

Stem Cell Therapy for Musculoskeletal Conditions

Final evidence report: Peer review, public comment, and response

February 17, 2020

Health Technology Assessment Program (HTA)

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Stem Cell Therapy for Musculoskeletal Conditions

Provided by:



Aggregate Analytics, Inc.

Prepared by:

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Shelby Kantner, BA

February 17, 2020

Responses to clinical and peer reviewers

Aggregate Analytics Inc. is an independent vendor contracted to produce evidence assessment reports for the Washington Health Technology Assessment (HTA) program. For transparency, all comments received during public comment periods are included in this document and attachments. Comments related to program decisions, process or other matters not pertaining to the evidence report, are acknowledged through inclusion only.

Specific responses pertaining to peer reviewer comments are included in **Table 1**. Draft report peer reviewers include:

- Zorica Buser, PhD, Assistant Professor of Research Orthopaedic Surgery and Neurological Surgery, Department of Orthopaedic Surgery, Keck School of Medicine, USC, Los Angeles California
- Patrick C. Hsieh, M.D., Professor of Neurological Surgery Edwin M. Todd/Trent H. Wells, Jr. Professor of Neurosurgery, Department of Neurological Surgery, Keck School of Medicine, USC, Los Angeles, California

Table 1. Responses to Clinical and Peer Reviewers

Comment		Response
Zorica Buser, PhD, Assistant Professor of Research Orthopaedic Surgery and Neurological Surgery, Department of Orthopaedic Surgery, Keck School of Medicine, USC, Los Angeles California		
Specific comments		
Introduction/ Key Questions	<ul style="list-style-type: none"> Overview of topic is adequate? Topic of assessment is important to address? Public policy and clinical relevance are well defined? <p>Response to Q1: Yes, in particular the ambiguity regarding how stem cells are defined and categorized.</p> <p>Response to Q2: Yes</p> <p>Response to Q3: yes they are. It is also important to understand that stem cell treatments are not covered by the insurance companies which adds additional financial burden to the patients. Additionally, cell numbers and cell potential for differentiation will be influenced by the donor's demographics and comorbidities.</p>	Thank you for your comments.
Background	<ul style="list-style-type: none"> Content of literature review/background is sufficient? <p>Yes absolutely.</p>	Thank you for your comments.
Report Objectives & Key Questions	<ul style="list-style-type: none"> Aims/objectives clearly address relevant policy and clinical issue? Key questions clearly defined and adequate for achieving aims? <p>Response to Q1: Yes.</p> <p>Response to Q2: Yes.</p>	Thank you for your comments.
Methods	<ul style="list-style-type: none"> Method for identifying relevant studies is adequate? Criteria for the inclusion and exclusion of studies is appropriate? Method for Level of Evidence (LoE) rating is appropriate and clearly explained? Data abstraction and analysis/review are adequate? <p>Response to Q1: Yes.</p> <p>Response to Q2/3/4: Yes.</p>	Thank you for your comments.
Results	<p>Yes amount of detail is appropriate, with figures, tables and appendices easy to understand. Key question 1 and 2 have been answered. Findings and gaps in the studies have been well addressed. Some studies are missing information on follow-up procedure (if patients went to have a surgery), but I assume that this information was not provided within the published manuscript. Final conclusions highlight the lack of</p>	<p>Thank you for your comments.</p> <p>Information on follow-up procedures (i.e. need for subsequent surgery) was specified <i>a priori</i> as an outcome of interest. As data were available, this</p>

