And the reason why it's a little bit stronger is because I focused on the second part of the question. So the first question really refers to efficacy of the treatment, and I really do feel that this question focuses more on the tolerability of the treatment as well as the indicational appropriateness for patients that have had pain that's refractory to standard non-operative interventions.

So, the general consensus of all the paper is that we reviewed, discussed its tolerability. And the consensus was that these, you know, treatments are extremely well-tolerated, with, you know, their tolerability has always been cited as high, with minimal adverse outcomes, and no serious adverse events, at least in these studies related to the treatments.

There were dropouts, for example, in the paper that looked at the large number, the 660, they were - I believe they ended up analyzing, let's see, 456 patients. There were dropouts. But it wasn't for adverse events. It was for failure or worsening of the condition, or in some cases patients were enrolled in the study as an interim measure and then suddenly have their surgery dates expedited.

So I think that we can't see it as the same thing as, you know, intolerability of the treatment, but rather just, you know, these were patients that were at the end of the line, they were trying to do anything to avoid a surgery, but they also knew that they probably would be getting surgery.

As far as entry criteria, most of the studies required that the patients had failed other non-operative interventions and conventional therapy. So I think that that applies with, again, you know, conform with my answer.

Stephen Boren: Well, thank you very much. I do appreciate it. Does anyone else have any comments on this question?

Okay. Nothing to add? Okay.

The next expert will be Dr. Portugal, who will be asked, if at least intermediate confidence, greater or equal to three, is noted in questions one or two, how confident are you that there's sufficient published evidence that the use of intra-articular hyaluronate shoulder injection should be limited to one injection for a six-month duration?

So, thank you very much, Dr. Portugal. Wanting to hear your opinions on this, and also we need you to mention any possible conflicts of interest.

Salvador Portugal: Sure. Hi, my name is Salvador Portugal. I'm an interventional spine and sports medicine physiatrist at NYU. I've been in clinical practice since 2012. I serve as the Sports Medicine Fellowship Program Director here within the Department of Rehabilitation. I'm also the current President of the New York Society of Physical Medicine Rehabilitation.

Regarding conflicts of interest, I did serve on an advisory panel for Hymovis for HA use in the knee. But I am not currently serving as an advisor for them. So, no current conflicts of interest.

To answer the question regarding, if at least intermediate confidence of equal or greater than three, I'm in agreement with Dr. Blumstein that I feel as though there is a good amount of evidence to suggest that HA is appropriate for to use in glenohumeral joint arthritis, in answer on one and two.

Do I feel there's sufficient evidence for the use of HA injection should be limited to one injection for a six-month duration or not. So, to specify, I think that, just to be clear, that there are certain formulations, as we all know, of

HA, which may be one injection or up to five injections. And then an available evidence that we have reviewing osteoarthritis for the shoulder, as well as for other joints, is that there is no agreed - or varying formulations have been used.

So I would not limit to one injection, but I would say to one treatment within six months, given the fact that in most of these studies there has been a duration of effect anywhere from three to six months, and even beyond six months. So I think it is very useful to limit to one treatment to six months, but I don't necessarily feel it should be one injection, specifically as some of these formulations are anywhere from one to five injections.

Stephen Boren: Thank you very much. Does anyone have any other comments about this question?

Howard Blumstein: This is Dr. Blumstein. I would just concur with Dr. Portugal with regard to one treatment's course. Of course, I would not recommend, you know, doing it more frequently than that.

And I also think that, given that we don't have great comparative studies of one versus three, versus five. In one of the papers that we looked at, we did see that there was an earlier treatment response with the five series as opposed to three. So there may be some benefit to longer courses for certain patients. But I would not limit it to one injection. I think that that would be, you know, compromising our Medicare population.

Stephen Boren: Thank you very much. Anyone else?

Okay. The next expert is Dr. Bush-Joseph. The question - the first question we're going to ask him is number four. How confident are you that there's adequate published evidence that HA is an objective treatment option in patients with moderate to severe glenohumeral joint osteoarthritis as a means to avoid/delay arthroplasty?

Also, before you speak, Dr. Bush-Joseph, if you would just introduce yourself and mention any potential conflicts of interest.

Chuck Bush-Joseph: Sure. Thank you for the opportunity. I'm Chuck Bush-Joseph, I'm an orthopedic surgeon. I'm a professor of orthopedic surgery at RUSH University Medical Center in Chicago. I've been in practice for over 34 years. I currently sit on the board of the AOSSM or the American Orthopedic Society for Sports Medicine. And I'm the chair of the AOSSM publishing committee, which overseas its family of journals.

