



Childhood Arthritis and Rheumatology Research Alliance

Standardized *CARRA Consensus Treatment Plan (CTP)* Development Process

February 25th, 2018

Background

Randomized controlled trials, although often considered the gold-standard for determining treatment effects, are costly and depend on the availability of sufficient numbers of patients. Determination of treatment effects using observational studies is less expensive, but is hampered by the extensive variability in the treatments used in our community. Thus, CARRA is working to reduce treatment variability by developing standardized regimens (Consensus Treatment Plans, CTPs) with the goal of supporting the conduct of comparative effectiveness research (CER). CTPs should be close enough to treatment regimens currently used in the community, that they will be accepted for widespread use by the physicians who care for the patients. Eligible patients should be enrolled in the CARRA registry to allow for data collection to conduct future CER.

CTPs may be used for patient care, but they differ from Practice Guidelines. Practice Guidelines are also developed by experts using consensus methodology, but they depend on the availability of sufficient evidence, which is often lacking for the pediatric rheumatic conditions. White papers, authoritative reports about complex issues that include the issuing body's philosophy on the matter, can also provide valuable guidance for patient care and research. They often do not utilize consensus methodology, but may be appropriate for some clinical scenarios.

CARRA CTP Advisory Committee

The CTP Advisory Committee provides oversight and support for investigators. The members have expertise in CTP methodology, consensus methods and clinical research. They provide pre-approval, ongoing oversight and final approval of CTPs for CARRA endorsement. A member of the committee is assigned to each CTP project to assist the investigators with the development of a study design that is appropriate for the individual CTP project and will allow them to meet the requirements below. Any disagreement about the guidance being provided should be sent to the CARRA Executive Committee.

CARRA endorsement

"CARRA endorsement" allows investigators to use the CARRA name in the CTP, to state on the manuscript, "this project received CARRA endorsement" and to have be eligible for accessing CARRA registry data for assessment of the CTPs, if the data is available.

Standardized CTP development procedures

Investigators wishing to obtain CARRA endorsement should follow this process and meet the targets below. This standardized process will ensure that there is uniform rigor and quality of the CTPs that are endorsed by CARRA and ensure that the same standards are applied to all published CTPs that contain the CARRA name.

- ❑ Project plan pre-approval
 - Investigators submit their proposed project plan to the CARRA CTP Advisory Committee for pre-approval using the *Project plan pre-approval form*. In this form investigators describe their plan for addressing the following required steps.
- ❑ Select a clinical problem that meets the following criteria
 - There is variability in treatment approaches and clear evidence for best treatment is lacking. Variability is important to ensure that there are treatments to compare, and if the best treatment has already been identified CER is not indicated. Investigators will complete the *Documentation of CARRA-wide Priority form* to support their choice of clinical focus.
- ❑ Define an available intended “target population”
 - This should include specifying the characteristics of the patients to be treated with the CTPs, as well as those patients that should not be treated with the CTPs. These characteristics will inform the development of standardized cases. There should be sufficient numbers of patients with these characteristics to support future CER using data collected on these patients who are treated with the CTPs.
- ❑ Perform a literature review to determine best available published studies of treatments and measures.
- ❑ Prepare and utilize standardized clinical cases to solicit opinion from the CARRA members who care for these patients
 - All important information that might influence treatment choice in practice should be included in the cases
 - The study team is encouraged to solicit input on the cases to ensure that all factors that influence treatment choice are included. This can be achieved by circulating the cases via email or posting for member feedback.
- ❑ Assessment of CARRA member’s opinion regarding the best measures to assess response to treatment, considering both disease response measures and tolerability.
- ❑ Define and justify the selection of the CARRA members that you plan to poll for the different phases of the CTP development project
 - Initial survey. Purpose is to determine the usual treatment approaches in the community. Information should be solicited by using standardized cases as examples. The survey should be sent to individuals who reflect the entire CARRA membership. This is important to ensure buy-in and broad use of the CTPs once they are developed, which will be critical to the conduct of future CER studies. Either the entire CARRA membership can be surveyed or a random subset of the membership can be surveyed. Inclusion of opt-out options (examples-I do not know, I do not want to participate,



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please do not include me in future surveys on this topic, etc) is permissible. The survey should remain open until an 80% response rate is met. Reminders may be used.

