



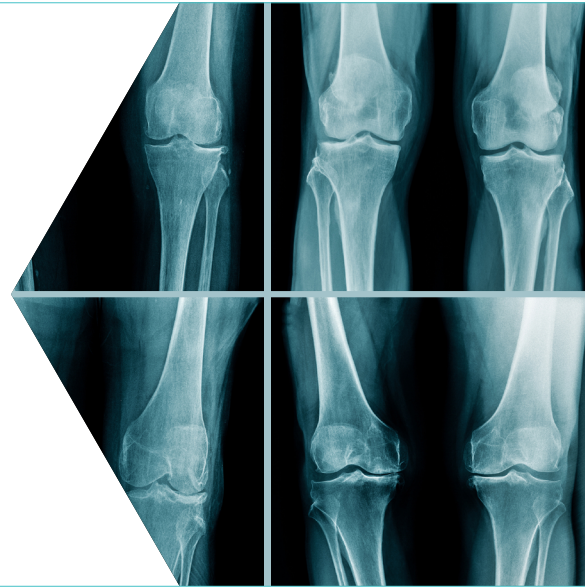
CLIENT REPORTED OUTCOMES

OSTEOARTHRITIS

This study overview illustrates the benefits seen using one's own MSCs, cultured by Celltex, to help alleviate symptoms of osteoarthritis.

DISCLAIMER: The Celltex study on osteoarthritis is being shared with you at your request. It reflects actual outcomes from individuals who received therapy using Celltex-produced mesenchymal stem cells. The study shows positive results for these individuals. It is important to note that the study is not scientific. No representation is being made that you or any other individual would get similar positive results. You should consult with your physician on what is best for you. Please call us if you wish to find out more about Celltex and the positive results individuals are having as reflected in this study.

STEM CELLS AND OSTEOARTHRITIS: HOW IT WORKS



Osteoarthritis (OA)

Osteoarthritis is a condition nearly synonymous with aging, causing pain and loss of mobility as the cartilage and underlying bone of a joint degenerate.

While the cause of OA is understood to be the wear and tear of a joint over time, inflammation is thought to play a significant role in how damage to the joint manifests.^[1]

Conventional OA treatments attempt to manage pain and inflammation until the joint deteriorates to the point that surgery becomes unavoidable, highlighting the need for alternative methods of care that are less invasive.

Why Mesenchymal Stem Cells?

Mesenchymal Stem Cells (MSCs) are a unique, naturally occurring type of stem cell known to possess powerful anti-inflammatory and regenerative properties that could help alleviate the symptoms of OA while helping maintain joint function over time.

An abundant amount of scientific literature already points to the efficacy of MSCs for OA, particularly of the knee. The radiological and functional improvements seen in these studies reveal how MSC therapy is one of the most promising potential avenues for addressing joint dysfunction in the near future.^[2]

This study overview illustrates the benefits seen using one's own MSCs, cultured by Celltex, to help alleviate symptoms of OA.

Data is based on reported outcomes of Celltex clients with OA.

Overview based on studies conducted by the Celltex Research & Development Team: *Safety of Autologous Adipose-Derived Mesenchymal Stem Cells in OA of the Knee & Safety of Autologous Adipose-Derived Mesenchymal Stem Cells in OA of the Shoulder.*

CLIENT REPORTED OUTCOMES FOR OA

Study Overviews

Celltex conducted two registry studies based on the reported results of our clients with osteoarthritis of the knee (OA-K) and osteoarthritis of the shoulder (OA-S) respectively.

MSC Therapy and Osteoarthritis (OA)

OA is a condition in which MSC therapy is thought to show particular promise, with an abundance of scientific literature pointing towards MSC therapy being effective for alleviating symptoms of OA.

Celltex has evaluated outcomes of MSC therapy for our clients with OA through **two registry studies**:

- Safety of Autologous Adipose-Derived Mesenchymal Stem Cells in **OA of the Knee**
- Safety of Autologous Adipose-Derived Mesenchymal Stem Cells in **OA of the Shoulder**

Table of Contents

OA of the Knee (OA-K)	
A Closer Look: OA-K	03
Key Findings: OA-K	04
Impacting the Symptoms: OA-K	05
Administering MSC Therapy: OA-K	06
OA of the Shoulder (OA-S)	
A Closer Look: OA-S	07
Key Findings: OA-S	08
Impacting the Symptoms: OA-S	10
Administering MSC Therapy: OA-S	11
Moving Forward	12
Supporting Information	13



A CLOSER LOOK: OA-K

Osteoarthritis of the Knee

The study used three surveys to assess the reported results of clients with OA-K who received MSC therapy between January 2011 and January 2019.