I'm also the representative of the Illinois Association of Orthopedic Surgeons. And I have no conflicts at all on this topic.

So with regard to the question number four, am I confident about the adequate published evidence that hyaluronate is an effective treatment option for patients with moderate to severe glenohumeral arthritis as a means to avoid or delay surgery.

I think there's no evidence for that, and I believe the answer to that is, one, I believe that, as in other joints, as noted by Dr. Portugal and Dr. Blumstein, that the primary indication for these medications is really the symptomatic control. There's no evidence, I believe, in any joint where it's provided or - led to a significant delay in treatment on the basis of the structural properties of the disease.

I would comment that, you know, Dr. Blumstein did a wonderful job of pointing - of describing the several studies, and there are very few in this area that of high quality in dealing with the use of hyaluronates in the shoulder primarily for arthritis. I will, you know, comment on the two - just the paucity of the amount of literature would suggest the weakness of the evidence.

The meta-analysis review by Mao, et al. did have the largest series of patients, essentially had 504 patients, which is the largest collection, even though it only represented seven studies, of which two of those studies have variations in outcome measurements and short-term duration. All of the studies, the longest duration of follow-up with six months in the majority of them were shorter than six months.

And then, if I review the two papers from the orthopedic literature, the Zhang, et al., which is the Journal of Shoulder and Elbow Surgery in 2019, and the earlier study from Dr. Portugal's institution, senior author Joe Zuckerman from 2013, really just found reasonable safety, I think as alluded above, but really no clear lasting - no clear lasting demonstration of efficacy.

And in fact, the 2019 study, the senior author Moin Khan who I'm very familiar with and is a high-quality researcher and publisher, note that there's strong concerns that any indications of relief of symptoms are based on the placebo effect and the intention to treat, I think as Dr. Blumstein appropriately pointed out.

So, in response to question number four, I'm going to say it's a one.

Stephen Boren: Thank you very much. Any other comments?

If not, we'll go on to question number five.

Howard Blumstein: The only question/comment, I was just wondering if you're familiar with the work that was done by Bannuru at Boston at Tufts New England Medical Center. Because he's published in the past, not necessarily about shoulder, but about knee osteoarthritis, and he has had a number of papers that discuss, you know, delay of, let's say, knee arthroplasty. And it wasn't poor-quality literature. And if you want, I could certainly forward, you know, some of the references to you.

Chuck Bush-Joseph: Yes, I would certainly be happy to look at it, but I was just speaking directly about the shoulder itself. I am a, you know, just from my clinical practice, I am a regular user and believer of hyaluronates in the knee and weight-bearing joints, but just, you know, again, this is just anecdotal, personal experience, I discontinued the use of it. And I also surveyed the senior member - the board members of the shoulder and elbow society, ASES, the American Shoulder and Elbow Society, before this meeting. And none of the senior - none of the current leadership use it in their algorithm.

Now, again, this is an orthopedic surgery bias as opposed to a physiatry or rheumatology bias...

Howard Blumstein: Yes.

Chuck Bush-Joseph: but it's the information that I have.

Howard Blumstein: Yes. Got it. Thanks.

Stephen Boren: Thank you. Okay.

Chuck Bush-Joseph: I'll go to number five. How confident you are that there's adequate published evidence that intra-articular injection of hyaluronan with physical therapy is more effective than physical therapy alone in patients who have glenohumeral arthritis.

Chuck Bush-Joseph: I had a three on that, and I believe the evidence is intermediate. I believe that Dr. Blumstein quoted a couple of the articles earlier that did show benefit with hyaluronate, again, in relatively short term timeframes. But I believe the evidence is reasonable and in my, again, clinical experience, patients who really are placed into a physical therapy protocol with isolated, uncontrolled pain, do very poorly.

And so the comparators are using, whether it be steroids or hyaluronate, as providing symptomatic pain relief. Certainly in my clinic experience, I believe that to be the case. I don't believe the evidence for it is of high confidence, however, based on the studies that we've mentioned before. The more recent study from (Tuffs), I'm not familiar with.

So I'll stop at that on number five.

Stephen Boren: Thank you. Does anyone have any other comments?