- Subsequent iterative surveys. Iterative voting by the same group as described above (after excluding those who do not want to participate) should be completed to narrow down the list of treatment options. The survey should remain open until an 80% response rate is met. Reminders may be used.
- Preparation of the CTPs. The survey responses collected above are used to develop a limited set of CTPs. This may be done with a small group of experts either in face-to face meetings or virtually. The resultant CTPs must be based on the voting results from the membership, and any “clean up” decisions should be made with consensus methods.
- Final CARRA-wide announcement. After complete, the CTPs should be distributed to the entire CARRA membership by survey to ensure dissemination and to solicit preferences for the different CTP options. The survey should remain open until an 80% response rate is met. Final agreement is achieved if at least 75% of the respondents indicate willingness to use at least one of the CTPs described..

Use of accepted consensus methods

- The consensus methods must include collecting input from individuals, controlled feedback of the compiled individual responses to the group, an iterative process so that individuals can change their opinions and quantitative reporting of any resultant voting
- Surveys must be approved by the CARRA CTP Advisory Committee and beta tested prior to dissemination
- Survey response rates must achieve 80%. The following strategies can be used to support achieving this response rate: survey a random subset of the CARRA membership, provide individual and personalized reminders, provide an opt out option.
- Level of consensus will be set at 75% for agreement with CTPs
- Investigators will obtain appropriate approval from a local ethics board of record for all CTP related surveys
- See resources below for description of several consensus methods that can be used

Preparation of a manuscript for publication which includes the following elements:

- The defined disease and patient characteristics intended for treatment with the CTP (as well as those characteristics that are not appropriate for CTP use)
- Updated literature review, including both pediatric and adult studies where appropriate, summarizing gaps in knowledge and best published evidence related to the defined disease and treatments
- Summary of current practice in the CARRA community based on feedback using standardized cases



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- Quantitative results of voting (percent and actual numbers) and dates of surveys and face to face meetings
 - Limited number of final treatment options (CTPs) suitable for evaluating through CER studies
 - Definitions for response variables to assess improvement and worsening
 - Definitions for outcome measures to assess toxicity/tolerability
 - Data collection items necessary to determine patient response and outcome measures
 - Time points for data collection
- ❑ Post-approval
- The CARRA CTP Advisory Committee will review the final manuscript and recommend approval for CARRA endorsement to the Steering Committee who will provide final sign-off prior to submission for publication.

Tracking

All CTP development projects will be tracked from pre-approval to publication by the CTP Advisory Committee with administrative support. A member of the committee will be assigned as the liaison to each project. Investigators will submit brief progress reports using standardized forms to their liaison at the following steps:

- Project plan pre-approval (complete *Pre-approval form*)
- Beta testing and approval of each survey or planned consensus meeting (complete *Survey/consensus meeting pre-approval form*)
- Results of surveys and consensus meeting votes (submit *Survey/consensus meeting log and results form*)
- Review of final CTPs prior to manuscript preparation
- Review of final manuscript

Resources and examples of how to do this

Facilitating face-to-face groups

The Facilitators Toolkit, Tools and Techniques for generating ideas and making decisions in groups, Lynn Kearny

Moderator chapter (see appendix)

Facilitator chapter (see appendix)

Types of Consensus Methods

Nominal Group Technique:



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NGT is an approach for conducting a structured in-person meeting with an orderly system for collecting the group's opinions. It depends on the skills of the facilitator and willingness of the group to work together

Delphi:

First described in 1948. This strategy is used to systematically collect the opinion of experts. It includes conducting a series of anonymous individual surveys. In between the data is collated and returned to the participants. The Delphi is complete when there is convergence of opinions or when you reach the point of diminishing returns. Advantages include flexibility in the number of rounds, no need for in-person polling and it allows for individuals to express their own opinion but still generates the groups consensus at the end. Limitations include the cost associated with having large number of rounds, impersonal process as data is not collected in person.

