

Returning Individual Research Results to Participants

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Acknowledgements

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Participants Value Access To Their Individual Research Results

But historically it has not been common practice to return individual research results to participants.

- Participants want their individual research results to:
 - Inform clinical and life decisions.
 - Understand a health condition (e.g., to end diagnostic odyssey).
 - Learn something of interest about oneself.
- Many believe it's paternalistic for investigators to withhold test results.
- In a few areas returning individual results is becoming more common (e.g., genetics, environmental exposure research).

Return of Results Study Aims

- Examine research participants' preferences and actual decisions for return of secondary genomic results
- Evaluate psychosocial and behavioral outcomes for participants who receive secondary genomic results

Study Design

WES group N = 140

Baseline questionnaire and vignettes

Initial counseling session

Pre-disclosure appointment questions
Disclosure session

1 week post-disclosure phone interview

1 month f/u questionnaire

1 year f/u questionnaire

In-depth interview (some participants)

Comparison group N = 85

Baseline questionnaire and vignettes

1 month f/u questionnaire

1 year f/u questionnaire

Survey instruments

- **Psychosocial impact**
 - Beck Anxiety Index
 - Personal Health Questionnaire-9 (depression)
 - Brief COUP (coping mechanisms)
 - Multidimensional Impact of Cancer Risk Assessment (MICRA)
 - General Self-Efficacy Scale (GSE)
 - Genetic Secrecy*
 - Genetic Stigma*
 - Satisfaction with results*
 - Worry about health, death and family health*
- **Behavioral Impact**
 - Internal Locus of Control Scale (IHLC)
 - Duke Social Support Index
 - Health Related Behavior*
 - Life Changes *
 - Sleep behavior*

*newly developed scale

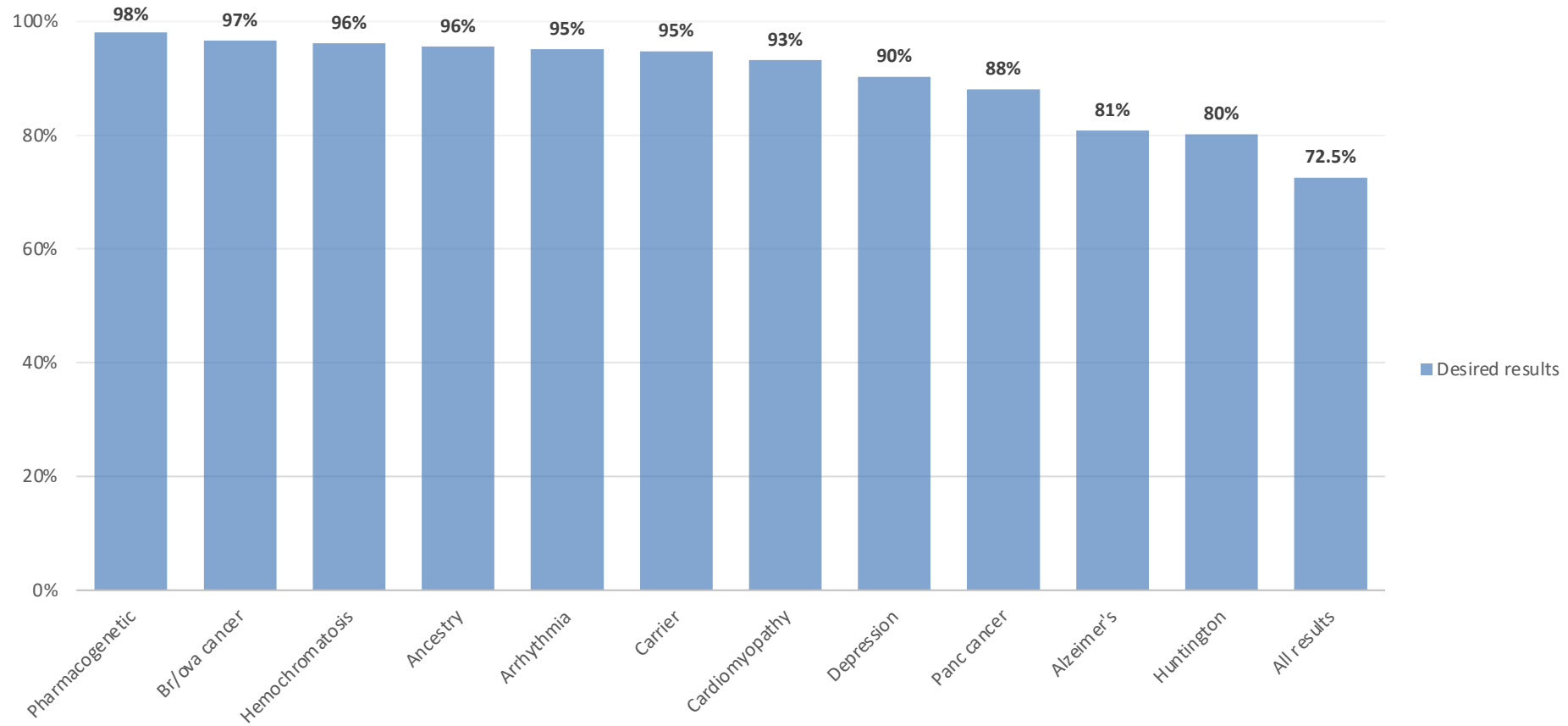
Cohort characteristics

Demographics	N	%
Female	164	75%
Married	186	85%
Age		
Mean and SD	48	14.3
Ethnicity and race		
White, Not-Hispanic	180	82%
White Hispanic	9	4%
Black	7	3%
Asian or Pacific Islander	7	3%
More than 1 race	2	11%
Other or not specified	14	6%