Rich Chang: Sorry, this is Dr. Chang. I agree with Dr. Bush-Joseph's comments. You know, definitely in terms of pain control, as Dr. Blumstein sort of alluded before, you know, definitely it's a comprehensive approach, especially for patients that want to avoid, you know, surgical options.

So, you know, defined as structural disease, again, we try to modify in terms of activity, and as well as to make sure that they accompany that, it's just not one single treatment, and get a multi-disciplined approach in terms of approaching these patients.

So, I agree, although the literature is not as robust and they're heterogeneous, especially in terms of the types of hyaluronic acid formulations, I, you know, there are a few studies that Dr. Blumstein mentioned, that synergistic effect. But, you know, a targeted physical therapy program, rotator cuff and scapular stabilization as well posture strengthening, in addition to an injection treatment, would allow patients at least to have some kind of improved function and quality of life.

Stephen Boren: Thank you. Any other comments? Okay.

Okay. The next question?

Chuck Bush-Joseph: This is Dr. Bush-Joseph again, I'll go on to number six.

Stephen Boren: Yes.

Chuck Bush-Joseph: How confident are you that there's adequate published evidence that supports the intra-articular hyaluronan injection to improve pain or function with glenohumeral joint arthritis?

So I'm going to give that a four. Again, this is the same literature, we're really discussing the same measures. And I do believe that the - certainly the papers that we have discussed so far have shown reasonable pain improvement, albeit over short durations, in patients.

I believe that many patients, they get symptomatic relief from an arthritic flare. And whether it's from stabilization of the synovium, I believe that's the primary source, and certainly in the knee, the orthopedic biases that the majority of orthopedic surgeons use, high molecular weight hyaluronans, we believe it would be much more effective.

Again, the literature here in the shoulder is, in my mind, not definitive. But I would - I rated this as a four.

Stephen Boren: Thank you very much. Anyone else to add on to this? Okay.

Okay. Well, thank you very much then.

Dr. Chang is next. And he will respond to number seven. How confident are you that there's adequate published evidence that the subacromial bursa injection of HA with steroids in patients with periarticular shoulder disorder improves function of the affected shoulder, including range of motion?

Please introduce yourself Dr. Chang and also state whether you have any conflicts of interest or not.

Rich Chang: Sure thing. Dr. Boren, again it's a pleasure and honor to speak with you all today. My name is Rich Chang, I am a sports and spine physiatrist, and also in New York, at the Icahn School of Medicine and Mt. Sinai. I'm the associate program director for the Primary Care Sports Medicine Fellowship in the Department of Rehabilitation and Human Performance.

I'm also a team physician for the local Division 3 city college, Medgar Evers College, as well as serve as a medical consultant for USA Fencing, USA Boxing, and Professional Combat Sports with the New York State Athletic Commission.

In terms of conflict of interest, in respect to hyaluronic acid injections, I did publish a study where I was a co-investigator, comparing ultrasound guided low molecular weight hyaluronic acid versus leukocyte poor platelet rich plasma injections for glenohumeral osteoarthritis, which was published in the Clinical Journal of Sports Medicine, November 2022.

So I'm happy to help answer this question, question seven. So I would say, intuitively, with the use of hyaluronic acid with respect to rotator cuff tendinopathy or shoulder impingement syndrome, you know, at glance, first glance, it's somewhat surprising. But based on existing literature, there is a number of, I would say, smaller studies, actually a number of randomized controlled studies, looking at its efficacy in terms of pain control, function, and difficulty.

So, one of them which I did send more recently, which is a study published last year by Mohebbi et al. in the journal, Annals of Pharmacotherapy in 2021. And that was a triple-blind randomized controlled study looking at high versus low molecular weight hyaluronic acid for rotator cuff tendinopathy.

That wasn't that large. It was about 60 patients. There was 30 patients in each group. And patients were - had to include rotator cuff tendinopathy and had to have MRI imaging confirming no evidence of rotator cuff tears or tendinopathy.

Patients were randomized to either actually a single injection dose of either a low molecular weight hyaluronic acid which was 500 to 700 kilo-Daltons or high molecular weight hyaluronic acid which was greater than 2000 kilo-Daltons. And patients were followed for range of motion, pain, in terms of their DASH scores from one month, three - one, three months, and six months.

Here they did show a significant improvement in terms of pain and range of motion in both groups. I would say in between groups there wasn't much difference, and there wasn't really any adverse outcomes.