Example of how to use Delphi for a CARRA CTP project*

1. Assessing treatment patterns in the community: Delphi survey - round 1

Create an "open-ended" treatment survey (for example see Dillman et al) that asks respondents how they would treat the standardized case(s). Respondents include either all, or a representative sample (using a random sampling methodology) of the CARRA membership. Sampling continues until an 80% or higher response rate is achieved.

2. Treatment collation

Under the supervision of an expert panel, the researcher collates the open-ended treatments and classifies them under similar themes, doses, routes, time course, etc. to come up with a smaller, manageable, number of treatments that reflect the similarities in the data originally collected. These might have several treatment strategies that look similar, but that are only slightly different.

3. Rating preferred treatments: Delphi survey - round 2

The collated treatments are re-sent, using the same survey methodology as above, to the same set of respondents. Respondents are asked to rate their preference for the different treatment responses (as applied to the same standardized case) by ranking their top treatment strategies in order. The survey continues until an 80% response rate is achieved.

4. Collation of round 2 responses

The research team, supervised by the expert panel, combines the individual rankings to generate the overall prioritized list of all respondents, which is used for voting in round 3.

5. Delphi survey - round 3

Using the same survey methodology, same respondents, and same response rate (80% at least), the round 2 responses are circulated to the respondents asking them to vote for their top 3 preferences in no particular order. Those treatments that achieve a vote from at least 75% of the respondents will become the CTPs. Those that achieve fewer than 25% will be dropped from further rounds.

6. Delphi survey - additional rounds



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Repeated rounds of electronic surveys with voting will continue, as above, until a modest set of CTPs achieve at least 75% approval. Each previous round will be fed back to the respondents. Ending the survey will be at the discretion of the expert panel.

7. Final CTP production.

An in-person meeting of the expert panel is convened to determine the fine points of the CTPs so that they can be practically applied. A formal nominal group process will be used to achieve consensus of the expert panel.

*Developed by Brian Feldman

References

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Jones J, Hunter D. Consensus methods for medical and health services research. *BMJ : British Medical Journal*, 1995; 311(7001):376-380. PMID: PMC2550437.

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Hansen B, Ombler F. 1000minds Decision-making and Conjoint Analyses Software. 1000minds Ltd., 2003; <https://www.1000minds.com>.

CARRA CTP Development Submission Forms:

CARRA-wide prioritization Form

Project Plan Pre-approval Form

Survey/consensus meeting pre- approval form

Survey/consensus meeting log and results form



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CARRA CTP Development Submission Form: CARRA-wide Prioritization Request	
Date:	Contact person:
Study team:	
CTP Name:	
Prioritization will be based on the following criteria. Please justify each of the following:	
1) Importance of the clinical problem	
2) Lack of adequate available information to guide treatment decisions	
3) Variability in current treatment practice	
4) Ability to collect data necessary to conduct CER, such as through the registry	
5) Sufficient sample size to conduct CER analyses	



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CARRA CTP Development Submission Form: Project Plan Pre-approval Request	
Date:	Contact person:
Study team:	
CTP Name:	
Clinical Problem: describe the clinical problem that you are addressing	
Target population: describe the characteristics of the intended patients for treatment with the CTP. Include "inclusion" and "exclusion" characteristics	
Literature review: describe your strategy for conducting a literature review (dates, key terms, etc)	
Cases: describe your plans for creating cases to solicit feedback on preferred treatment approaches	
CARRA-wide survey: describe your approach for conducting a survey to obtain feedback on the cases from the entire CARRA membership, or a representative sub-group	
Consensus methodology: describe what consensus methods will be used	
Timeline: provide an estimated timeline for the project	

**Attach survey for review*



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CARRA CTP Development Submission Form: Survey / consensus meeting pre-approval request*	
Date:	Contact person:
Study team:	
CTP Name:	
Survey Name:	
Purpose of survey:	
Respondents (who and how many):	
Target date for dissemination:	



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CARRA CTP Development Submission Form: Survey/consensus meeting Log						
Date:			Contact person:			
Study team:						
CTP name:						
Survey/meeting name	Description of Recipients/participants	Number respondents	Date survey opened/meeting held	Date survey closed	Number (%) responses	Summary of results*

*attach summary of survey responses