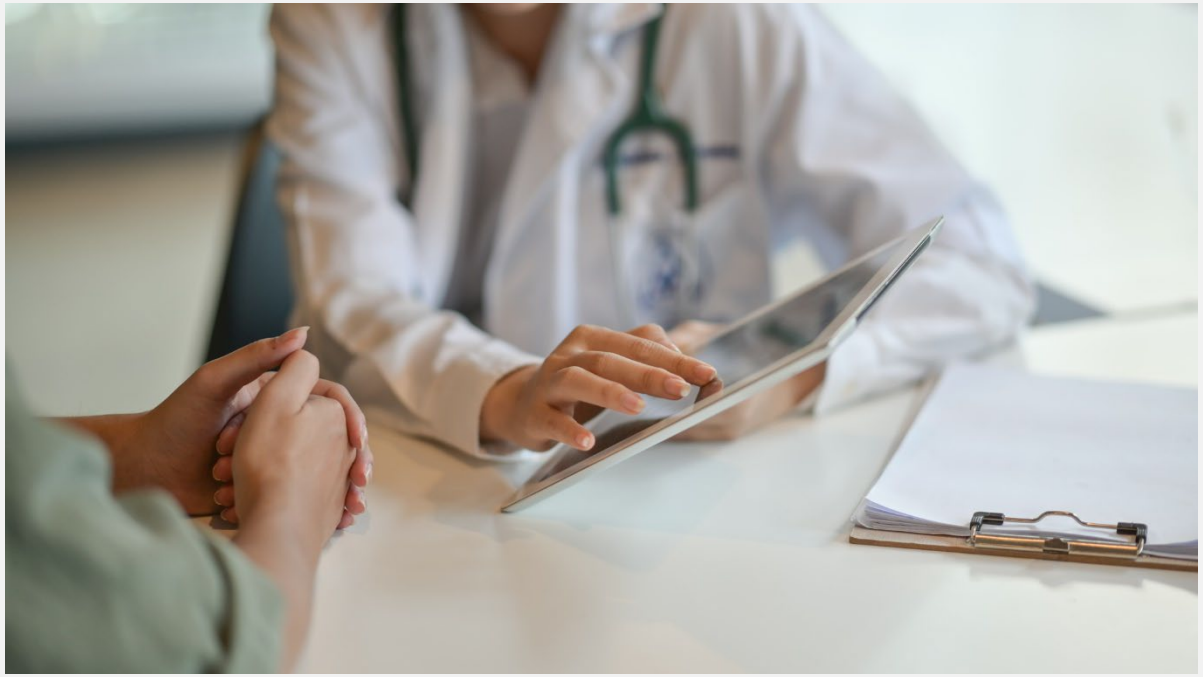
Launching the Return of Individual Research Results (IRR) Project & Website

The webinar will begin shortly

Thank you to the taskforce members who contributed to this project:

- Sylvia Baedorf Kassis
- Barbara Bierer
- Linda Coleman
- Anna Kang Liu
- David Leventhal
- Megan McBride
- Lisa Murray
- Nancy Levitan Poorvu
- Sandra Prucka
- Kate Robins
- Jessica Scott
- Jamie Tyrone
- Carol Weil
- Sarah White



MULTI-REGIONAL CLINICAL TRIALS

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

Return of Individual Research Results (IRR) Website Launch Webinar

MODERATOR
Lisa Murray
MRCT Center
Project Manager

GUEST SPEAKER
Jamie Tyrone
Patient Advocate

INTRODUCTION
Barbara Bierer
MRCT Center
Faculty Director

24 March 2022
1-2 pm EDT
https://mrctcenter.org/

Session Agenda

- MRCT Center Introduction
- Importance of Returning Individual Research Results (IRR)
- Evolution of this work
- Remarks from Jamie Tyrone, Patient Advocate
- Review of project update
- Website Demo
- Q&A

MRCT Center

The MRCT Center is a research and policy center focused on addressing the conduct, oversight, ethics and regulatory environment for clinical trials.

Brigham and Women's Hospital
Founding Member, Mass General Brigham

HARVARD UNIVERSITY

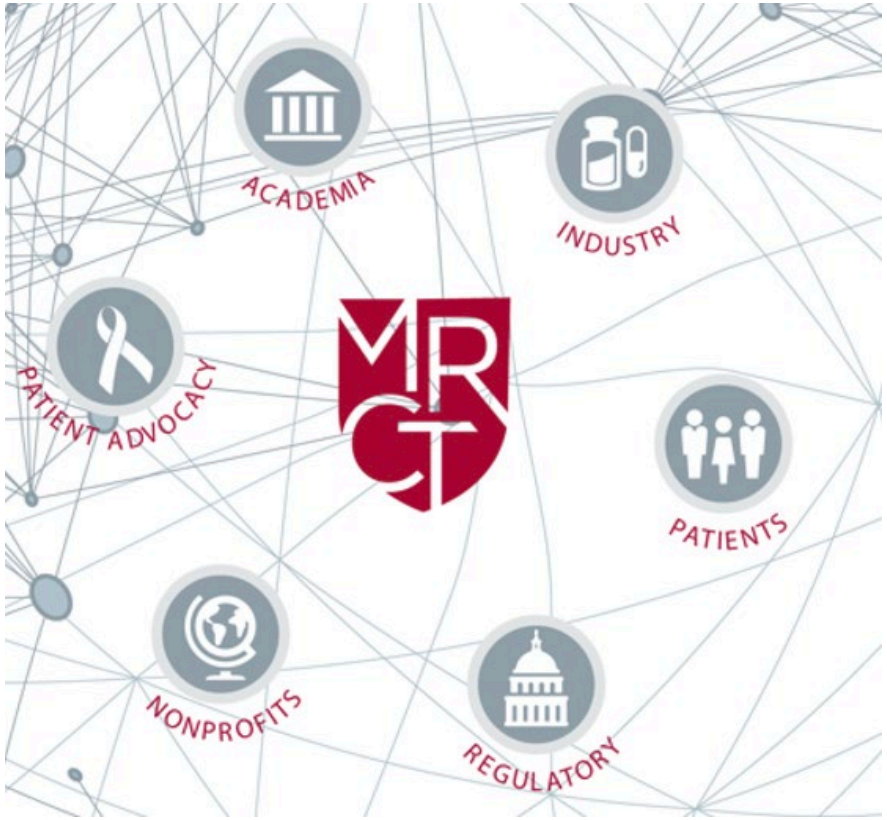
MRCT Center

Our Vision

Improve the integrity, safety, and rigor of global clinical trials.