They're smaller size. I mean, there was one under the bibliography, the last one, Citation 13, the Byun study, which was looking at two arms trial, randomized controlled trial looking at ultrasound guided subacromial bursa injections with hyaluronic acid versus hyaluronic acid with corticosteroid or triamcinolone. That was a smaller study, only 13 patients in each group.

Both groups did improve, but the hyaluronic acid group appeared to have a longer duration, it's like up to three months.

When you look at more - previous studies, there was one study in 2013 done by Moghtaderi et al., and they had a small sample size, 40 patients. And there they actually compared once for three weeks hyaluronic acid compared to placebo or normal saline injected into the subacromial space

under ultrasound guidance. And there was improvement in 3 months with both groups with range of motion, pain and activities of daily living favored for the hyaluronic acid group.

There are other studies such as Merolla also in 2013, Meloni in 2008, that showed similar sort of outcomes. Again, the mechanism is not quite understood or intuitive, given that hyaluronic acid, we think at face value seems more of a lubricant, but according to the basic science research, there is some evidence in both basic animal studies and in human studies actually that it has some kind of anti-inflammatory and viscoelastic effect on tendons with decreasing expression of type 3 collagen, also some healing effects in terms of decreasing abnormal angiogenesis in tendons, and some effect in terms of inflammation, in terms of decreased promotion of (pro) inflammatory radicals and cytokines.

So, in terms of my overall answer, I would say, if we were to give it, I would give it between the three and four. I'd give it a 3.5, in terms of while I agree that the studies are small, it is safe.

And, you know, the next question, number eight, I feel that it would be an option, especially with patients in our older Medicare population where the orthopedic surgical, I think we're trying to stay away from corticosteroids, and if we are having a little bit of option, hyaluronic acid to the subacromial space would be a viable option for patients and that would be safe.

And that will lead into the question about the disadvantages or pitfalls.

Stephen Boren: Thank you very much. Does anyone else have any comments concerning this question or what Dr. Chang said?

Okay. Then let's go on to question number eight, which is also going to be addressed by Dr. Chang. How confident are you that further randomized controlled trials are not necessary to evaluate the efficacy of hyaluronan injection for shoulder, and to identify optimum dose and route of administration?

Rich Chang: So, a great question. So, somewhat of a trick question. So I'll first answer before I give the score, that, you know, I feel that the further randomized controlled trials and studies are much needed, especially in the - for the use of hyaluronic acid for - in rotator cuff tendinopathy.

And that, you know, there isn't really any one study that I see that has comparative data and our current standard of care is corticosteroid. Or I would say in some instances, some physicians have started to use injectable non-steroidal anti-inflammatory drugs such as ketorolac as an alternative to avoid the potential detrimental effects for rotator cuff tendinopathy or post-surgical shoulders.

I would say, in terms of score, out of five, I would give, you know, in terms of it's not necessary, I would say it is necessary. So I would give it - I would give it like in the middle of the road, a three. I feel that, you know, definitely more studies are needed, especially with the current standard of care. It does seem promising. But again, I would - it would have to be with larger n, sample sizes, and to a standard current group.

And again, just to allude back to Dr. Blumstein's comment about when we conduct these pain studies, again, even - every placebo group has a type of potential treatment response. So, you know, even with saline. So, yes, that's my answer.

Stephen Boren: Thank you very much. Anyone else wants to comment on question number eight?

Howard Blumstein: I just want to comment about the difficulty of doing a study. On top of the pain and all of the other things that were mentioned before, it's also just the nature of the material and getting an appropriate placebo.

So, giving someone a placebo visco injection, especially in a double-blinded fashion, is even more difficult, because most of us, you know, are - if we're conducting the study, will probably be the assessor also, and you can usually tell the difference between a, you know, viscous material that you're injecting and something that goes in much, you know, it will be the burden

of the companies, of course, to come up with an acceptable placebo that could mimic the viscosity, you know, to truly blind effectively. But that's another area that can confound the interpretability of the studies.

Stephen Boren: Thank you very much. Any further comments about this?

Chuck Bush-Joseph: This is Chuck Bush-Joseph. I would just say that I concur, you know, that, yes, these studies are almost impossible to do on a completely blinded fashion. But certainly, you know, if we go back to the, you know, the Kwan and Zuckerman studies from 2013 with phosphate buffer, you know, you're at least removing bias from the patient about what they're receiving, what they're not.

And I think what - as, you know, Dr. Chang said, we just need more numbers. You know? We're citing small cases, you know, the largest series was 40, you know, most of these are, you know, very small, anecdotal cohorts that are really difficult to make judgments on.