Survey Tools

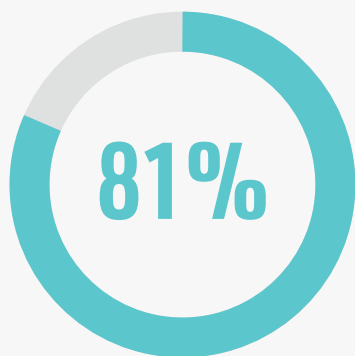
Clients were given three surveys, each meant to measure the impact of MSC therapy in a different way.

CLIENTS WITH OA-K WERE GIVEN 3 HEALTH SURVEYS:

1 survey was a custom retrospective survey developed by Celltex.

2 of the surveys were validated health assessment tools:

The Knee Orthopedic Outcomes Survey & The Rand Short Form 36



OF CLIENTS WITH OA-K
INDICATED IMPROVEMENT IN
ONE OR MORE SYMPTOMS

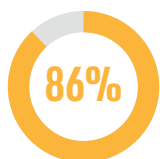
The majority of respondents reported improvements in one or more symptoms.

Most clients with OA-K saw improvement in at least one symptoms.

While these results are very promising, how each client's symptoms improved, and to what extent, varied from client to client.

Client-Reported Impact

Within the custom retrospective survey, clients were also asked to characterize whether they thought MSC therapy had helped them:



would recommend MSC therapy to others with OA-K.



felt their need for pain medication had decreased.

KEY FINDINGS: OA-K

The KOOS Assessment

Clients were given the Knee Orthopedic Outcomes Survey (KOOS) to measure the impact of MSC therapy.

The KOOS is a validated, patient-reported survey used to measure detectable differences to areas like pain, symptom severity, and quality of life. Higher KOOS scores indicate better outcomes.

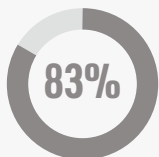
Clinically Important Improvement

Improvement in a KOOS score is often categorized as either a **Minimal Detectable Change (MDC)** or a **Minimal Clinically Important Difference (MCID)**.

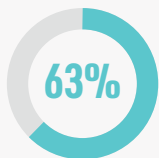


MDC is the minimum amount of change in score that isn't attributable to chance or measurement error. ^[3]

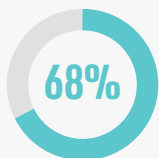
MCID is the minimum amount of change in score that may be considered important to a patient or clinician. ^[3]



improved **beyond the MDC** in overall KOOS score.



improved **beyond the MCID** in the Pain Domain.



improved **beyond the MCID** in the Quality of Life Domain.

Improvements in pain level and quality of life

A large majority of client respondents demonstrated improvements beyond the MDC in their overall KOOS score.

Additionally, most client respondents demonstrated clinically important improvements in level of pain and quality of life 12+ months after receiving MSC therapy.

Statistically Significant Improvements

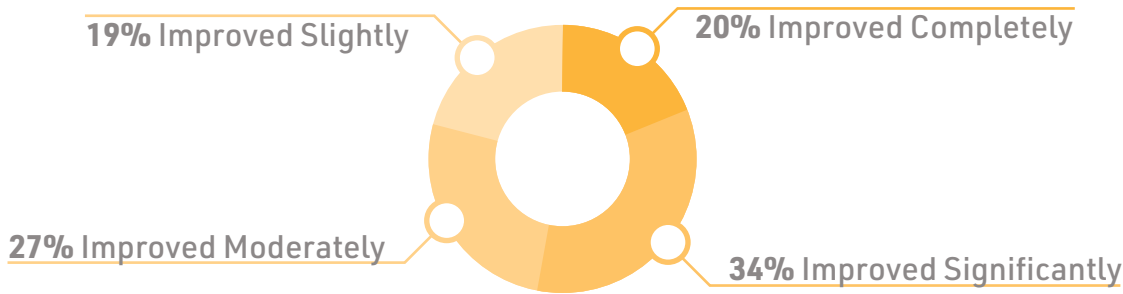
Improvements seen in the KOOS are supported by results from the Rand Short Form 36 (SF 36) survey, which saw statistically significant improvements in clients' physical health following MSC therapy.