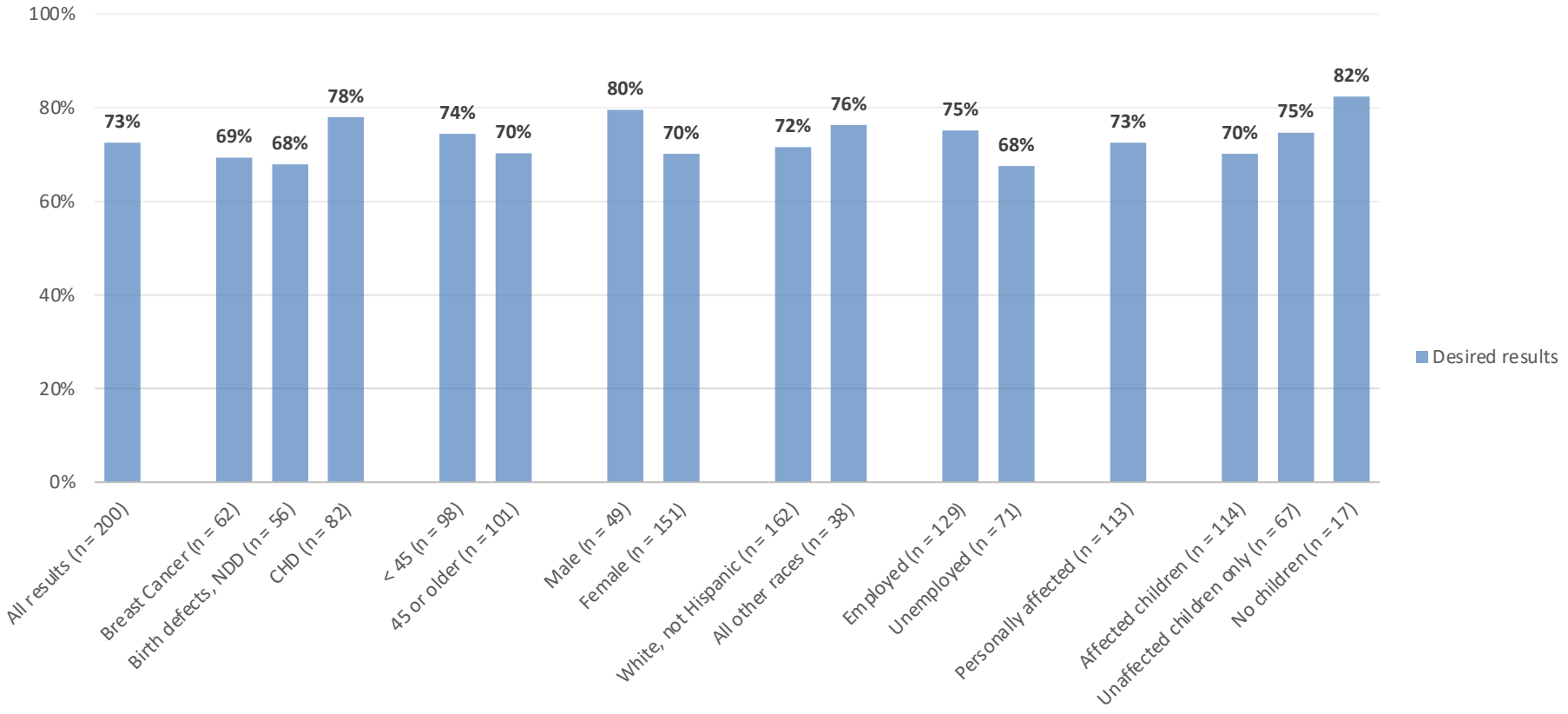
N = 219

	N	%
Education		
Up to HS or vocational training	30	14%
Some college/ Associate	43	20%
College graduate	61	28%
Advanced degree	85	39%
Employed (full or part-time)	141	64%
Parent study		
Breast cancer	64	29%
Congenital heart disease	94	43%
Birth defects, neurodevelopmental disorders	61	28%
Personally affected	83	38%
Children		
Affected children	126	58%
Unaffected children only	78	36%
No children	17	8%

