2ND DISCLOSURE AND TRANSPARENCY FOR CLINICAL DATA SUMMIT

August 13-14, 2018 | The Inn at Penn | Philadelphia, PA

Balance Your Commercial Values and Ethical Responsibilities Through the Vigilant Execution of National and Global Data Transparency
Sharing Aggregate and Individual Results of Clinical Trials with Study Participants

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Disclaimer

• The opinions contained herein are those of the authors and are not intended to represent the position of Brigham and Women's Hospital or Harvard University.

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• We are committed to autonomy in our research and to transparency in our relationships. The MRCT Center—and its directors—retain responsibility and final control of the content of any products, results and deliverables.
Our Mission

Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.

- Academic credibility
- Trusted collaborator
- Independent convener
Outline

1. Different types of data that may be returned in a research study
2. Current practice and opinions about sharing results from study participants
3. Principles, processes and tools for sharing aggregate results and individual results
Different types of data that may be returned in a research study
Overview of data types that may be returned in a research study

A: Urgent Results & Urgent Incidental Findings

C: End of study Individual Results
  • Study Group Assignment
  • 1° Endpoints
  • 2° Endpoints
  • Safety endpoints

B: Routine Results & Non-Urgent Incidental Findings

D: Exploratory Results
  • Includes exploratory endpoints
  • During or after close of study
  • May lead to future research

E: Aggregate Results
  • 1° Endpoint
  • 2° Endpoints
  • Summary of Conclusions

Data types recommended for return, at a minimum, are highlighted in yellow

From: MRCT Center Return of Individual Results to Participants Recommendations Document, Version 1.2, November 2017
Why?
Current practice and opinions about sharing results with research participants
• **EU Parliament Regulation (EU) No 536/2014 (2014):**

  Sponsor of a clinical trial must submit “a summary of the results of the clinical trial together with a summary that is understandable to a layperson, and the clinical study report, where applicable, within the defined timelines.”

• **Do study participants want to receive results?**
  – 90% of study participants want to know the results of their clinical trial\(^1\)
  – 91% never hear back from study staff or sponsor\(^2\)

The MRCT Center designed and conducted 2 studies among study participants

| Study objectives: | • Understand expectations and preferences for sharing aggregate clinical trial results among patients who had received integrative medicine interventions |
| Study populations: | • Study 1: Cancer patients  
• Study 2: Individuals with various medical conditions |
| Questionnaire development: | • Questionnaire developed by MRCT Center, in collaboration with US and Korean colleagues  
• Filled out Template for returning aggregate results from MRCT Center Toolkit for review |
| Dissemination method: | Online survey |
| Data collection period: | Study 1: June 2016  
Study 2: April – June 2017 |
| Response size: | Study 1: n=77 (23% response rate)  
Study 2: n=134 (17% response rate) |
Respondent profile: Sex and Age

Study 1

- 88% Female
- 12% Male
- 67% 51-70 years
- 20% 31-50 years
- 12% 71 years & older
- 1% 18-30 years

Study 2

- 62% Female
- 38% Male
- 52% 51-70 years
- 25% 31-50 years
- 13% 18-30 years
- 9% 71 years & older
Clinical Trial Experience

Study 1

Ever participated in clinical trial?

- 52% Yes (n=38)
- 44% No (n=32)
- 4% Not sure (n=3)

Read or heard anything about results?

- 58% No (n=22)
- 37% Yes (n=14)
- 5% Not sure (n=2)

Study 2

Ever participated in clinical trial?

- 51% Yes (n=63)
- 45% No (n=45)
- 4% Not sure (n=5)

Read or heard anything about results?

- 76% No (n=48)
- 16% Yes (n=10)
- 8% Unsure (n=5)
Should Researchers share the overall results of a study with participants?

**Study 1**
- 90% Yes (n=68)
- 11% Not sure (n=8)
- 0% No (n=0)

**Study 2**
- 89% Yes (n=111)
- 10% Not sure (n=12)
- 2% No (n=2)
Preference for sharing results

Preferred Format for Sharing Results

- Email: Study 1: 45.00%, Study 2: 40.00%
- Website: Study 1: 10.00%, Study 2: 15.00%
- Phone Call: Study 1: 0.00%, Study 2: 0.00%
- Letter mailed to home address: Study 1: 20.00%, Study 2: 15.00%
- In-person meeting: Study 1: 25.00%, Study 2: 20.00%
- Other: Study 1: 20.00%, Study 2: 25.00%
- As long as results are shared, it doesn't matter how: Study 1: 30.00%, Study 2: 35.00%

8/27/2018
Why should researchers share results with participants?