Comment		Response
	data and adequate study designs to draw any recommendations.	outcome was abstracted from the studies and included in the report. For example, see section 4.2.1.2 under secondary outcomes.
Overall Presentation and Relevancy	Yes, well structured and presented. The report is very important for clinicians, research and patients, and for public policy makers.	Thank you for your comments.
Quality of Report	Superior	Thank you for your comments.
Other	<p>Attached is the form with my comments, report is well executed. I went over the report and appendix. I have not cross referenced guidelines & information in the tables. Same applies to tables and referenced studies, I have not double-checked that data in tables was correctly transferred from published papers.</p> <p>I mainly focused on the content, how it was presented, what was presented and if conclusions are supported with what was presented in the report.</p> <p>I was not looking for typos but noticed that K4 was sometimes swapped for K5 (no Q5 in this review).</p>	Thank you for your comments.
Patrick C. Hsieh, M.D., Professor of Neurological Surgery Edwin M. Todd/Trent H. Wells, Jr. Professor of Neurosurgery, Department of Neurological Surgery, Keck School of Medicine, USC, Los Angeles, California		
Specific comments		
Introduction	The overall introduction is a nice review of the impact of musculoskeletal diseases in our society, the description of stem cells sources and types, and the regulatory process involved in stem cell processing and therapy.	Thank you for your comments.
Background	The background section is well-written and provides an appropriate introduction to the need to assess the data behind stem cell therapy in musculoskeletal conditions.	Thank you for your comments.
Report Objectives & Key Questions	The most relevant and critical information for clinicians and patients on any clinical products and services are related to safety and efficacy. The objectives of this report on investigating the short-term and long-term clinical outcomes and adverse events related to stem cell therapy is on target. It is particularly worthwhile for clinicians and patients that are interested in utilization of stem cell therapy in musculoskeletal diseases.	Thank you for your comments.

Comment		Response
Methods	The overall methodology of this report is appropriately stringent and consistent with high quality systematic reviews. I agree with the evaluation of relevant literature based on the Cochrane Handbook for systemic reviews of interventions and Agency for Healthcare Research and Quality (AHRQ). The assessment of literature reports based on level of evidence, quality of study design, sample size, consistency of data, and publication or reporting bias is appropriately conducted by the reviewers. I believe this is an overall well-written review of current state of literature and evidence based on solid methodology of accepted standard for quality systematic review.	Thank you for your comments.
Results	The results of this reports are appropriately comprehensive and inclusive. The tables and figures are presented in concise and well-presented fashion.	Thank you for your comments.
Overall Presentation and Relevancy	Overall, I believe this is well-conducted systematic review of current literature and evidence on the efficacy and safety of stem cell therapy in the treatment of musculoskeletal conditions. The reviewers have prepared a comprehensive and yet concise report that detail the available evidence and support for treatment of degenerative orthopedics conditions with autologous and allogenic stem cells therapy. Readers of this report will find the information is presented in a well-written and engaging article. In addition, the data is salient and pertinent to clinician and patients that are interested in pursuing treatment of musculoskeletal diseases with stem cell therapy. This report will serve as a great addition to current literature and reports on stem cell therapy in clinical medicine.	Thank you for your comments.
Quality of Report	Superior	Thank you for your comments.
Other	I think it's overall a well done review and well written. I don't have any concerns or criticisms of the review or the content. I've tried to use the form as well as I understand it for my review. Let me know if it's not adequate. Thanks!	Thank you for your comments.

Responses to public comment on draft report

This second section responds to comments received during the public comment period from the following:

Table 2. Responses to public comments

No public comments were received on either the draft key questions and scope or to the draft report.

APPENDIX: Clinical/peer reviews and public comments received**Peer Reviewer #1: Zorica Buser, PhD, Assistant Professor of Research
Orthopedic Surgery and Neurological Surgery, Department of Orthopedic
Surgery, Keck School of Medicine, USC, Los Angeles California**

Thank you for your willingness to read and comment on the Comprehensive Evidence-Based Health Technology Assessment Review for the **Stem Cell Therapy for Musculoskeletal Conditions**. Your contribution and time are greatly appreciated.

The general time commitment ranges between 2 and 4 hours; we are able to pay a maximum of 6 hours.

