
The New World of Transparency for Clinical Trial Results
Return of aggregate research results to participants

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Disclaimer

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

• Rationale for returning aggregate results to participants

• Return of Results Guidance Document
  – Process flow of returning results
  – Methods for returning results
  – Content of results summaries
  – Numerical literacy

• Return of Results Toolkit
  – Templates for communicating study results
  – Neutral language guidance
  – Endpoint table
Rationale for returning aggregate results to participants
## Patient/Participant Perspective in the U.S.

<table>
<thead>
<tr>
<th>Patients / Study Volunteers</th>
<th>Research Professionals</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 90% want to know the results of their clinical trial&lt;sup&gt;1&lt;/sup&gt;</td>
<td>• 98% of study staff would like to provide results to their volunteers&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>• 91% never hear back from study staff or sponsor&lt;sup&gt;2&lt;/sup&gt;</td>
<td>• 95% of research ethics board chairs strongly support (Canadian survey)&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>• If not informed, 68% would not participate in future trials&lt;sup&gt;3&lt;/sup&gt;</td>
<td></td>
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</tbody>
</table>

Declaration of Helsinki –

Ethical Principles for Medical Research Involving Human Subjects

Paragraph 26:

All medical research subjects should be given the option of being informed about the general outcome and results of the study.


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.”

**Article 37:** Irrespective of the outcome of a clinical trial, within one year from the end of a clinical trial in all Member States concerned, the sponsor shall submit to the EU database a summary of the results of the clinical trial.

**EU Requires posting laypersons summary to EU Portal beginning in 2017**
Multi-Regional Clinical Trials Center Response
Return of results: MRCT Center workgroup

**Academic/Medical Center:**
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Mark Barnes - Ropes & Gray, LLP / MRCT Center
Barbara Bierer - Brigham & Women's Hospital/MRCT
Assunta De Rienzo - Brigham & Women's Hospital
Alla Digilova – MRCT Center
Rebecca H Li – MRCT Center
Holly Fernandez Lynch - Harvard Law School
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Amish Shah - MRCT / Harvard Law School
Zachary Shapiro – MRCT/ Harvard Law School
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**Industry/Trade Associations:**
Salvatore Alesci – PhRMA
Richard Bergstroem – EFPIA
Elizabeth Garofalo - Novartis Pharma AG
Laura Hagan - Merck Serano
Sandra Hayes-Licitra – Johnson & Johnson
Angelika Joos – Merck Sharp & Dohme
Barbara Kress – Merck
Sarah Larson – Biogen Idec
David Leventhal – Pfizer
Craig Lipset – Pfizer
Laurie Myers – Merck (CO-CHAIR)

**Institutional Review Boards:**
David Forster - WIRB Copernicus Group
Mary Oster – NE IRB
Jim Saunders - NE IRB

**Nonprofit:**
Behtash Bahador – CISCPR
Phyllis Frosst - Personalized Medicine Coalition
Zach Hallinan – CISCPR
Marc Wilenzick – International AIDS Vaccine Initiative

**Patient Advocates:**
Nicola Bedlington – European Patients Forum
Deborah Collyar – PAIR (COCHAIR)
David Haerry – European AIDS Treatment Group
Cheryl Jernigan - Susan G. Komen
Yann LeCam – EURODIS
Marcello Losso - HIV RAMOS
Jane Perlmutter – Gemini Group

**Research/Consulting Firms:**
Barbara Godlew - The FAIRE Company, LLC
Pierre Gervais - QT Research
Paulo Lacativa - CCBR Clinical Research
David Walling – Collaborative NeuroScience
Goals

• Develop standards and best practices.
• Ensure principles are respectful of global cultural expectations.
• Address perceived barriers to widespread implementation.

Rationale:

Returning results allows sponsors and investigators to recognize and honor the essential contributions and volunteerism of clinical trial participants. Expectations of academic, industry, not-for-profit sponsors similar. Returning results is a key aspect of improving transparency and increasing public trust.