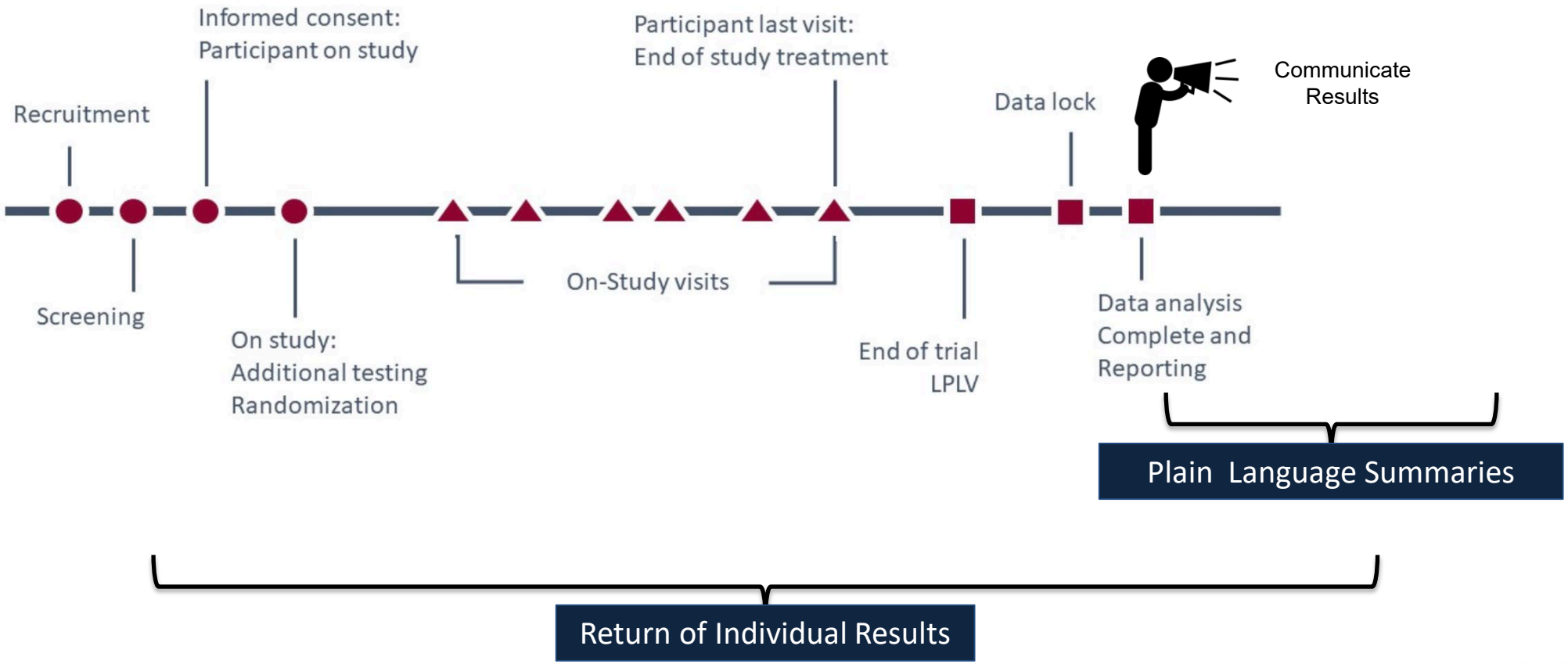
Our Mission

We engage diverse stakeholders in the research enterprise to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.



Framework

Decision to return aggregate and individual results begin with commitment at study design, requires planning, and embodies respect



Privacy, Confidentiality, Security, Data Utility

Defining Individual Research Results (IRR)

IRR **is**:

Any data or test result from a research study that is specific to an individual, such as study arm assignment, lab results, or genetic sequencing data

IRR **is not**:

Aggregate results, plain language summaries, or lay summaries that provide study participants with overall findings of a research study

The Importance of Returning IRR

Research participants consistently desire and expect to receive both individual and aggregate research data from the research studies in which they have participated

Expectations about data transparency and ownership are evolving in society; returning IRR anticipates and responds to those expectations

Foundational ethical principles in research can and should be applied to the return of IRR to participants

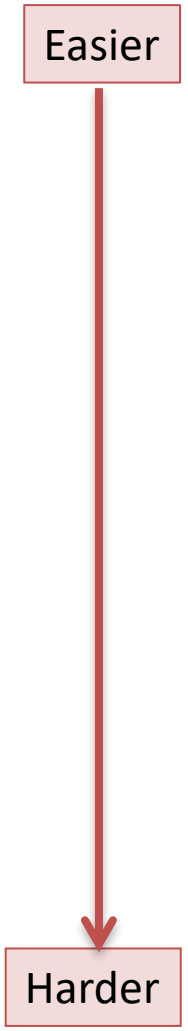
The MRCT Center's IRR Initiative – Version 1 Background

Version 1, Released in 2017

- Strong case was made for the ethical imperative of returning IRR
- Introduced classification of result types based on timing, actionability, etc.
- Robust set of considerations for returning genetic information
- Presented as a starting point for external stakeholders to build upon

Spectrum of results to return to participants:

- Aggregate research results (plain language summaries)
- Assignment to and results of study arm
- Routine clinical results performed in the course of research
  - Urgent
  - Actionable
  - Personally valuable
  - No known implications
- Incidental findings discovered in the course of a clinical trial
  - Of potential clinical significance or actionable
  - Of uncertain significance
- Research results
  - Of likely or uncertain significance
  - Of potential proprietary importance
  - Genetic/genomic results
- Other results



What 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?
- Are the results of personal utility?
- Does sharing the result impact the integrity of the study?
- Does returning the result comply with institutional policies, legal and national laws, and regulations?

Remarks from Jamie Tyrone, Patient Advocate

The MRCT Center's IRR Initiative – Expansion and Update

Need for an update:

- Identified the need for practical, implementation-based resources
- Update/expansion of certain recommendations

IRR Taskforce:

- Convened 10-person taskforce to update the original materials and overall project
  - Included representation from industry, academia, IRB/HRPP, government, and patient advocates
- Objectives:
  - Find **common problems and barriers** throughout the process of returning IRR
  - Provide guidance/resources to help organizations **address and overcome barriers**
  - **Promote the value** of organizations to prepare for and prioritize returning IRR

The MRCT Center's IRR Initiative – Version 2

Challenges Identified

- Perception of a high barrier to entry
- Concerns around liability/fear of the unknown
- Unclear differentiation of responsibilities between and among stakeholders
- Absence of regulatory requirements or guidance on what to return, when, and how
- Difficulty in achieving buy-in throughout the organization

Solutions Created for Version 2 Release

- Guidance on getting started and planning for a gradual progression
- Roadmaps to clarify stakeholder roles and responsibilities
- Re-classification of result types to frame the return of IRR
- Guidance on how to create a return of IRR plan
- Specific tools for implementing the return of IRR
- Topics to review common concerns/complexities with returning IRR

Intended Audience

Research Sponsors

Those developing treatments and financing clinical trials.

SEE ROADMAP

IRBs & HRPPs

Those providing ethical reviews of research or managing human research protections programs.

