



**MULTI-REGIONAL
CLINICAL TRIALS**

THE MRCT CENTER OF
BRIGHAM AND WOMEN'S HOSPITAL
and HARVARD

Sharing Summary Level Study Results with Participants: Current Landscape

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- I have no financial conflicts of interest.
- I am, however, biased. I believe that we should be offering to return results to participants, patients, and people unless there is a justifiable and continuing reason not to.





MRCT Center is an applied research and policy center focused on addressing the conduct, oversight, ethics and regulatory environment for clinical trials around the world.

What is Return of Results?

In the context of clinical research, the topic of “return of results” refers to the process of giving participants:

Plain Language Summaries: an overall, understandable report of what the study found and how individual participation contributed to the creation of generalizable knowledge.

Individual Results and Data: personal data that was collected throughout the study.

Only discussing
Return of Summary Results
today

Why give participants their results and data?

- Participant request and expect to learn the results of their participation
- Fulfilling that expectation supports transparency and trust
- Return of summary results is:
 - Concordant with ethical principles
 - *Justice*: people have a right to their own data and information
 - *Beneficence*: research should maximize the possible benefits to participants
 - *Respect for Persons*: honor and acknowledge participant contributions to science
 - Consistent with international standards
 - Compliant (actually, not non-compliant) with federal regulations

International guidelines support the return of results

➤ **ICH E6(R3) Annex 1: Good Clinical Practice Guidelines**

Paragraph 2.9.3 “Where relevant, the investigator should inform the participant about the trial results and treatment received when this information is available from the sponsor after unblinding, with due respect to the participant’s preference to be informed.”

➤ **World Medical Association Declaration of Helsinki (2024)**

Paragraph 26: All medical research subjects should be given the option of being informed about the general outcome and results of the study.

➤ **CIOMS (2016)** (Appendix 2. Obtaining informed consent: essential information for prospective research participants)

Paragraph 6: that, after the completion of the study, participants will be informed of the outcomes of the research in general, if they so wish;



Regulations

- **US federal laws** require listing aggregate results of many studies on ClinicalTrials.gov (but not in plain language)
- **Revised Common Rule addition 45 CFR 46.116(c)(8)**
“A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.”
- **EU Parliament Regulation (EU) No 536/2014 (2014):**
The 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.”
 - Timelines are defined as “12 months after the study ends unless delay is scientifically justified.”

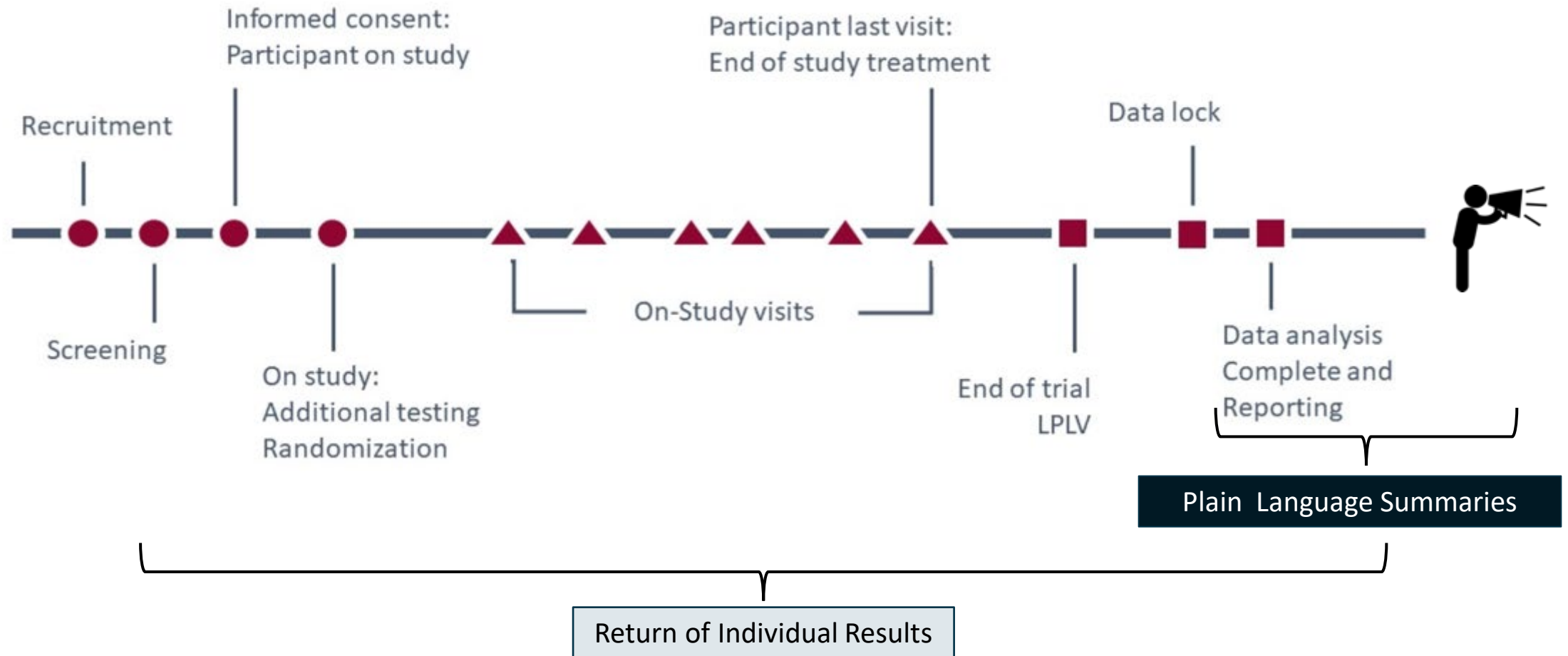
Article 37:

“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.”

<https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-regulation>

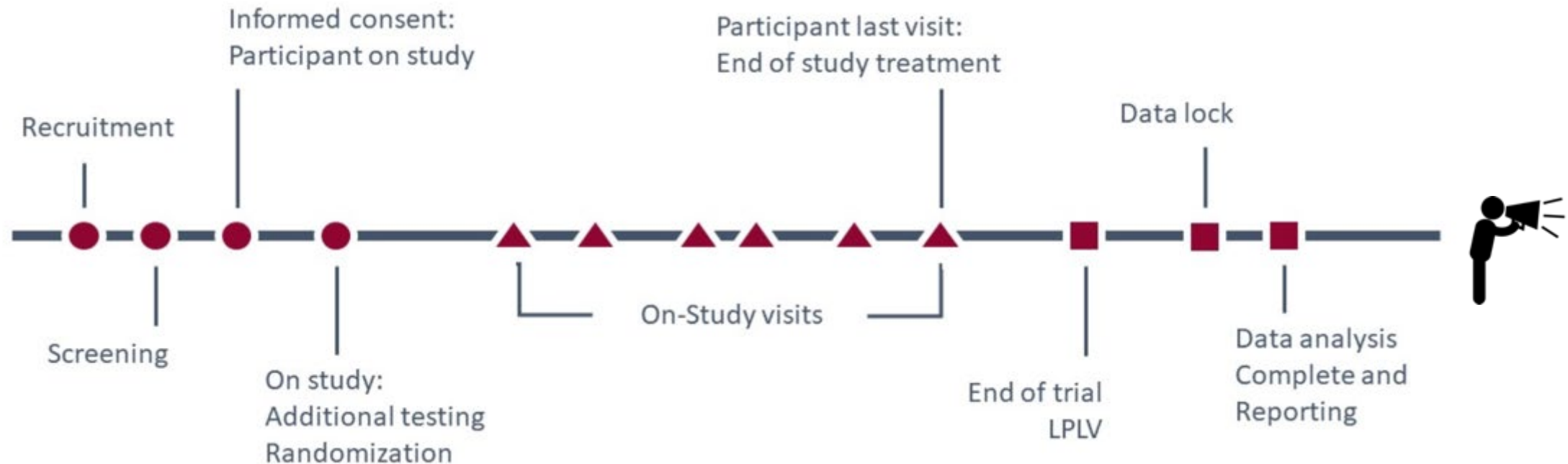
Return of Study Results and Data: The Participant Journey

Returning aggregate results begins with commitment and requires planning



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Find out early what participants most want to learn through the research.