Most frequent themes from both studies:

• Interest in research results
• Ethical expectation

“It'd be interesting to see what the outcomes are for something that you'd personally participated in” (first study)

“As a participant you are lending your body or experience so sharing results in my opinion is a respectful practice.” (second study)
Key Learnings

• Vast majority of integrative medicine patients and research participants think that researchers should share results

• Most clinical trial participants don’t hear about the results of the trial they participated in

• A plurality prefers Email for receiving results
Principles, processes and tools for sharing aggregate results
Return of Individual Results to Participants: Principles

1. Providing individual research results responses to the expressed interests and expectations of
   clinical trial participants and their representatives, and ensuring that these results are communicated
   in a manner that is comprehensible to them.

2. Considerations relating to the return of individual research results to clinical trial participants
   should be integrated into the clinical trial's overall communication plan.

3. The informed consent process should include information about the participants' right to
   receive their research results, which can be delivered by an independent committee that oversees
   the return of these results.

4. If results are offered, participants should be able to choose whether or not to receive these
   results.

5. Participants have the right to request the return of individual research results, which is
   facilitated by an independent committee responsible for communicating these results.

6. The purpose of research in clinical trials is to determine the efficacy and safety of the study
   intervention or approach, and to return individual research results to participants in
   a manner that is comprehensible to them.

7. Return of individual research results should be planned and executed in consultation with
   other stakeholders, including regulatory agencies, ethics review boards, and investigators.
• **Return of Aggregate Results Guidance Document**
  (Version 3.1, November 2017)

• **Return of Aggregate Results Toolkit**
  (Version 3.1, November 2017)

• **Return of Aggregate Results to Participants Principles**
  (November 2017)
What & When?
MRCT Center Return of Results Workgroup Recommendations:

• Before the study starts
  – Establish level / timing / delivery method of sharing study results
  – Update organizational policies, processes, procedures to include return of results
  – Allocate Budget for sharing study results
  – Develop and incorporate sharing of aggregate results into study documents (e.g., informed consent, communication and publication plan)
  – Build staff capacity
Before the study starts

• Protocol development
  – Anticipate that participants will be given an opportunity to receive study results

• Informed consent development
  – Include a general statement that explains the intent to provide study results
  – Example: “In the future, you can decide whether or not you wish to receive the general results of the study. You do not need to decide now about this.”

• Resource planning
  – Discuss and agree upon resources for plain language summary (PLS) sharing execution
During study conduct

- Discuss Informed Consent with participant: process and anticipated timing of aggregate results
- Stay connected with participant; e.g., thank you letter after ICF is signed, letter of appreciation after last visit, annual holiday card, periodic letters explaining stage of the study
- Prepare for participant end-of-study visit: written summary, including opt-in or opt-out for receiving aggregate results; if opted-in, how to access PLS when available
After study ends or all data for primary endpoint concluded

- Develop PLS according to template
- Have PLS reviewed by clinical trial team and medical communications group, and, optimally, internal and/or external reviewers with varied backgrounds
- Identify study participants who agreed to receive PLS and notify them
How?
1. Study name
2. Who sponsored this study?
3. General information about the clinical trial
4. What patients/people were included in this study?
5. Which medicines [or vaccines] were studied?
6. What were the side effects?
7. What were the overall results of the study?
8. How has this study helped patients and researchers?
9. Are there plans for future studies?
10. Where can I find more information about this study?
• A Pilot Study on a Mind-Body Intervention for Irritable Bowel Syndrome and Inflammatory Bowel Disease
Feedback on Template for sharing summary results

**Study 1**
Was summary **helpful** to understand study results?

- 82% Yes (n=62)
- 18% No (n=14)

Was anything unhelpful or unclear?

- 30% Yes (n=23)
- 70% No (n=53)

**Study 2**
Was summary **helpful** to understand study results?

- 94% Yes (n=123)
- 6% No (n=8)

Was anything unhelpful or unclear?