IMPACTING THE SYMPTOMS OF OA-K

Degrees of Improvement

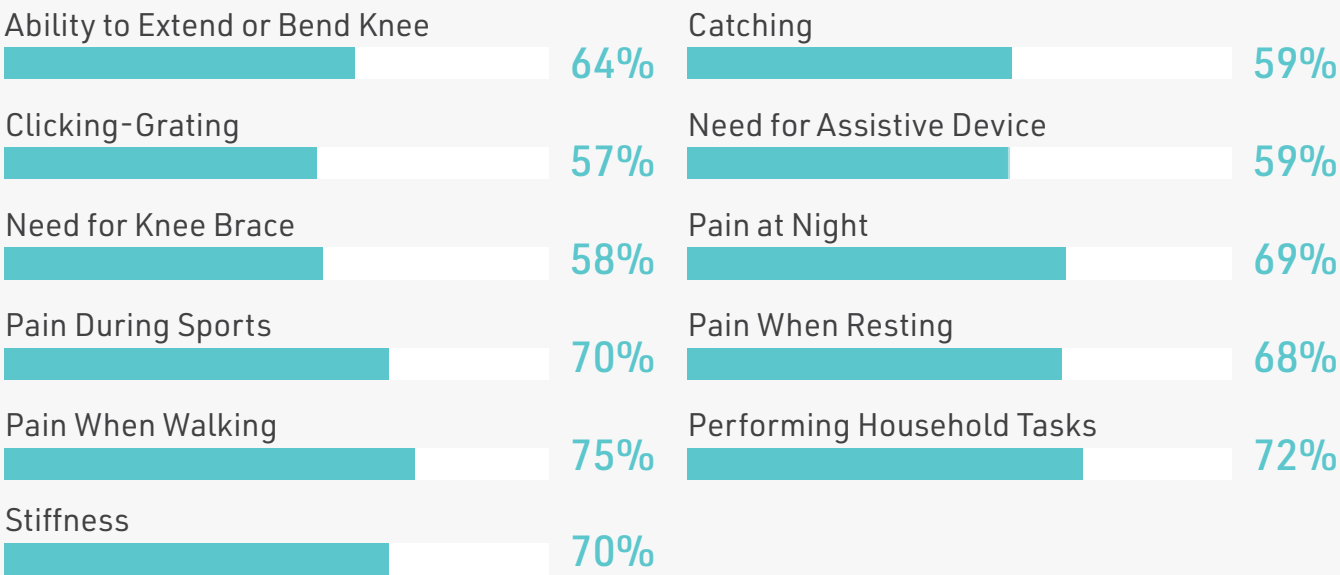
While each client experienced individualized improvements across different areas, most reported that the severity of their OA-K symptoms had reduced in some way.

OF THE SYMPTOMS THAT SHOWED IMPROVEMENTS:



Frequency of Symptom Improvements for OA-K Clients

The chart below represents the percentage of respondents that reported seeing improvement for the indicated symptom. Not every individual had every symptom.



ADMINISTERING STEM CELL THERAPY: OA-K

While the type of administration and frequency of therapies often varies based on a clients' specific circumstances, **each respondent received at least one intraarticular injection during this study.**

Routes of Administration

How MSCs are administered into the body varies based on physician recommendation and the individual client's needs.

Intraarticular (IA)

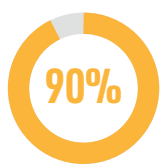
The MSCs are injected directly into the affected joint(s).

Intravenous (IV)

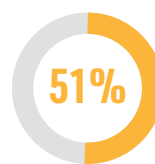
The MSCs are infused into the body through an IV.

Physicians often recommend IV infusions, regardless of condition, because they allow MSCs to travel via the circulatory system and regulate inflammation systemically.

ADMINISTRATION DETAILS AMONG SURVEYED CLIENTS:



of MSC therapies included one or more IVs in addition to IA.



of clients had MSC therapy for both of their knees.

Are Repeat Therapies Needed?

It's possible that repeated rounds of MSC therapy could enhance benefits.

Clients who had more than one IA injection within the duration of this study were 8% more likely to report improvements on one or more surveys.

Additional studies are needed to adequately determine whether multiple IA injections, and at what intervals, are most effective.

A CLOSER LOOK: OA-S

Osteoarthritis of the Shoulder

The study used four surveys to assess the reported results of clients with OA-S who received MSC therapy between October 2011 and July 2020.