SEE ROADMAP

Study Staff & Investigators

Principal Investigators, study team members, and staff at research sites.

SEE ROADMAP

Patients & Participants

Those participating in or considering clinical trials, and their family members/caregivers.

SEE ROADMAP

The MRCT Center invites review, comment, and suggestions for revision from all stakeholders to MRCT@bwh.harvard.edu

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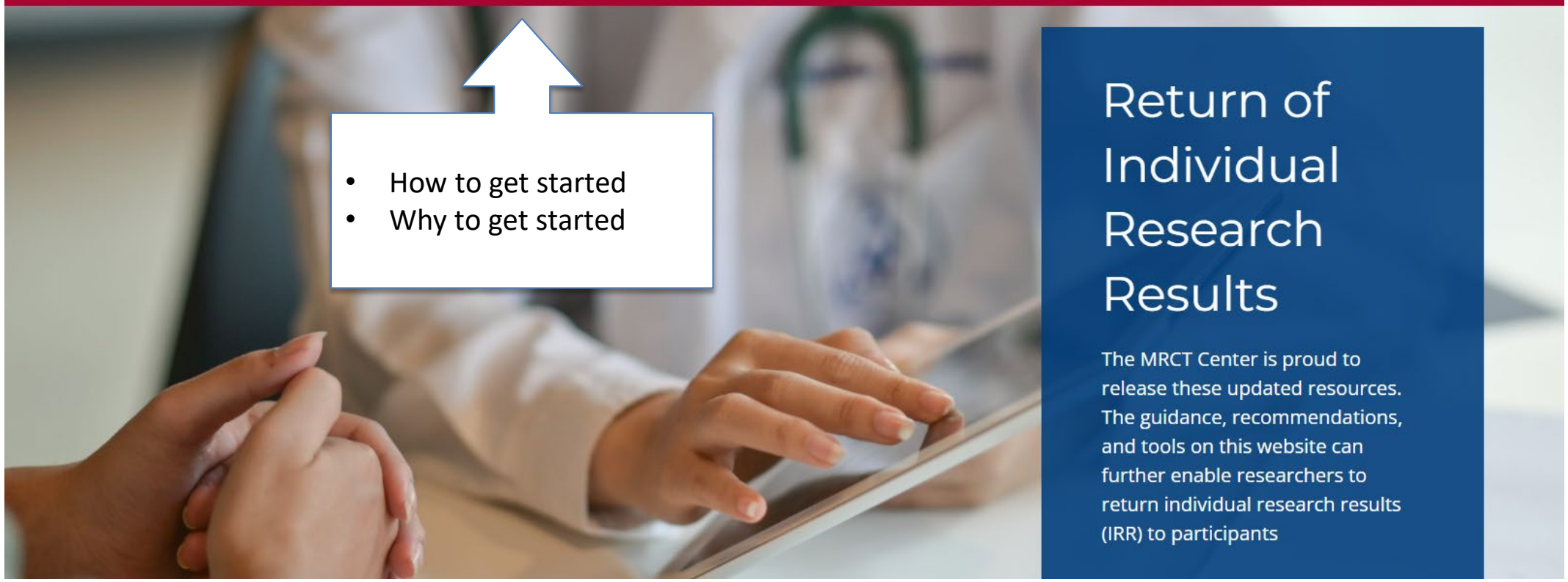
RETURN OF INDIVIDUAL RESEARCH RESULTS