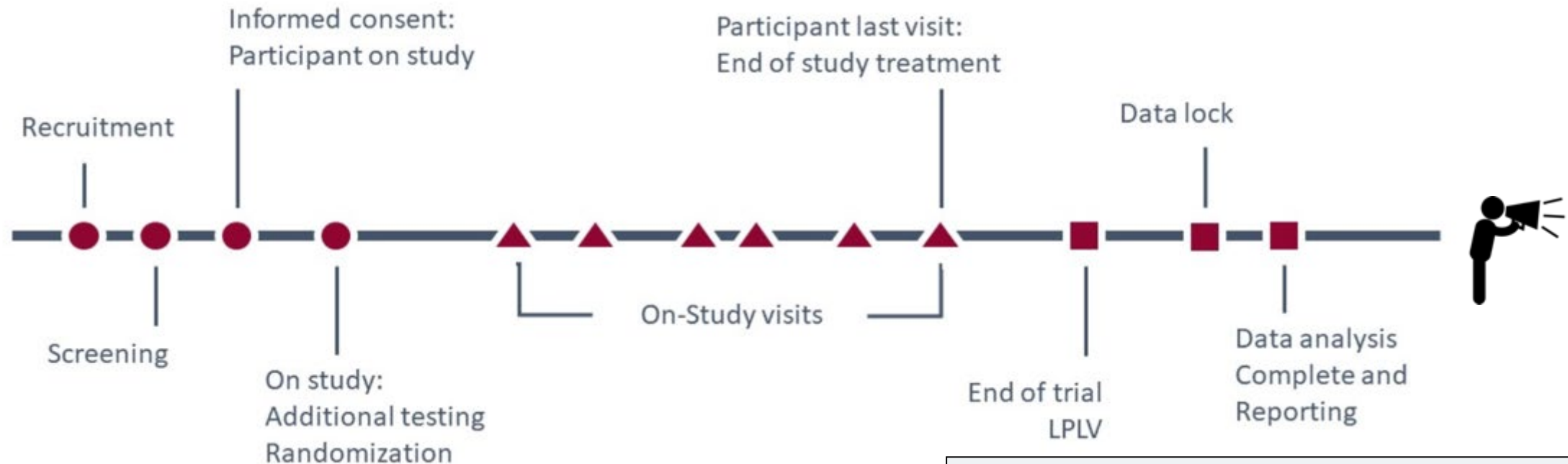
Get input on what, when, and how to return results to the participants, caregivers, communities, and public

Keep track of study issues and findings that may be important to address in the results summary

Collect feedback on the summary itself before it is posted/distributed widely. Learn from experience

Return of Study Results and Data: The Participant Journey

Returning aggregate results begins with commitment and requires planning



- Address whether, what, who, when, and how to return PLS
- (IRB review and approval of plan)

When, how, what

- Introduce plan to participants
- Manage expectations
- Engage and communicate

Who, how

- Prepare PLS aligned with original plan, IC, CSR, manuscript and communications
- Website/individual outreach through PI/sites
- Follow up if needed

When, how, what

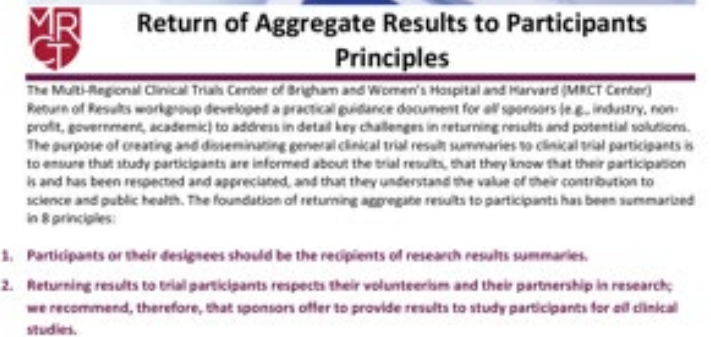
MRCT Center Return of Aggregate Results Guidance and Toolkit



Return of Results Guidance Document

<http://mrctcenter.org/wp-content/uploads/2017/03/2017-03-20-MRCT-Return-Aggregate-Results-Guidance-Document-3.0.pdf>