And you know, there's two perspectives here. There's the medical, number one, of safety. I think everybody's feeling safe about this procedure. The efficacy we're having some confidence to some degree, some higher than others. But the third side of this is, say, efficacy value and value of the expense or the value to what we're performing, I don't think we have any literature that provides a value calculation for Medicare or CMS.

Stephen Boren: Thank you. Okay. The next two questions, number 9 and number 10, are also for Dr. Portugal. Number nine is, how confident are you that there's adequate published evidence that intra-articular HA injections for treatment of patients with frozen shoulder or adhesive capsulitis are safe and effective?

Salvador Portugal: Within the bibliography provided, there was a systematic review in meta-analysis of the available literature, which was essentially a reproduction of an article that was done in 2016, given the lack of evidence or lack of studies that evaluate this. And what they look at are a number of studies from - or sorry, 1998 to 2021. And there's a total of seven of them, of small

numbers, the largest one being having 160 patients. And generally, a heterogeneous population.

In terms of the fact that adhesive capsulitis, the response is going to be dependent on the staging of when a patient - what to expect in terms of are they in a freezing time or frozen stages, which is not well-defined within these studies.

In addition to that, the treatment or the controls are all very different, in terms of one group - one study is comparing HA to NSAIDs, another study comparing HA to corticosteroids, another saying HA plus hydrodistension versus steroid, HA plus PT versus PT alone, HA versus triamcinolone PT stretching, HA plus steroid versus PT plus steroid, corticosteroid versus HA versus corticosteroid plus HA plus saline.

In the study overall, it found that there was very little difference in outcomes with regards to pain. However, there's a slight improvement in external rotation. However, not much of a difference in terms of abduction or flexion, which we mostly find to be the most limiting in terms of activities of daily living.

So, in terms of confidence that there's adequate published evidence that the use of HA for adhesive capsulitis is effective, I give that maybe a two. In terms of safety, what's been reported is there's no significant difference in adverse outcomes to the standard treatment, as mentioned.

Stephen Boren: Thank you. Thank you very much. Does anyone else have anything to add to what Dr. Portugal said?

Okay. Let's go on to question number 10. How confident are you that there is adequate published evidence that is generalizable to the Medicare patient population?

And before Dr. Portugal answers that, I would like to mention that CMS has on their Web site, and you - kind of hard to navigate through their Web site, but it can be done. That about maybe three years ago, 17% of all Medicare beneficiaries were under 65, and then last year, I think the figure had

dropped out to 15. The last figure I think is 12%, even though I'm not sure that that is a true valid number, because I believe that was only for traditional Medicare and excluded people on Medicare Advantage.

So I don't know. I'm trying to find another site. So I'm just (figuring up) that there are a number of people who are under 65 who are, you know, on Medicare. For a number of different reasons, there are those people.

Now, Dr. Portugal, could you answer the question please?

Salvador Portugal: Yes. So, as it pertains to osteoarthritis, osteoarthritis is largely thought to be a condition, a degenerative condition, associated with aging, but not necessarily so. Osteoarthritis is much more common in patients over the age of 65 and patients that are in these studies are - can be under the age of 65. But given the fact that this entity of osteoarthritis mostly affects patients on the Medicare population, I feel like this is generalizable to the Medicare patient population.

Stephen Boren: Thank you very much. Does anyone else have anything to add to what Dr. Portugal said?

Rich Chang: This is Dr. Chang. I definitely agree that it's generally - I agree the literature is somewhat heterogeneous, but definitely applicable to the Medicare population, especially, you know, the population could be more active and, you know, given the topic that we're discussing, patients may not be great surgical candidates or they may have comorbidities that may prevent them from using, for example, corticosteroid, like diabetes.

So, you know, while, you know, a number of the evidence is not the best or robust, I would say that having options to use will allow us to maybe keep us in pace with the international community. Of course, we can continue today, but if we have other options besides corticosteroids or NSAIDs, or, you know, to wait for surgery, then, you know, I feel it would definitely be appropriate.

And coming from the sports medicine side, for athlete, you know, for patient athlete, again, this injectable medicine may be an option to performance

while they're in season, without the fear, for example, like in tendons, like, tendon rupture, which is, you know, basic science, or fear of further degeneration, you know, or your eventual surgery on the joint. So that's my view on the - in terms of applicability to the Medicare population, and potentially, you know, with a younger population, since you mentioned there's some patients below the age 65.