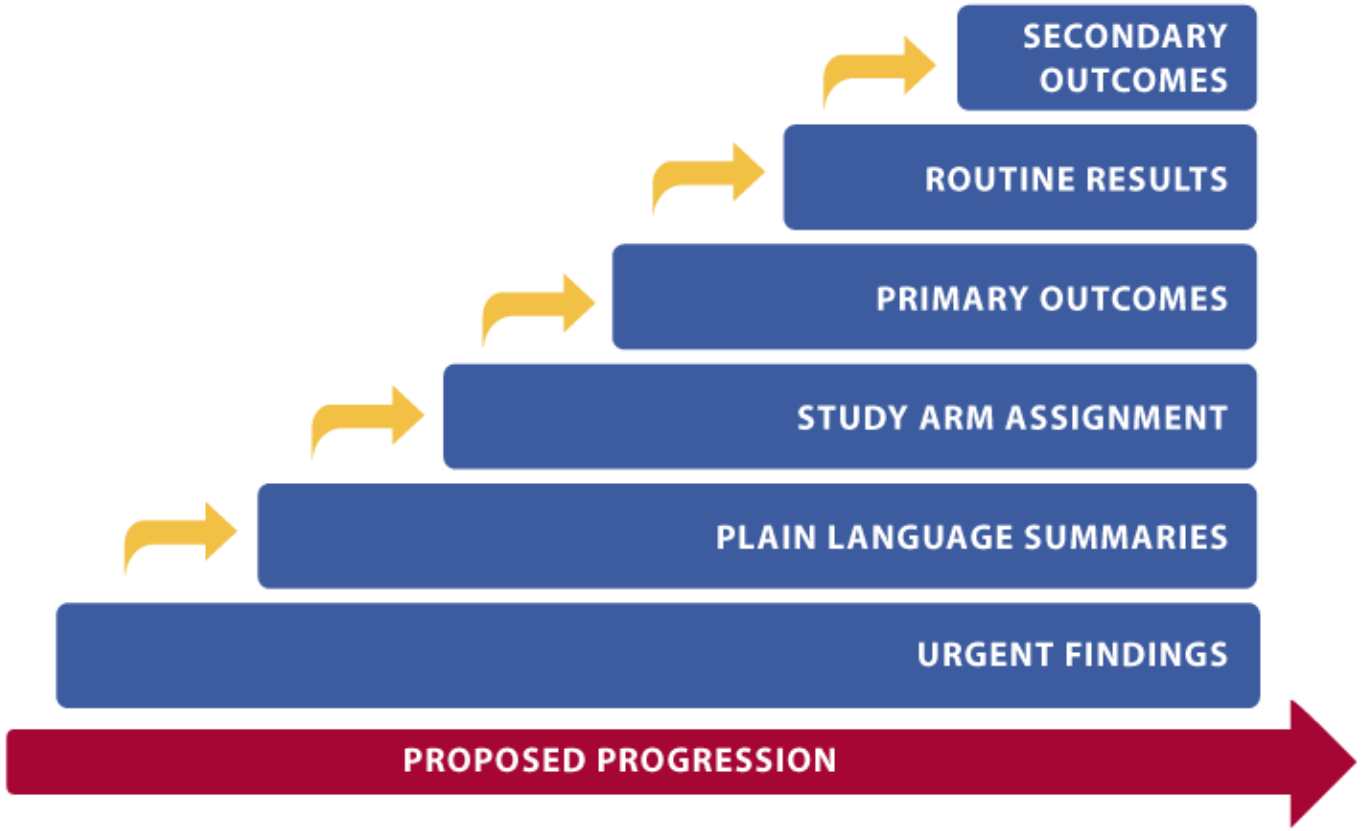
ABOUT | GETTING STARTED | HOW TO RETURN IRR | RESOURCES | TOPICS

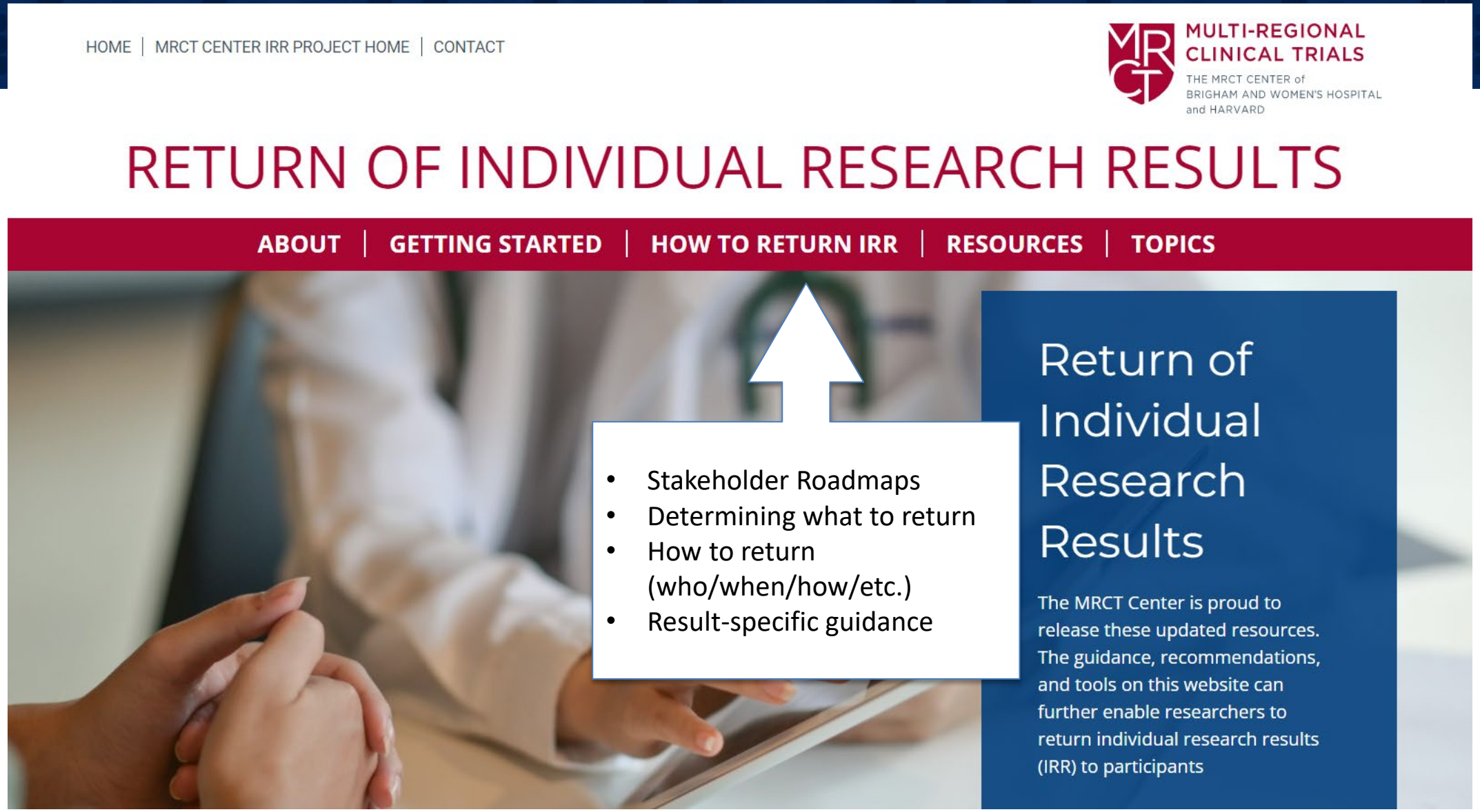


- How to get started
- Why to get started

How to Get Started

- Proposed progression of return
- Designing a pilot
- Who to involve
- Methods for returning IRR
- Establishing a policy

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RETURN OF INDIVIDUAL RESEARCH RESULTS
ABOUT | GETTING STARTED | HOW TO RETURN IRR | RESOURCES | TOPICS
Return of Individual Research Results
The MRCT Center is proud to release these updated resources. The guidance, recommendations, and tools on this website can further enable researchers to return individual research results (IRR) to participants
• Stakeholder Roadmaps
• Determining what to return
• How to return (who/when/how/etc.)
• Result-specific guidance

New Result Type Classifications

URGENT

ACTIONABLE

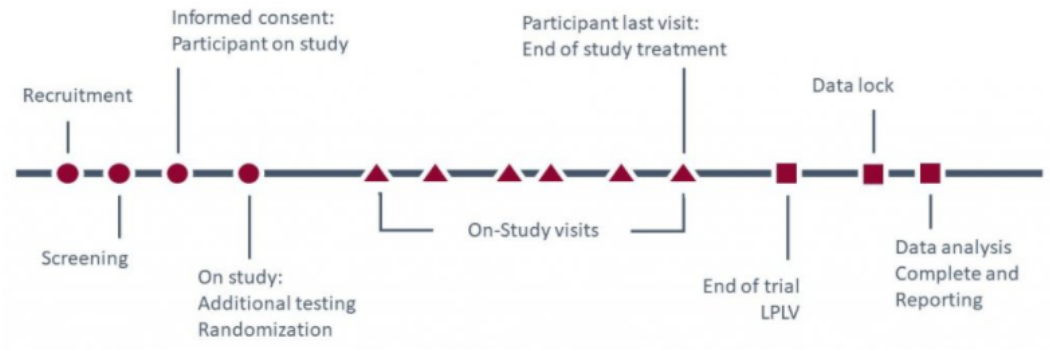
PERSONALLY VALUABLE

NO KNOWN IMPLICATIONS

Determining what to return

Step 1: During the study, when are you collecting data?

Consider the entire clinical trial lifecycle for a participant:



Step 2: What kinds of data will be generated during each period?