Process flow of returning results
Methods for returning results
Content of results summaries
Health and numerical literacy



Return of Results Toolkit

<http://mrctcenter.org/wp-content/uploads/2017/03/2017-03-13-MRCT-Return-of-Aggregate-Results-Toolkit-3.0.pdf>

Templates for communicating study results
Neutral language guidance
Endpoint table
Useful checklist

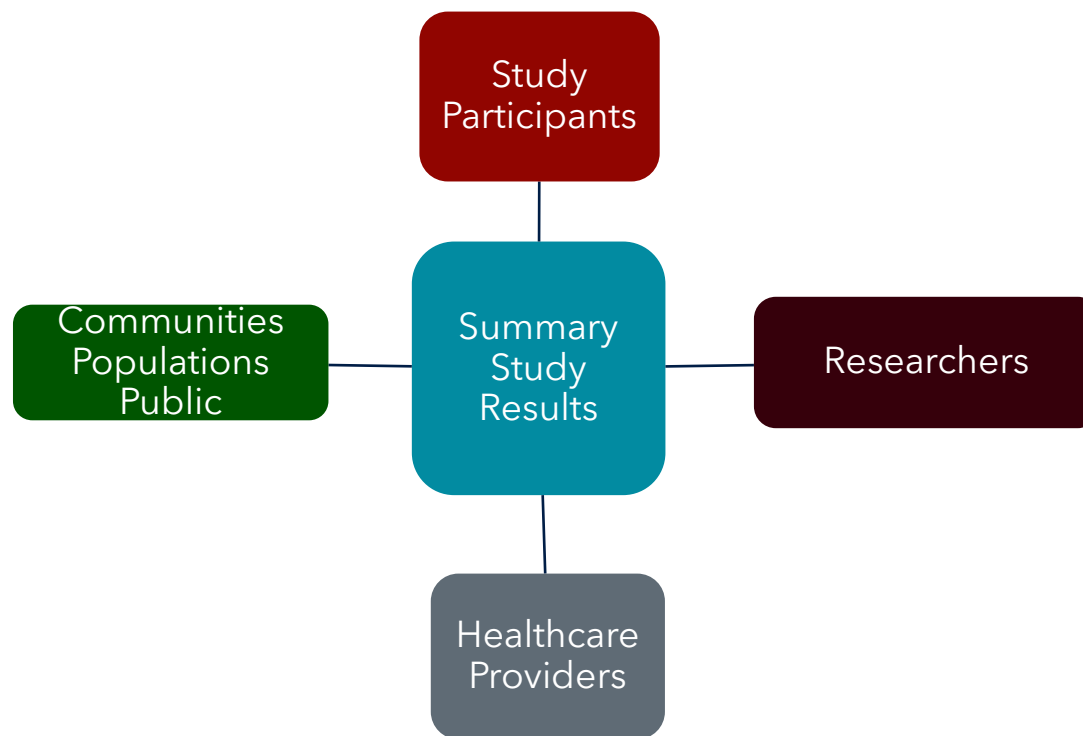




Audiences for research results



Summary Results



The process of returning aggregate results to participants

- Does the participant know they will receive results and/or know where to find them?
- Does the study team have a method to return (and/or contact info)?
- Are there others that the participant gave permission to share the results with?
- Is there a chance that the results could be sensitive or difficult to communicate?
- What method(s) will be followed to return the results?
- Does returning the results comply with institutional policies, legal and national laws, and regulations?

Role of HRPP and IRB

- Advocating for and respecting participants, resource to study team, and educators
- Convey the expectation of return of PLS to participants in the study protocol and/or consent form
- Reviewing the return of results plan
- If the plan is unchanged, no need to review or to review the PLS itself as the study will be closed.