Stephen Boren: Thank you very much, Dr. Chang. Anyone else have any comments?

Chuck Bush-Joseph: This is Bush-Joseph again. I would support Dr. Chang. I've taken care of professional athletes for 20 years, and Division 1 athletes for almost 30 years, and we use hyaluronics very commonly in the lower extremity, and obviously patients well below Medicare age.

But I do believe that the literature is supportive and the majority of the literature really is aimed at Medicare-based patients. Either those on Medicare disability secondary to diabetes, or other significant comorbidities.

So the last point is I think what Dr. Blumstein noted earlier, again, these things never occur in isolation and we will never have the perfect evidence because these conditions are so confounded in so many ways. And I do believe that there's wide use and adoption in other lower extremities with value. And there is some value in the upper extremities. But I am still skeptical as to the literature support of it, so.

Stephen Boren: Thank you very much. Are there any other comments in general?

Howard Blumstein: I'll add one more comment.

Stephen Boren: Okay.

Howard Blumstein: One thing that I think that every panel member can agree on is that, if a patient is not responsive, this wasn't one of the questions, but I do - I would just throw this out there. You know, again, all of us I think, in our respective specialties, realize that we are stewards of, you know, the healthcare system, and Medicare in particular in today's call. And there is, you know, so

one of the questions dealt with how many shots or, you know, whether one shot would be adequate.

But I would say that, you know, one guideline that you could, you know, certainly get endorsement by most people, is that if a person doesn't respond, it shouldn't be continued. I know it goes without saying, but there are entities out there that exist just to provide fiscal supplementation, regardless of the outcome. But you know, if someone had the response, then that's one thing.

And you know, most of us, you know, we appropriately left all of the comments to our, you know, review of the literature, but, you know, all of us have had positive experiences, and, you know, you have patients that respond and you repeat it because it does afford them improved quality of life. But you know, I'd just consider that, you know, that's the reasonable guideline, you know, where, if a person has no improvement, you don't just switch to the next drug, into the next drug, into the next drug, you know. So, that's it.

Stephen Boren: Thank you. Okay. Any other comments?

Rich Chang: Sorry, last comments. Dr. Chang. So, I guess, from a cost perspective, just a little regarding cost. I would say, you know, given hyaluronic acid, different formulations, different companies make it, I would say if CMS does consider expanding to this joint, I would continue in terms of making sure that's evidence-based and that, you know, for example, patients have to try physical therapy or standardized - to provide exercise program probably four to six weeks and, you know, oral medications before they try this injectable treatment, in order to reduce any sort of - any potential misuse or fraud.

So, again, I'm sort of excited by the potential promise of, you know, based on what we've discussed today. But again, from a cost perspective, you know, we're in the U.S. and we have a very diverse patient population. So

again, that is - if Medicare is thinking about guidelines, I think that's something that - to bear in mind.

Stephen Boren: Thank you very much. One thing I will add here, that many people don't know that contractors cannot, and the seven of us, contractors, NGS or Elevance's, either the largest or second largest depending which day of the week it is. Sort of like the difference, who's richer, you know, Bill Gates or the Oracle of Omaha Warren Buffet, that is which day of the week.

But contractors are not allowed to use cost as a reason for not covering or for covering any treatment. And related, even though there's a lot of people who don't believe this, Medicare contractors do not get any savings from, you know, turning down claims or anything like that. The only way it really affects us is as a taxpayer, which I'm just, you know, binging it out since cost has been brought up.

Linda, we are - we would like to have everyone who spoke to give their - a number on each thing. How do they go about doing that?

Linda: Hi, this is Linda. I sent you all an email with the questionnaire on. If you could fill it out and send it back to me. We would greatly appreciate that. And I will send it out again today, just in case you can't find it. Okay?

Stephen Boren: Thank you. And again, I want to thank everyone who participated in this, because, as I said at the beginning, we, you know, want to get people's opinions on things. We want you to have a voice in Medicare. We will listen to you. We might not always agree with you, but we will listen to you. And as I said before, I don't know too many other places in healthcare that you have a voice. But you have a voice with us.

So, thank you all very much, and we appreciate all your help. Thank you.

Man: Thank you so much.

Man: Thank you for participating. Thank you.

Man: Thank you. It was a pleasure.

Coordinator: That will conclude today's conference. And we thank you for participating. You may disconnect at this time.

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