Think about the kinds of tests you will perform during each of the above periods:

- Study arm assignment
- Laboratory tests
- Diagnostic Imaging
- Genetic sequencing
- Physical or visual examinations
- Socio-behavioral
- Surveys and questionnaires
- Digital or mobile health results
- Patient-reported outcomes (PROs)
- Exploratory results

Step 3: Consider the following questions/domains for *each* data type during *each* study period to determine whether to return and what plans must be made to return:

A. URGENCY

- **Is there a possibility for a result to require urgent medical attention?**
  - **Example:** A "routine" blood pressure found to be 220/120 mmHg
  - **Example:** A participant reports suicidal ideation

Steps in a clinical trial

Types of data that may be generated in the trial

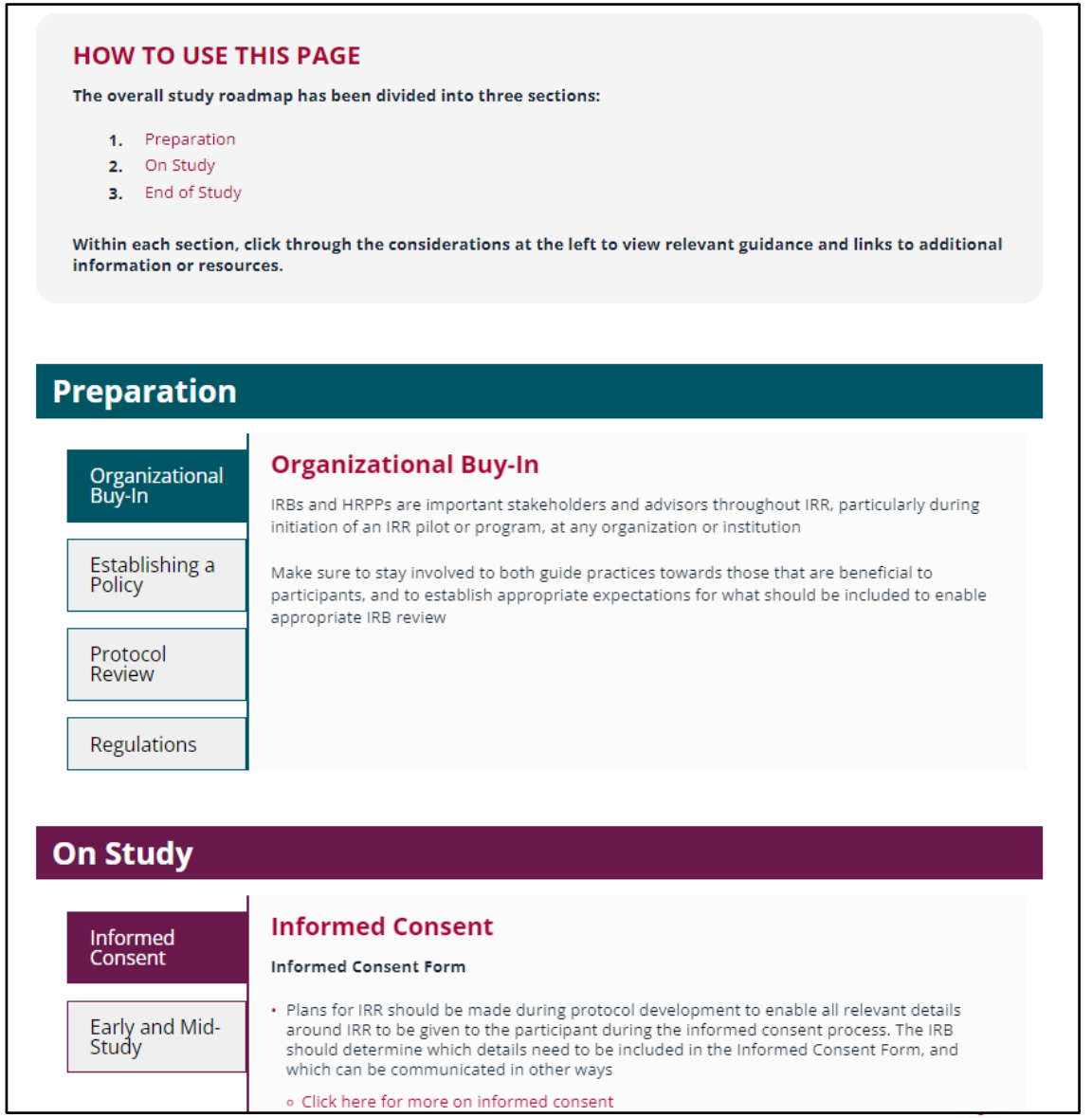
Classification of result

Stakeholder Roadmaps

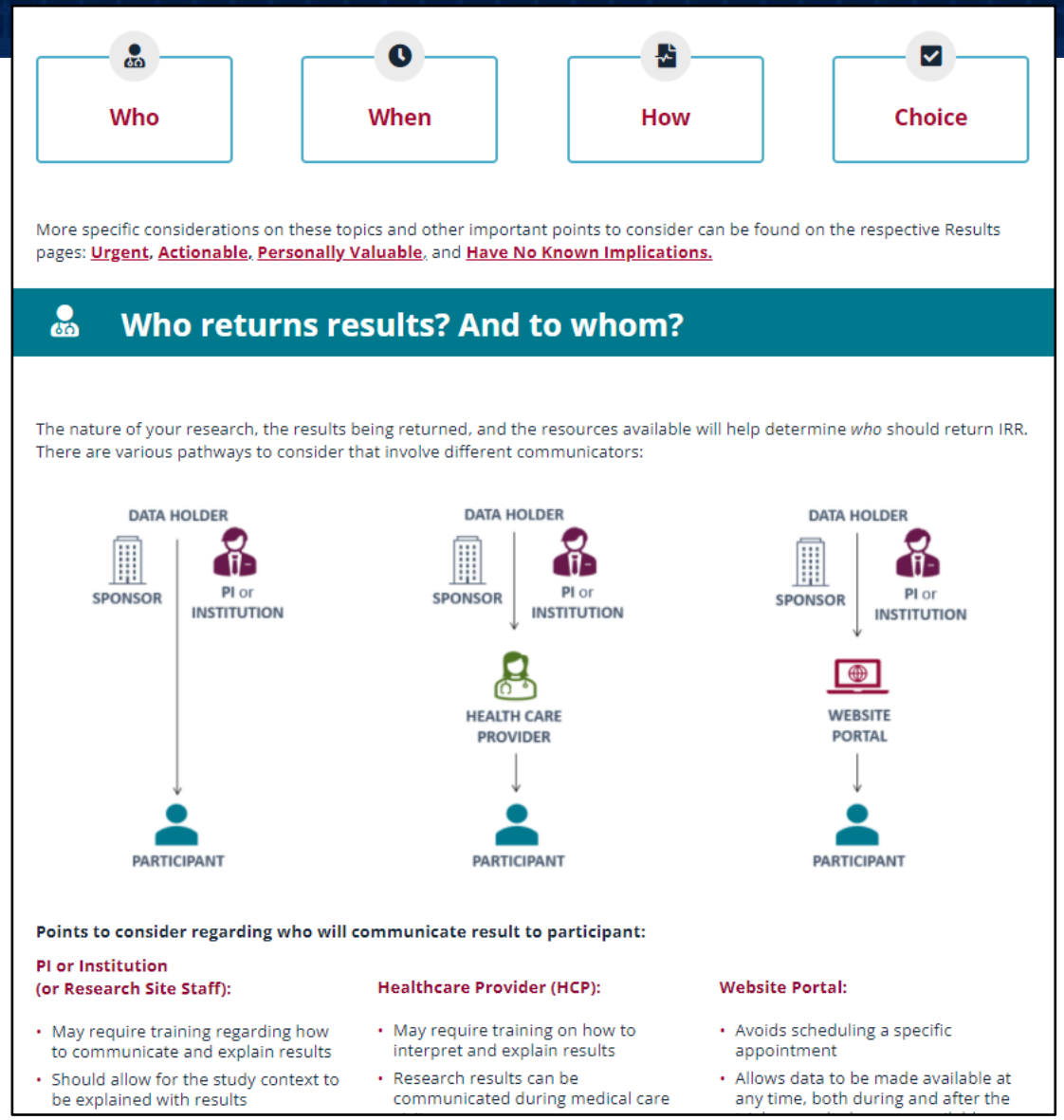
- Roadmap for each stakeholder group
- Provides a basic overview of each role's responsibility/task during a given time period
- Links to additional guidance or tools relating to each responsibility/task