Survey Tools

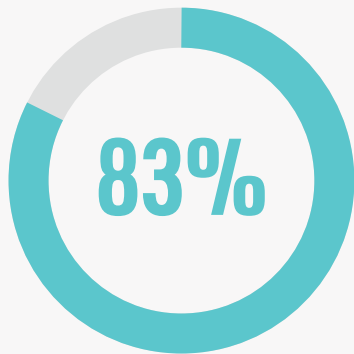
Clients were given four surveys, each meant to measure the impact of MSC therapy on the shoulder.

4 HEALTH SURVEYS WERE USED TO COLLECT DATA:

3 surveys were completed by clients themselves

1 survey was completed by clients' physicians

The most compelling data came from this physician-submitted survey



OF CLIENTS WITH OA-S
INDICATED IMPROVEMENT IN
ONE OR MORE SYMPTOMS

The majority of respondents reported improvements in one or more symptoms.

Most clients with OA-S saw improvement in at least one symptoms.

While these results are very promising, how each client's symptoms improved, and to what extent, varied from client to client.

Client-Reported Impact

Within the custom retrospective survey, clients were also asked to characterize whether they thought MSC therapy had helped them:



would recommend MSC therapy to others with OA-S.



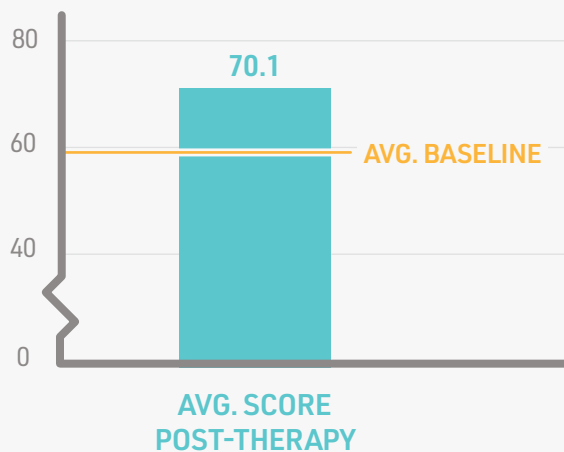
felt their need for pain medication had decreased.

KEY FINDINGS: OA-S

Physician-Validated Results

The Constant-Murley Score (CMS) is a validated, physician-administered assessment that compiles objective observations regarding shoulder range of motion, function, and radiology. Higher CMS scores indicate better outcomes.

Of all the data collected in our study, the most compelling came from this physician-completed survey tool.

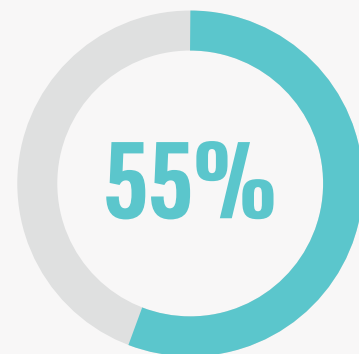


The average client saw range of motion in their shoulder improve.

After MSC therapy, physicians completing the CMS assigned a score based on the client's range of motion in the affected shoulder and compared it to the client's baseline score. On average, clients' scores improved by 10.3 points.

The majority of respondents' physicians reported objective improvements in radiology.

Of the clients whose physicians opted to compare their client's shoulder to previously recorded radiology, **55% demonstrated an improvement** following MSC therapy.



OF CLIENTS' PHYSICIANS NOTED IMPROVEMENT COMPARED TO PRE-THERAPY RADIOLOGY

KEY FINDINGS: OA-S

The ASES Assessment

Clients were given the American Shoulder and Elbow Survey (ASES) to assess the impact of MSC therapy.

The ASES is a validated survey used to measure improvements based on an individual's pain, quality of life, and ability to perform activities of daily living.

Substantial Improvements

Improvement in an ASES score is often categorized as either a **Minimal Clinically Important Difference (MCID)** or a **Substantial Clinical Benefit (SCB)**.

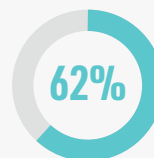


MCID is the minimum amount of change in score that may be considered important to a patient or clinician. ^[4]

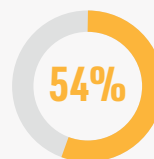
SCB is the minimum amount of change in score needed for a patient to feel that they improved significantly. ^[4]

Both clinically and substantially important

Most client respondents were found to have **both** clinically important and substantially important improvements 12 months after MSC therapy.



improved **beyond the MCID** after MSC therapy.



improved **beyond the SCB** after MSC therapy.