The report and appendices are available at: <https://www.hca.wa.gov/about-hca/health-technology-assessment/stem-cell-therapy-musculoskeletal-pain>

This form can be filled out electronically on your personal computer. Enter your identification information and comments directly into the shaded areas; use the **TAB** key to move from field to field. Please enter the section, page, and line numbers where relevant. The shaded comment field will expand as you type, allowing for unlimited text. You have been provided comment fields in each section. Should you have more comments than this allows for, please continue with a blank page. Additionally, we are very interested in your evaluation of the ease of use of our Peer Review Form. Please use the last field to enter suggestions for improvement.

We will be going through the draft for typographical errors as well as grammatical and minor edits, allowing you to focus on the substance/content of the report.

When the Peer Review form is complete, save it to your hard drive and return as an e-mail attachment to: andrea@aggregate-analytics.com

I will need your review by Monday, January 27, 2020 at the latest.

If you have questions or concerns please contact andrea@aggregate-analytics.com. Thanks!

Reviewer Identification Information

Reviewer Name	Zorica Buser
Address	Street 156 E Commercial St City San Dimas State CA Zip Code 91773
Phone	
Fax	
E-mail	buserzori@gmail.com

INTRODUCTION Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Overview of topic is adequate?
- Topic of assessment is important to address?
- Public policy and clinical relevance are well defined?

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Response to Q1: Yes, in particular the ambiguity regarding how stem cells are defined and categorized.

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Response to Q2: Yes

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Response to Q3: yes they are. It is also important to understand that stem cell treatments are not covered by the insurance companies which adds additional financial burden to the patients. Additionally, cell numbers and cell potential for differentiation will be influenced by the donor's demographics and comorbidities.

BACKGROUND Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Content of literature review/background is sufficient?

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Yes absolutely.

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REPORT OBJECTIVES & KEY QUESTIONS Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Aims/objectives clearly address relevant policy and clinical issue?

- Key questions clearly defined and adequate for achieving aims?

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Response to Q1: Yes

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Response to Q2: Yes

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METHODS Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Method for identifying relevant studies is adequate?
- Criteria for the inclusion and exclusion of studies is appropriate?
- Method for Level of Evidence (LoE) rating is appropriate and clearly explained?
- Data abstraction and analysis/review are adequate?

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Response to Q1: Yes

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Response to Q2/3/4: Yes

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RESULTS Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Amount of detail presented in the results section appropriate?
- Key questions are answered?
- Figures, tables and appendices clear and easy to read?
- Implications of the major findings clearly stated?
- Have gaps in the literature been dealt with adequately?
- Recommendations address limitations of literature?

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Yes amount of detail is appropriate, with figures, tables and appendices easy to understand. Key question 1 and 2 have been answered. Findings and gaps in the studies have been well addressed. Some studies are missing information on follow-up procedure (if patients went to have a surgery), but I assume that this information was not provided within the published manuscript. Final conclusions highlight the lack of data and adequate study designs to draw any recommendations.

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OVERALL PRESENTATION and RELEVANCY Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Is the review well structured and organized?
- Are the main points clearly presented?
- Is it relevant to clinical medicine?
- Is it important for public policy or public health?

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Yes, well structured and presented. The report is very important for clinicians, research and patients, and for public policy makers.

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QUALITY OF REPORT

Quality Of the Report

(Click in the gray box to make your selection)

☒ Superior

☐ Good

☐ Fair

☐ Poor

**Peer Reviewer #2: Patrick C. Hsieh, M.D., Professor of Neurological Surgery
Edwin M. Todd/Trent H. Wells, Jr. Professor of Neurosurgery, Department of
Neurological Surgery, Keck School of Medicine, USC, Los Angeles, California**

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Reviewer Identification Information

Reviewer Name	Patrick Hsieh
Address	Street 1520 San Pablo Street, Suite 3800 City Los Angeles State CA Zip Code 90033
Phone	3234097422
Fax	
E-mail	phsieh@usc.edu

INTRODUCTION Comments

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QUALITY OF REPORT

Quality of the Report

(Click in the gray box to make your selection)

☒ **Superior**

☐ **Good**

☐ **Fair**

☐ **Poor**