Scope:
Communication and dissemination of summary research results to individual participants.
The MRCT Center Tools

An **ROR Guidance Document** for groups wishing to return results including:

- Logistics and detailed processes for results sharing
- Content of research result summaries
- Cultural and health literacy considerations
- Timing
- Special considerations


An **ROR Toolkit** including:

- Templates for Phase 1, 2 & 3, studies ending early
- Neutral language guide
- Endpoints language guide
- Ethics Committee Checklist

http://mrctcenter.org/resources/2015-10-02-template-mrct-ror-toolkit-version-2-0/
Process Flow for Returning Results

• Pre-Study preparation
  • Include data transparency in organizational preparation, policies, processes
  • Establish level/timing/delivery
  • Resource planning

• Protocol Development
  • Offer participants an opportunity to receive study results
  • Include a section on returning results in ICF

• During study conduct
  • Consider letter of appreciation
  • Prepare for last study visit of participant
  • Keep intermittent engagement with participant thereafter

• When study ends
  • Prepare and review summary document
  • Adhere to global regulatory framework and health literacy principles
Methods of returning aggregate results

• **To Whom:**
  All participants who have been enrolled and agreed to receive results

• **Several Methods of Return:**
  • Internet based methods (flexible, cost-effective, current, security may be important)
  • Interactive methods (e.g., face-to-face meeting(s), telephone call(s), two-way online meeting(s), dynamic email exchange, etc.)
  • One-way communications (e.g. video summary, automated phone message, printed materials)

**Timing**

• Within 1 year of completion or ‘end of study’
Participant Clinical Trial Results Summaries - Content

• Thank You
• Title of the study
• Why the study was done
• Study information (patient population, drugs, start & end date, countries)
• How the study worked (how participants were divided into groups)
• Side effects
• Summary of results
• Final comments (official study title, where to get more information)
Participant Clinical Trial Results Summaries - Process

- Unbiased and not promotional
- Reviewed by independent and objective editor(s) and patient representative(s)
- Plain language (sixth-eight grade reading level) and apply health literacy principles. Health and numeracy principles applied.
- Translation into additional languages consistent with translations of informed consent
- An individual from the study site or neutral informed third party should be available to answer questions for participants
- Provisions should be made for vulnerable populations and other instances
- Consideration as to whether to, and whom to, inform in the event of a participant’s death
Numeracy or Mathematical Literacy

14%
Or
About 1 in 7
Template for Communication of Study Results

**SPONSORS**: This template helps create clear summaries of clinical trials. Replace the [guidelines in red brackets] with your text; delete this heading.

[If written to study participants, include the following:]

*Thank you for participating in this study.*

You and other volunteers helped researchers answer important health questions.
Here we describe the results of this study.

[If written for the general public, start here:]

This summary was completed on [month/year]. Newer information since this summary was written may now exist. This summary includes only results from one single study. Other studies may find different results.

**Phase 1 Study**

*This study searched for a safe dose of [interventions/treatments] for people with [disease/condition].*

[Place a simple title for the study in the box above. Sponsors may consider using the same simple title as in the registry. If drug names are used, list both generics and also where brand names® can be found.]

**Phase 2 and 3 Studies**

*This study compared [interventions/treatments] for people with [disease/condition].*

[Place a simple title for the study in the box above. If drug names are used, consider including both generic and brand names®. If brand names are not used, help participants find brand names elsewhere.]

**Why the study was done**

**Phase 1 Study**

This was the first time this [treatment/drug/device/intervention] was studied in humans. This study was done to find the highest [dose/amount] of the drug/treatment that people could take without having severe side effects. Side effects include unexpected medical...
### Neutral Language Guide

