Summary

Minimal Clinically Important Difference Module: Summary, Recommendations, and Research Agenda

INTRODUCTION

In preparation for the conference, methodological papers on minimal clinically important differences (MCID) and the current status and need for MCID on core measures in the 4 content areas of interest [osteoarthritis (OA), rheumatoid arthritis (RA), osteoporosis (OP), and low back pain (LBP)] were written and distributed to the conference participants. At the conference, these papers were presented in plenary and the participants were then divided into 8 breakout groups (3 groups each for OA and RA, and one group each for OP and LBP) to further consider the issues. Questionnaires were distributed to participants in the breakout sessions to help focus discussions during these sessions. All questionnaires had a similar core set of questions on MCID, as well as questions that were specific to the content area (OA, RA, OP, LBP). Completed questionnaires were collected by the breakout session leaders at the end of the sessions and the information was entered into a database and analyzed. At the closing plenary session of the conference, the results of the breakout questionnaire and discussions were presented and conference participants voted on key issues associated with MCID.

This paper presents results from the questionnaire and voting, summarizes the associated discussions, and identifies some areas for further research.

RESPONSES TO BREAKOUT QUESTIONNAIRE

A total of 136 questionnaires were returned. Most were from the larger number of RA and OA sessions (RA 58; OA 54; OP 19; LBP 5). The specific results presented here primarily relate to RA and OP.

Of the 30 cells in the "cube" defined by who is the focus (groups, individuals), which scores are contrasted (differences between, changes within, both), and what type of change (minimum potentially detectable, minimum actually detectable beyond error, observed in the population, observed in those estimated to differ/change, observed in those estimated to have important difference/change), the cell of most interest was the "individual" setting for "within change" scores on "important change."

In the RA breakout sessions, participants discussed the classification in the cube of the current RA response criteria according to type of change/difference. The response to the question, "Where are the RA criteria currently placed in the cube," indicated that the majority of participants believed that the ACR20 improvement criteria and the EULAR response criteria were considering change/difference observed in those estimated to have changed or estimated to have an important change (ACR20 52%; EULAR 73%). Based on the assumption that ACR and EULAR criteria have defined response or improvement corresponding to MCID, the participants ranked priority areas for further research. The percentage of priority rankings (rank 1 or 2) for the different areas considered were as follows: defining major improvement (25%); studies that focus on defining individual response as opposed to group change or difference (18%); studies that attempt to define MCID for individual elements of the core set including functional status measures (16%); further validation of ACR/EULAR definitions against independent definitions of response (15%); and studies that focus on whether thresholds for response differ for different core set items (14%). Only 1% gave a priority ranking to studies that evaluate whether core set items have particular statistically measurable thresholds for MCID. An area of study not listed but given a priority ranking by 5% under category of other was validating short term response criteria in predicting longterm outcome received 5% priority ranking.

The issue of major improvement was further explored, with 76% indicating that it was important or useful to establish criterion for a major clinically important improvement as well as a minimal clinically important difference. A qualitative analysis of participants' comments in considering major improvement indicated the following supporting themes: MCID is only a lower bound of improvement change; major change comes after determination and understanding of MCID; treatment decisions are more often made based on major change; and major change is important in interpreting trials of 2 active treatments.

In the OA breakout sessions, the adequacy of current estimates for the OA core set of measures (pain, function, and patient global assessment) were considered from the perspective of the different types of change, namely: (1) minimum potentially detectable; (2) minimum actually detectable beyond error; (3) observed in the population; (4) observed in those estimated to differ/change; and (5) observed in those estimated to have important difference/change. The current estimates for pain were considered at least adequate ("very adequate or adequate") by over 70% of the respondents for type 1, 2, and 3 change.

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Only 42% and 23% considered it at least adequate for the categories observed in those estimated to differ/change and observed in those estimated to have important difference/change, respectively. For function, about 70% found it at least adequate for all types of change except for the category observed in those estimated to have important difference/change, which received only 22%. Patient global assessment had a similar pattern to pain with a large percentage indicating it was at least adequate for type 1, 2, and 3 change (over 65%) but a smaller percentage for type 4 (34%) and type 5 (21%) change.

The small number of participants in the OP and LBP breakout groups made it difficult to analyze and interpret their individual breakout session results. The information obtained in these sessions will be relayed to and considered by their respective societies and interest groups as a basis for possible further studies.

In all the breakout sessions, the participants were asked whether a MCID should be defined in terms of percentage change only, absolute change only, or both. The vast majority indicated both (85%), with an equal percentage of respondents indicating support for percent (7.5%) or absolute (7.5%) change only.

RESPONSES TO PLENARY QUESTIONS

Four questions were posed and voted on in the final plenary sessions. The questions were designed to confirm discussions that took place among the participants and the interpretation of the questionnaire results. The goal was to set a broad overview on a research agenda.

Question 1: Do you support the development of clinical response criteria for individuals in other diseases?

Yes	96%
No	1%
Don't know	3%

The MCID module concentrated on 4 content areas (OA, RA, OP, LBP). To address whether other areas should consider clinical response criteria in this way, a question was posed to draw on the various expertise of the participants, as well as the information they were provided with and their specific experience at the OMERACT conference. The vote by all the conference participants at the final plenary session resulted in 96% supporting the development of clinical response criteria for individuals in other diseases.

Question 2: Do you agree that it is important to define "major" clinical important improvement for RA?

Strongly agree	47%
Agree	33%
Neutral	13%
Disagree	3%
Strongly disagree	2%
Don't know	1%

The results of the questionnaire for the RA breakout sessions indicated that "major" clinically important improvement may be an important area of consideration for research. This question was posed to and voted on by all the conference participants at the final plenary session, with a resulting 80% in agreement.

Question 3: Do you agree that it is important to validate short term response/improvement criteria in predicting longterm outcome?

Strongly agree	61%
Agree	23%
Neutral	8%
Disagree	2%
Strongly disagree	4%
Don't know	2%

The issue of validating short term response/improvement criteria in predicting longterm outcome received an important priority ranking but was essentially considered by only one breakout session. This question was posed to and voted on by all the conference participants, with a resulting 84% in agreement.

Question 4: In OA should any response criteria developed be defined in terms of...?

Percent change alone	5%
Absolute change alone	4%
Both	91%

Based on the breakout questionnaire, a large majority of participants indicated that a MCID should be defined in terms of both percentage change and absolute change only. This is an important concept in the development and interpretation of MCID and confirmation of this finding was sought for OA response criteria. This question was posed to and voted on by all the conference participants, with a resulting 91% indicating that both absolute and relative should be considered. After the vote, Maxime Dougados presented the recent work and decisions made by OARSI in which both percentage and absolute change were used in the definition of OA response criteria.

RESEARCH AGENDA OVERVIEW:

1. Develop clinical response criteria for individuals in other diseases?
2. Consider both relative and absolute change in developing response criteria.
3. Consider "major" clinically important change in the further development of a clinical response criteria.
4. Validate short term response criteria in predicting longterm outcome?
5. Consider the patient perspective in developing response criteria.

CONCLUSION

Progress has been made in considering changes/differences related to clinical outcomes of interest in some of the disease areas. Through a multidisciplinary approach at OMERACT involving academic investigators, clinicians,

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and regulatory experts, it is anticipated that this work will progress further in areas in which it is more established, with the possible development of "major" response criteria, and be initiated in areas in which it needs more consideration. During the discussions, two important themes evolved that were in need of more consideration — taking a patient perspective of response and validating the longterm clinical consequences of short term response criteria.

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