Understanding the perceived barriers

- Content and Comprehension
 - What do patients and participants want to know? Do they understand the implications and, if not, whose responsibility is it to enhance understanding?
- Practical Considerations
 - What, when, who, where, and how
 - Consistency of communications
 - For research other than interventional research
- Logistics
 - Methods, methodologies, and their implications
 - Costs
- Oversight, compliance, and enforcement

Understanding the perceived barriers

- Content and Comprehension
 - What do patients and participants want to know?
 - Primary outcome versus secondaries? Exploratory versus hypothesis-generating?
 - Patient-reported outcomes? Safety measures?
 - Other
 - Do they understand the implications and, if not, whose responsibility is it to enhance understanding?
 - Is assessment of comprehension expected, or is that a bridge too far?
 - Is the audience only participants and patients?
 - Caregivers, families, loved ones?
 - Populations? Communities, however defined?
 - The public?
 - Important to have consistency of communication, and of the summary itself
 - One pre-defined author of results summary, many authors, any author?
 - Must participants/patient communities vet the PLS or at least be in plain language?
 - Sponsor versus PI versus lead author of a publication?

Understanding the perceived barriers

- Practical Considerations: What?
 - Are there times, situations, or conditions in which summary results should not be returned?
 - Are there populations or communities to whom special considerations apply?
 - Are there exceptions to an NIH policy that should be considered as a policy matter?
 - Should there be a process for exceptions, and if so, what would that process be?

 - What do participants, communities, and the public want to know?
 - Beyond primary outcomes, what else about the entire study is relevant to return?
 - What study elements should be required (versus suggested) to be returned?
 - How does one ensure that the summary is fair, balanced, and not selective?
 - Does the PLS content need to be pre-defined, and if so, when, who, and how?

 - Does the study need to be completed to return results? Will that impact the “what?” is returned?
 - Master protocols, adaptive trials, interim results? Other?
 - Social behavioral/psychiatric/population-specific conditions?
 - How does one ensure information consistency?

Understanding the perceived barriers

- Practical Considerations: When?
 - What timeframe is appropriate as a requirement (versus a guideline) for return?
 - Is there a maximum time (e.g., 12 months adult, 6 months pediatric) and is that after study data-lock, study end, or some other set point?
 - What triggers for the timeline should exist (e.g., with publication, study close out, other?)
 - Are there situations or variables that would modify the timeline?

Understanding the perceived barriers

- Practical Considerations: Who?
 - Should the “who” be specified? If not, how does one ensure consistency of information?
 - Who develops the summary and who communicates it to the participant, community, and public?
 - Is “posting” sufficient or other form of impersonal communication or is human interaction important?
 - Generally, the study is over, and the study team may be disbanded. Then what?
 - Role of the healthcare provider or the sponsor, if one exists?
 - Who will answer questions in follow-up? And is that necessary or elective?
 - Does one need personal interaction or is a one-way communication sufficient?
 - Are there unique considerations for special populations (e.g., pediatrics)?
 - Are there unique considerations in a multi-site (multi-national) trial?
 - Outside of a clinical trial, who is responsible for sharing information? In an epidemiology study or a study using biobanked materials?
 - Are there any situations when we would opt not to return?
 - Who else should be considered? (HCP, family, parent, caregiver, etc).
 - Focus here has been (largely) on clinical interventional research. Are there different implications for the “who” in other settings?

Understanding the perceived barriers

- Practical Considerations: Where and How?
 - Should the “where and/or how” be specified or elective?
 - If the “where and/or how” is not specified, will the summary be findable?
 - Given variability in participants, communities, and the public, what considerations should be discussed in the NIH policy?
 - Should the summary be posted, or alternatively, are there settings or conditions where the results should *not* be posted? Is the public always entitled to the results, and if not, why not?
 - How should the results be made accessible?
 - What should be specified:
 - Plain language
 - Translation
 - Accommodations for disabilities
 - Other
 - If AI is used to generate the PLS, is privacy and confidentiality preserved?
 - Which human being remains responsible?

Understanding the perceived barriers

- Content and Comprehension
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Summary

Returning results is a participant expectation, ethical imperative, and should become a regulatory expectation beyond the required reporting of results on www.clinicaltrials.gov

Logistical and operational challenges are surmountable.

Help the NIH develop a policy that is fit-for-purpose, practicable, sustainable, and helps promote trust in the research enterprise.



OSP Website:



<https://osp.od.nih.gov/policies/return-of-research-results#tab2/>



Thank you
and
Thank you, NIH.

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