Time Period →

Responsibilities/Tasks →
- Organizational buy in
- Establishing a Policy
- Protocol Review
- Regulations



How to Return IRR



Who should return result
When it should be returned
How it should be returned
Choice for participant as to whether to receive

Guidance separated by result type

Recommendations for who should return results of different data types:

Urgent	Actionable but not urgent	Personally Valuable	No known Implications

PIs should generally give urgent results to the participant contextualized with appropriate medical information, connect with the healthcare provider, and document the handoff.

Documentation should include the result, referral, and verification of the transfer of responsibility.

It may be necessary to inform the healthcare provider first, and then inform the participant with recommended next steps. These situations include concerns around requisite psychological support systems (e.g. information indicating suicidality), or in settings wherein the nature of the problem might inhibit the ability of the participant to respond.

If the participant is unreachable in an urgent situation and no alternative person has been designated by the participant, the PI and study staff should revert to procedures deployed in clinical settings and submit a report to the IRB as soon as reasonably possible. The medically responsible person affiliated with the trial should be contacted and tasked with this responsibility whether or not that person is the principal or site investigator of the trial.

The PI should determine how to proceed in other special circumstances.

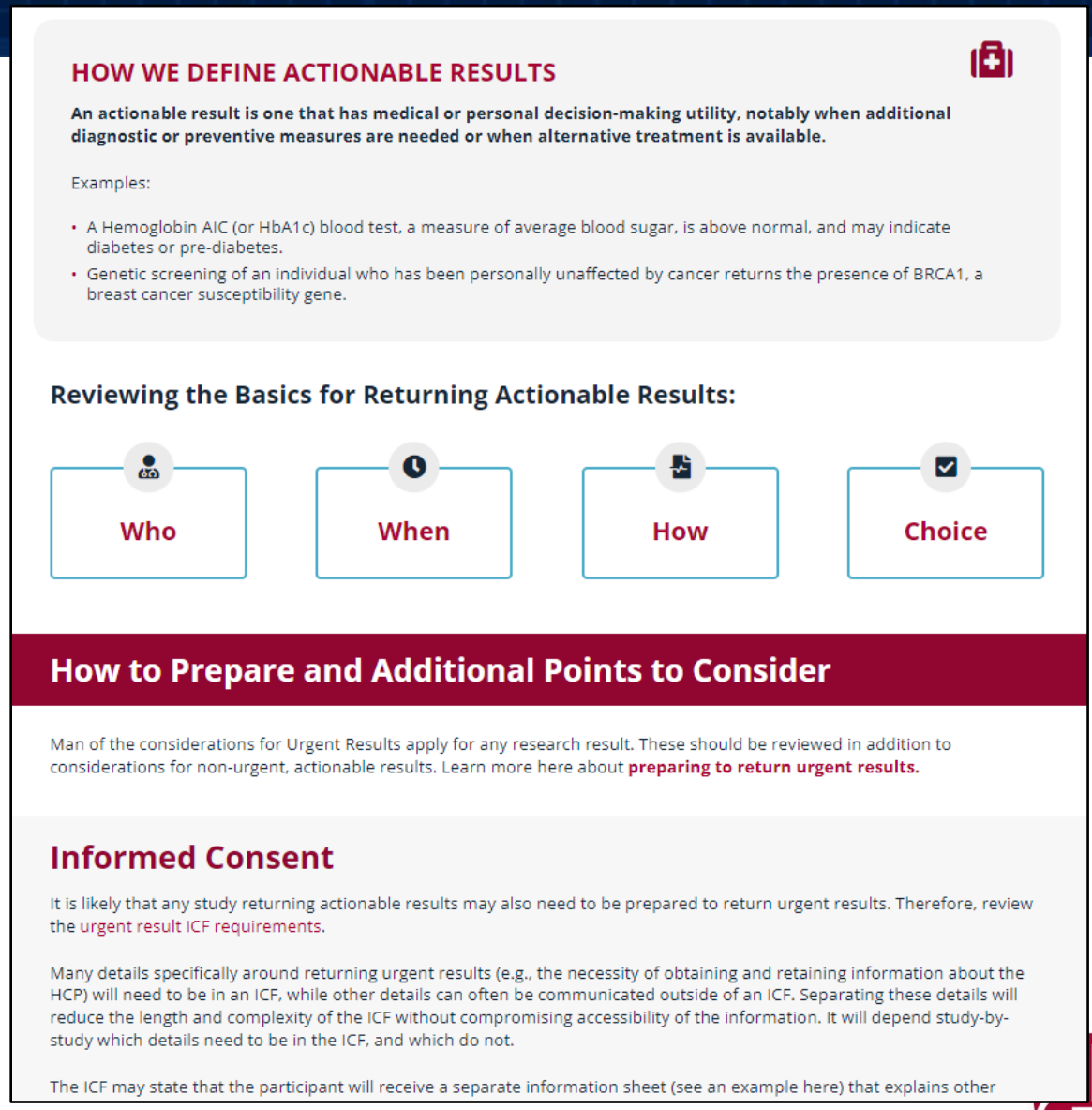
Click here for more about returning this data type.

Data-Type Pages

URGENT | ACTIONABLE | PERSONALLY VALUABLE | NO KNOWN IMPLICATIONS

For each result/data type:

- Definition & examples
- Links to basic considerations (who, when, how, choice)
- Informed consent (IC) guidance
- IC sample language
- Regulatory requirements
- Gathering the participant's healthcare provider contact info
- Accessing appropriate expertise to interpret results or advise in other capacities



HOW WE DEFINE ACTIONABLE RESULTS

An actionable result is one that has medical or personal decision-making utility, notably when additional diagnostic or preventive measures are needed or when alternative treatment is available.