Statistically Significant Improvements

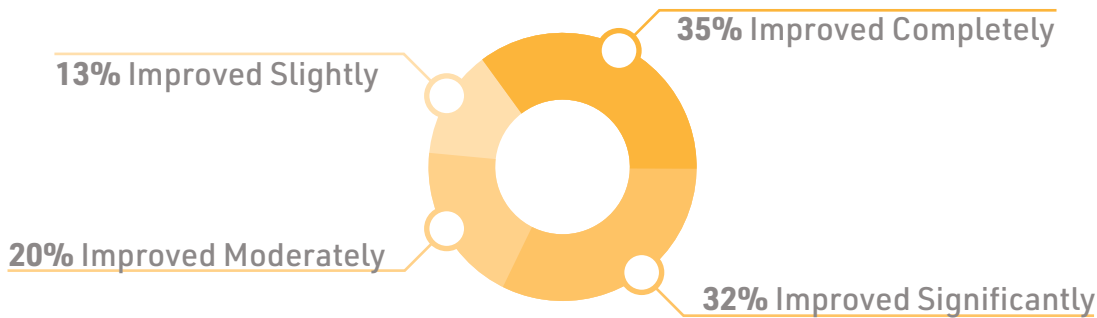
Improvements seen in the ASES are supported by results from the Rand Short Form 36 (SF 36) survey, which saw statistically significant improvements up to 12 months following MSC therapy.

IMPACTING THE SYMPTOMS OF OA-S

Degrees of Improvement

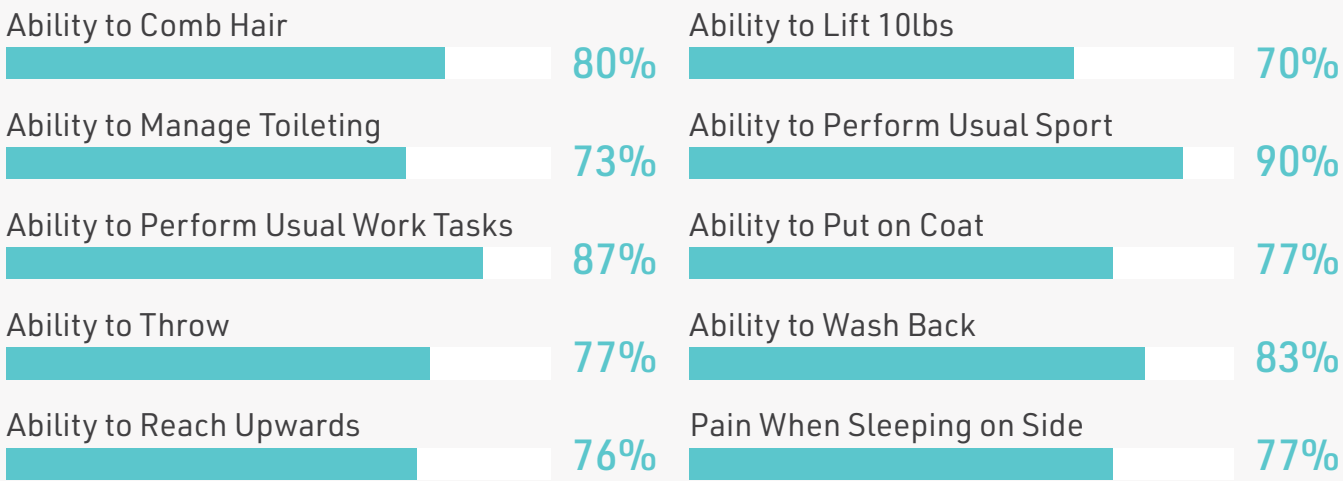
While each client experienced individualized improvements across different areas, most reported that the severity of their OA-S symptoms had reduced in some way.

OF THE SYMPTOMS THAT SHOWED IMPROVEMENTS:



Frequency of Symptom Improvements for OA-S Clients

The chart below represents the percentage of respondents that reported seeing improvement for the indicated symptom. Not every individual had every symptom.



ADMINISTERING STEM CELL THERAPY: OA-S

While the type of administration and frequency of therapies often varies based on a client's specific circumstances, **each respondent received at least one intraarticular injection during this study.**

Routes of Administration

How MSCs are administered into the body varies based on physician recommendation and the individual client's needs.