- 16% Yes (n=21)
- 84% No (n=108)
Feedback on Template for sharing summary results (cont.)

Conflicting responses:

• Could be more robust/detailed; explain results better
• Make it more succinct

Some specific suggestions:

• Use graphs
• Add “what does it mean for you”
• Provide a means to answer questions of study participants
• Make it relevant to personal experience
Principles, processes and tools for sharing individual results
• **Return of Individual Results Recommendations Document**
  (Version 1.2, November 2017)

• **Return of Individual Results to Participants Toolkit**
  (Version 1.2, November 2017)

• **Return of Individual Results to Participants Principles**
  (November 2017)
What & When?
What should be shared? Our Recommendations:

- **Urgent Results & Incidental Findings:**
  - Always return as soon as interpreted and confirmed as valid

- **Routine Results & Non-Urgent Findings:**
  - Balance potential benefits against resource requirements

- **End of Study Individual Results:**
  - At a minimum, offer information about study arm assignment and primary endpoints, after study concludes (unless it would compromise the integrity of ongoing studies)

- **Exploratory Results:**
  - Handle on a case-by-case basis

- **Aggregate Results:**
  - Return summary of primary endpoints and safety data, in accordance with applicable law and guidance
When should results be shared? Considerations:

- Has the participant opted in to receive results?
- Are the results analytically valid?
- Does the result have clinical validity?
- Are the results urgent, actionable?
- Does sharing the result impact the integrity of the study?
- Does returning the result comply with institutional policies, legal and national laws, and regulations?
How?
How to share results with participants?

• Considerations
  – Privacy of participant
  – Types of data
  – Access of participants to health care professional
  – Need for interpretation
  – Pros and cons of modalities

• Modalities
  – In-person meeting
  – Telephone/video-conference
  – Online patient communities or portal
  – Confidential letter
Template for Communication of Individual Study Results including Study Arm Unblinding

Which group you were assigned to

[Participants] in the study were put into [#] groups by chance. [If not randomized, list how many patients/people were in each group, and how this was determined.]

___ Group A received [simple explanation of study regimen for first arm, i.e., 100 mg of drug once per day]

___ Group B received [simple explanation of study regimen for second arm, i.e., 50 mg of drug once per day]

___ Group C received a placebo treatment (a sugar pill) once per day.

You were assigned to the Group checked above.
**Summary of individual results**

**Individual Results**

The following table describes your results compared to all the participants in the study. [the specific population that was studied, including age and gender breakdown. Include eligibility criteria, including specific genetic mutations (when appropriate).]

[Research Institution]

[Study Name]

Sample Study Participant Summary Report

Summary report for all participants in the same group you were assigned

<table>
<thead>
<tr>
<th>[Study Name] Participants For Ages [X – XX] Years [Total ( \pm ) xx patients]</th>
<th>YOUR INDIVIDUAL RESULTS</th>
<th>RANGE [the lowest and highest “normal” value]</th>
<th>MEAN [the average value for all participants in the group]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Endpoint 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Secondary Endpoint)*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Who?
Who should receive results? Who should share results?

Axes of Communication for return of individual results

- Sponsor (if applicable)
- Principal Investigator
- Study participant
- Primary Care Physician / Personal Physician
- Website
National Academies of Medicine
Guidance and
Summary
NAM Guidance agrees with MRCT Center recommendations:

- Respect for Persons/Autonomy
- Promote and safeguard the well-being of research participants
- Return clinically actionable results
- Maintain the integrity of the research
- Decisions vary on study-by-study basis
- Planning for return of individual results
- Setting participant expectations in the informed consent process
- Identify the appropriate communication modality

• Released July 10, 2018
• Refers to MRCT Center recommendations more than a dozen times
NAM Guidance offers additional emphasis on:

- Decision-making framework with feasibility and value dimensions
- Need for quality management system
- Need to harmonize federal regulations by reshaping legal and regulatory landscape
- No recommendations by types of data
Summary

• Decide what results to share and plan for it

• Utilize available resources

• Realize that most study participants do not receive results, but want to – what can you do to change this?
Comments, questions and discussion

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Go to “Resources” – “Return of Aggregate Results” and “Return of Individual Results”