Examples:

- A Hemoglobin AIC (or HbA1c) blood test, a measure of average blood sugar, is above normal, and may indicate diabetes or pre-diabetes.
- Genetic screening of an individual who has been personally unaffected by cancer returns the presence of BRCA1, a breast cancer susceptibility gene.

Reviewing the Basics for Returning Actionable Results:

Who | When | How | Choice

How to Prepare and Additional Points to Consider

Man of the considerations for Urgent Results apply for any research result. These should be reviewed in addition to considerations for non-urgent, actionable results. Learn more here about **preparing to return urgent results.**

Informed Consent

It is likely that any study returning actionable results may also need to be prepared to return urgent results. Therefore, review the urgent result ICF requirements.

Many details specifically around returning urgent results (e.g., the necessity of obtaining and retaining information about the HCP) will need to be in an ICF, while other details can often be communicated outside of an ICF. Separating these details will reduce the length and complexity of the ICF without compromising accessibility of the information. It will depend study-by-study which details need to be in the ICF, and which do not.

The ICF may state that the participant will receive a separate information sheet (see an example here) that explains other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endations,
and tools on this website can
further enable researchers to
return individual research results
(IRR) to participants
• Tools and Templates
• Resources for participants
• 2017 Guidance Documents
• Health Literacy
• Aggregate Results
• Coming soon: Case Studies

Tools & Templates – these and others!

Simple, downloadable tools supporting the adoption of returning IRR in a compliant and respectful way

IRB Approval Checklist:
Return of Individual Research Results

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	YES	NO	MORE INFO NEEDED	NOT APPLICABLE
The Study Protocol and/or Informed Consent Form (ICF) describes the plan for returning individual research results (IRR). If there is no intention to return IRR, plans and procedures in the event of urgent or incidental findings are still outlined.				
The following is included in the Study Protocol:				
Whether results will be returned	☐	☐	☐	☐
Which results will be returned	☐	☐	☐	☐
How results will be returned	☐	☐	☐	☐
Document templates and/or a website portal will aid in communicating results to participants and were included with submission	☐	☐	☐	☐
When results will be returned	☐	☐	☐	☐
Who will return and receive results	☐	☐	☐	☐
Healthcare provider contact information will be collected if necessary	☐	☐	☐	☐
Procedure in place for results returned to parent/guardian or Legally Authorized Representative	☐	☐	☐	☐
Designee (close friend or family member) to contact in case the participant is not reachable or available	☐	☐	☐	☐
Designee to contact in case the participant is deceased	☐	☐	☐	☐
Appropriate provisions are included for urgent results or urgent incidental findings that may occur during the study and *must* be returned	☐	☐	☐	☐
In the case of non-urgent findings, the participant or their legally authorized representative is able to make an informed choice as to whether to receive their individual results or not.				
Participants are given the choice whether or not to receive the information	☐	☐	☐	☐
There is a plan/system for tracking participant decisions	☐	☐	☐	☐
Participants will be consented or re-consented as needed when the results are available	☐	☐	☐	☐
Procedures for communicating results are respectful of the wishes of the participants	☐	☐	☐	☐

mrctcenter.org/return-of-individual-results

HEALTHCARE PROVIDER CONTACT FORM

<insert study name>
<insert PI/Study contact information>

What is this form?

In the *<insert plain language study title>* study there may be results about you that would be important for your healthcare provider or doctor to know. This form seeks permission to contact your healthcare provider or doctor if necessary. We also ask you for their contact information.

When we would be required to contact your healthcare provider (where you don't have a choice):

We must contact your healthcare provider if there is a result or medical finding that requires immediate attention, such as *<insert any plausible example from your type of study, e.g. A routine scan finding a tumor>.*

If you take part in this study, you agree that we can contact your healthcare provider when your study team decides it is necessary, generally for your safety and/or well-being.

Please know that medical care unrelated to the research will not be provided or paid for by the study, and you will need to follow up with your doctor.

Reasons you can choose to let us contact your healthcare provider:

<During and/or at the end of the study>, we will offer you some personal research results. If you like, we can also share these results directly with your healthcare provider so that they have them in the future. Examples include:

<insert feasible reasons from study>

Do you want us to share these optional results with your healthcare provider?
☐ Yes ☐No ☐ I don't have a healthcare provider

Print name: _____ Signature: _____

Please provide your healthcare provider's name, address, and contact information.
If you don't have a healthcare provider, please provide that last place you went for medical care.

Name of provider: _____

Name & address of clinic, hospital, or office: _____

Provider phone number: _____

Clinic/hospital/office phone number: _____

What if my healthcare provider changes?

If you change healthcare providers, you can contact us at any time with their new information at: <insert mode of contact>

We will also review this information at a later visit: <insert pre-specified review time if applicable>

RETURN OF RESULTS INFORMATION SHEET

Template instructions (delete after filling in template):
This sheet is intended to support the decision and discussion around a participants' choice to receive results. It should be adapted and/or adopted for the individual study and the choices that the participant may have.

The **<red type in brackets>** below should be changed to reflect the plan of the study and the types of results that a participant has the option to receive below.

Add and explain as many different types of results as necessary.

Record participants' choices in your study documents and/or the informed consent form. In addition, check the boxes on this form for participants to take home as a reminder of their decisions.

<Insert study name>
<Insert PI/Study contact>

What is this sheet?

This sheet describes the types of research results that you <may choose to/will/can> receive by participating in *<insert plain language study title here>.*

You can choose whether or not to receive these results.

Note, however, that we must return urgent results that require medical attention with you and/or your doctor. You do not have a choice with respect to urgent results. We will explain the reasons why below.

Can I change my mind about getting my results?

Yes, if you decided to receive results and you change your mind later, you can contact us at any time by: <insert mode of contact>

No matter what you decide, we will give you another chance to choose whether to receive results on: <insert pre-specified review time if applicable>

Result 1: Urgent results that require medical attention

☒ **Any result like this must be returned**

Description: If an urgent result arises, we must return it to you in order for you to receive additional evaluation and/or care. Examples from this study could be if: *<<insert any plausible example from your type of study, such as: A routine scan for this study found a tumor>>.*

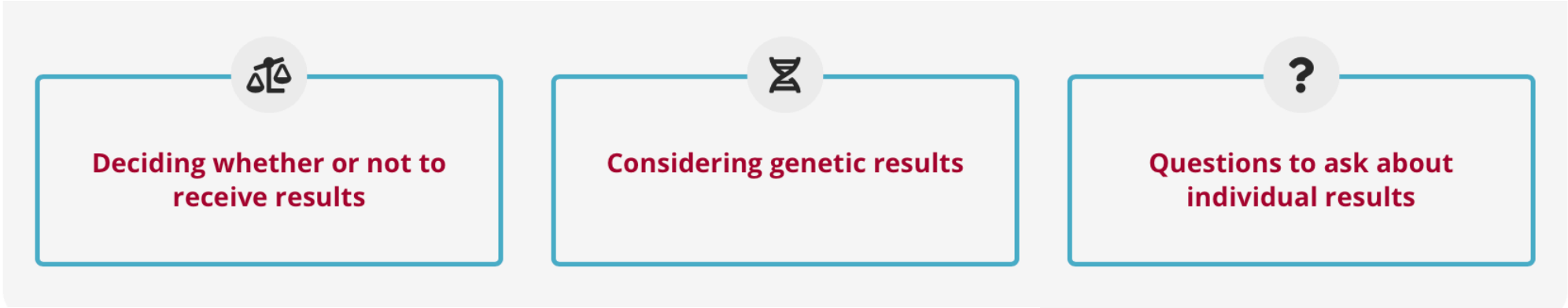
We might also need to share this information with your doctor or healthcare provider. Additional evaluation and/or care unrelated to this research, if you need it, will not be paid for by the study. You will need to follow up with your doctor.