<table>
<thead>
<tr>
<th>Language to avoid</th>
<th>Language to consider</th>
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<tbody>
<tr>
<td>This study proved...</td>
<td>This study found that... This does not mean everyone in that group had these results.</td>
</tr>
<tr>
<td>This study proved that using &lt;drug A&gt; to prevent &lt;disease/condition&gt; is effective.</td>
<td>This study found that people with &lt;disease/condition&gt; who got &lt;drug A&gt; had &lt;primary endpoint&gt;.</td>
</tr>
<tr>
<td>This means that &lt;Drug A&gt; is better than &lt;Drug B&gt;.</td>
<td>In this study, people who got &lt;drug A&gt; had more &lt;study endpoint&gt; than some people who got &lt;Drug B&gt; with the same health conditions.</td>
</tr>
<tr>
<td>&lt;Drug A&gt; works better than &lt;Drug B&gt;, but some people didn’t tolerate it as well.</td>
<td>In this study, more people received or were treated with &lt;study endpoint&gt; with &lt;Drug A&gt;. They also had more side effects that interfered with their daily lives, like &lt;list specific adverse events&gt;.</td>
</tr>
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Similar principles have been suggested by TransCelerate BioPharma: 
*Recommendations for Drafting Non-Promotional Lay Summaries of Clinical Trial Results*
## Endpoint Descriptions and Examples

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<tr>
<td>Composite</td>
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<tr>
<td>Dose Escalation</td>
</tr>
<tr>
<td>Mortality</td>
</tr>
<tr>
<td>Morbidity</td>
</tr>
<tr>
<td>Progression-free survival (or disease-free survival)</td>
</tr>
<tr>
<td>Patient-Reported Outcome on symptoms or functions (e.g., pain)</td>
</tr>
<tr>
<td>Exploratory Biomarker / Pharmacogenomics</td>
</tr>
<tr>
<td>Prevention or incidence endpoint</td>
</tr>
<tr>
<td>Non-inferiority endpoints</td>
</tr>
<tr>
<td>Surrogate</td>
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## Endpoint Descriptions and Examples

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<tr>
<th>Endpoint</th>
<th>Description of the type of endpoint</th>
<th>Example in simple, plain language</th>
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<tr>
<td>Composite</td>
<td>A composite endpoint, as the primary endpoint, combines multiple outcomes (e.g. death, getting sick again (relapse), serious event) and test results into one measure of how well the drug/therapy/device works. This is useful when there are many different outcomes that can happen during a trial. This can also be called a combined or multi-part endpoint.</td>
<td>“The XXX study measured [patients/people] to see if those in Group A (ABC treatment) or Group B (XYZ treatment) lived longer, had fewer heart attacks, or fewer hospital visits for heart failure. These events were measured together (combined) because each one is quite rare. Researchers also wanted to see if the drug worked in patients who had all 3 conditions. The study found that there was no change in the number of events for [patients/people] in Group A or Group B.”</td>
</tr>
<tr>
<td>Dose Escalation</td>
<td>Dose escalation is used in phase 1 studies to measure safety. People in the study start with a low dose of the medicine (drug). If that dose does not cause safety problems, then more people are given a higher dose until there are too many side effects. The highest dose that is tolerated is called the maximum tolerated dose (MTD) or dose limiting toxicity (DLT).</td>
<td>“This study was done to find the highest [dose/amount] of treatment that people could take without having too many side effects.”</td>
</tr>
</tbody>
</table>
Special Considerations

- Trials that close early
  - Futility
  - Efficacy
  - Safety
  - Low accrual
- Observational, long-term follow-up, and extension studies
- Notification of results to a 3rd party designated by the participant
- Vulnerable populations
- Legally Authorized Representatives and other designated parties
- Return of Results in the event of participant death
- Assent for Return of Results to Children
- Complexities of the Global Context
Summary

- Return of results may become the expectation and practice in clinical research.
- Funding for return of results should be provided as an anticipated component of human subjects research.
- If similar to the U.S. studies, research participants worldwide may want to receive information about the clinical trial to which they participated.
- Logistics, Content, Process and Standard methodologies and approaches must be delineated for populations inside and outside of US, UK and EU.
Next Steps

• Return of individual level results (incidental findings, results of study arm, clinical and research findings)
• Return of results in integrative medicine
• Adoption of guidance for non-Western cultures
• Return of aggregate results
  – Apply principles of guidance to a number of studies, collecting feedback from participants as to comprehension and preferences
Comments, questions and discussion