Intraarticular (IA)

The MSCs are injected directly into the affected joint(s).

Intravenous (IV)

The MSCs are infused into the body through an IV.

Physicians often recommend IV infusions, regardless of condition, because they allow MSCs to travel via the circulatory system and regulate inflammation systemically.

THROUGHOUT THE COURSE OF THIS STUDY, THE AVERAGE CLIENT RECEIVED:

1-2 IA injections into the affected shoulder

AND

2-3 IV infusions within a week of their IA injection(s)

Are Repeat Therapies Needed?

It's possible that repeated rounds of MSC therapy could enhance benefits.

Most clients (54%) felt like they would need repeat therapies.

Additional studies are needed to adequately judge whether multiple IA injections are more effective than just one.

MOVING FORWARD

Safety of MSC Therapy

There were no severe adverse events to MSC therapy in this registry study of Celltex clients with OA.

In fact, Celltex-produced MSCs have been used in over 10,000 therapies across various disease categories with no severe adverse events.

More Research is Crucial

Using MSCs to help alleviate the symptoms of OA certainly has potential, but more research is still a priority.

MSC therapy may already be an option for some. Learn more at [CelltexBank.com/Therapy](https://www.celltexbank.com/Therapy).

The Celltex Difference

Stem cell banking is the critical first step in the MSC therapy process that separates Celltex from other stem cell companies. Stem cell banking with Celltex involves (1) extracting a one-time sample of an individual's fat tissue, (2) isolating MSCs from that sample, (3) expanding the pure MSCs in quantity, and (4) cryopreserving a lifetime supply for future therapeutic uses.

Celltex's technology enables an individual's stored MSCs to be expanded into quantities exponentially greater than that of current same-day stem cell clinic offerings, greatly increasing the potential for positive results when therapeutic application is necessary.

This difference in cell quantity, along with the compatibility from using one's own cells, contributes to the superior quality of Celltex-produced MSCs. **Celltex-produced MSCs have the potential to succeed where same-day stem cell therapies have failed before.**

YOUR NEXT STEPS

Take Our Virtual Consultation

Visit [CelltexBank.com/OA-Eval](https://www.celltexbank.com/OA-Eval) to see if stem cell banking or therapy is right for you.

Talk to Your Celltex Representative

Here for you every step of the way, we can answer any question you might have about our process.

SUPPORTING INFORMATION

References

Overview based on studies conducted by the Celltex Research & Development Team:

- *Safety Registry Study Series using Autologous Adipose-Derived Mesenchymal Stem Cells: Osteoarthritis of the Knees – Retrospective Patient-Reported Outcomes.*
- *Safety Registry Study Series using Autologous Adipose-Derived Mesenchymal Stem Cells: Osteoarthritis of the Shoulder – Prospective and Retrospective Patient-Reported Outcomes.*

Additional References:

- [1] Griffin, T. M., & Scanzello, C. R. (2019). Innate inflammation and synovial macrophages in osteoarthritis pathophysiology. *Clinical and experimental rheumatology*, 37 Suppl 120(5), 57–63.
- [2] D'Arrigo, D., Roffi, A., Cucchiari, M., Moretti, M., Candrian, C., & Filardo, G. (2019). Secretome and Extracellular Vesicles as New Biological Therapies for Knee Osteoarthritis: A Systematic Review. *Journal of clinical medicine*, 8(11), 1867. <https://doi.org/10.3390/jcm8111867>
- [3] Singh, J. A., Luo, R., Landon, G. C., & Suarez-Almazor, M. (2014). Reliability and clinically important improvement thresholds for osteoarthritis pain and function scales: a multicenter study. *The Journal of rheumatology*, 41(3), 509–515. <https://doi.org/10.3899/jrheum.130609>
- [4] Werner, B. C., Chang, B., Nguyen, J. T., Dines, D. M., & Gulotta, L. V. (2016). What Change in American Shoulder and Elbow Surgeons Score Represents a Clinically Important Change After Shoulder Arthroplasty?. *Clinical orthopaedics and related research*, 474(12), 2672–2681. <https://doi.org/10.1007/s11999-016-4968-z>

Acknowledgments

We would like to acknowledge the generous contribution of those who received their own MSCs under the registry study in which this overview is based on. Their willingness to perform and submit surveys throughout repeated data collection cycles made these analyses possible.

We give our deepest thanks to these people for their contribution to help advance understanding in stem cell research.

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