Who would return this to me and how?	When would it be returned to me?
<explain your return plan for urgent results> Example: If this situation occurs, the principal investigator for this study will contact you by phone.	*<explain your return plan for urgent results>* Example: This would happen as soon as possible/as soon as the result is confirmed by another test/etc.

Tools & Templates

- IRB Approval Checklist for Returning IRR
  - A checklist to assist IRB members and Ethics Committees in reviewing return of IRR plans, based around the U.S. regulatory criteria for IRB approval.
- Healthcare Provider Contact Form Template
  - A template for obtaining permission to contact a participant's healthcare provider or doctor about individual research results, along with their contact information.
- IRR Information Sheet for Participants Template
  - A template for supporting the decision and discussion around a participants' choice to receive results, which should be adapted to reflect the plan of the study and the types of results that a participant has the option to receive, along with their decisions to receive them.
- Informed Consent Sample Language
  - Sample language to use in informed consent forms when explaining the different types of individual results that will be generated/returned to participants in a study.
- Resources for Participants

Resources for participants

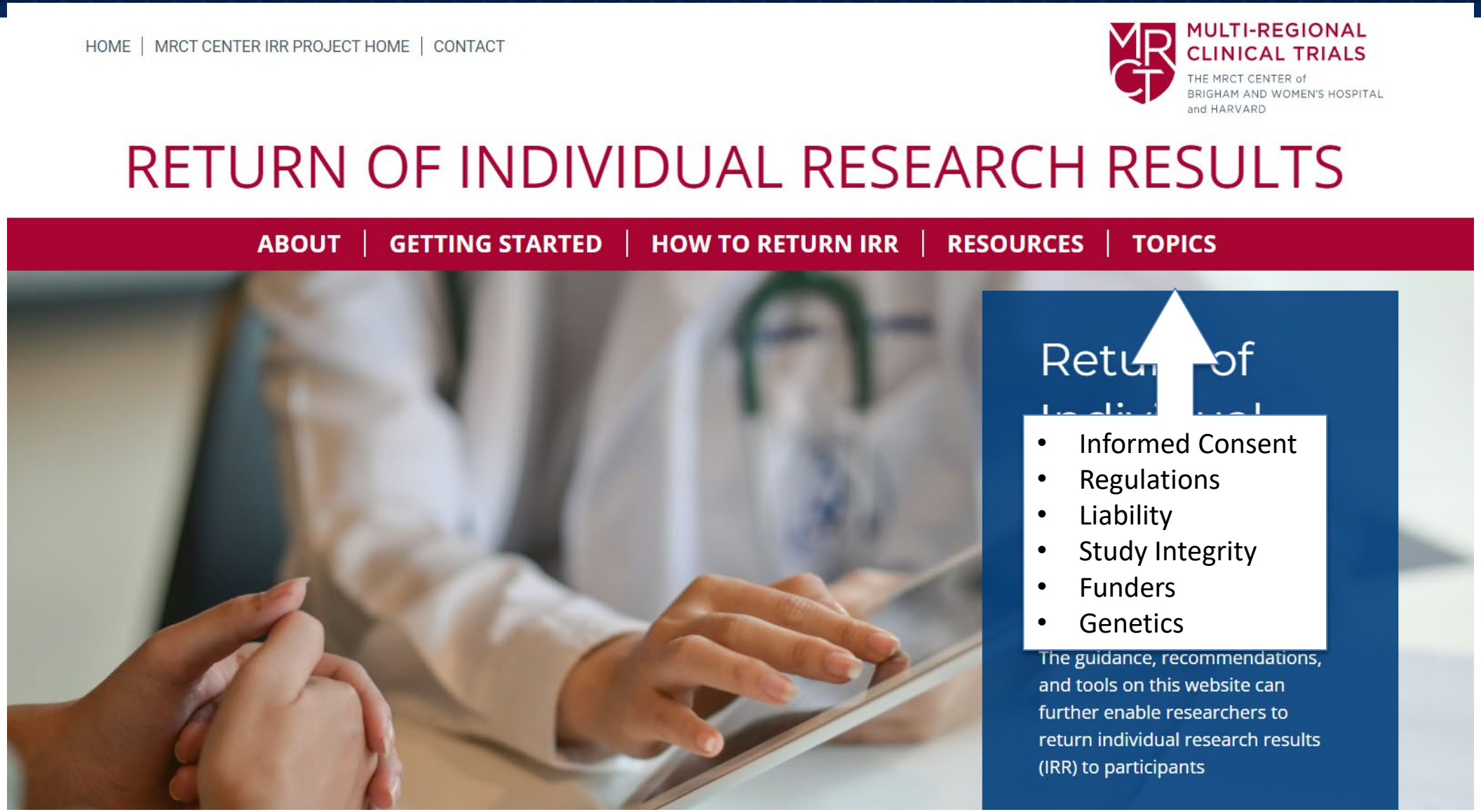


Remember, joining a research study is an important personal decision, and participating in a study is your choice. Be informed. Ask questions. Get answers.

- What kinds of results will you share with me? If you are not sharing any results with me, can you tell me why?
- What happens if you find out something serious or other information about my health?
- Do I have a choice about which findings you share with me? What if I don't want to know?
- Can I change my mind later about receiving these results?
- How can these results help me?
- Will you tell me about results that might affect my health or a member of my family's health?
- Could results/findings affect my family planning decisions?
- Could you learn something new about my family history?
- Will you be able to make sure any findings are correct?
- Who can I talk to about these findings?
- Are my research data placed in my regular medical records?
- How will you protect my privacy?
- Who will pay for my follow-up care and treatment if a new medical issue is uncovered as part of the study?
- Will there be future research on any of my samples? Will I learn any of those results?

Ask questions
Get answers

Additional topics



Coming Soon: Identified Areas for Continued Work

Further review of returning genetic information

Guidance for biobanks

Returning IRR to parents, guardians, representatives

Additional case studies

And more!

Please reach out to us if you would like to collaborate or have suggestions

Website Demo

mrctcenter.org/return-of-individual-results/

Discussion

Thank you!

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