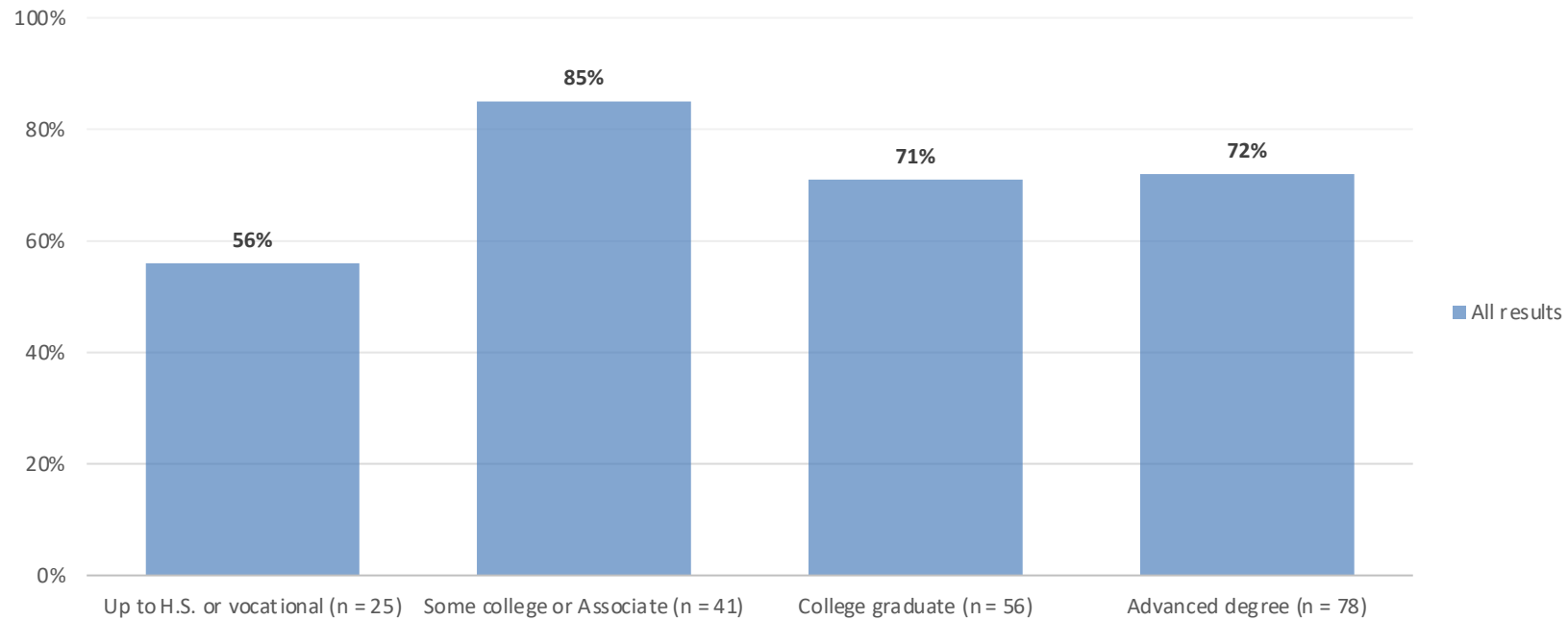
Preferred results for return by type of result



Preferences for results by demographic category



Preferences for results by education level



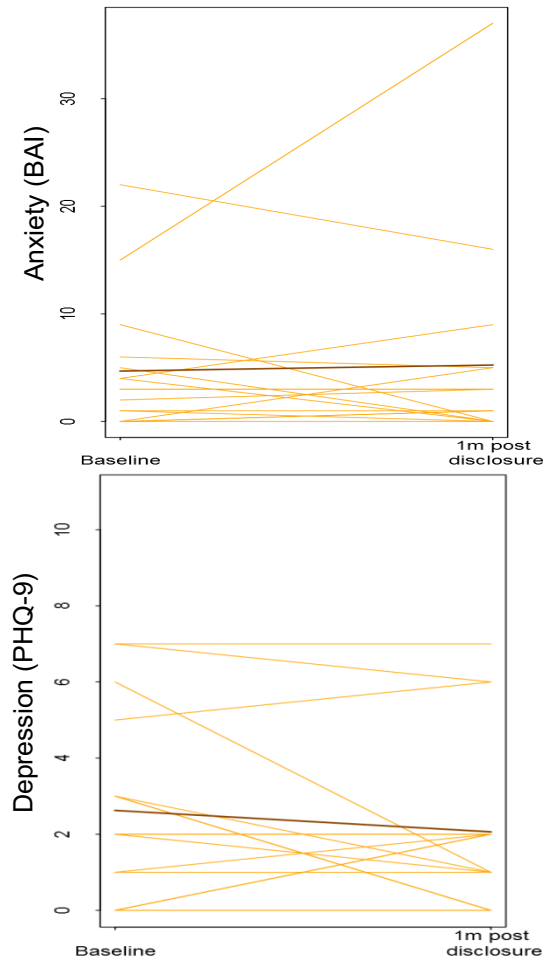
Chi-squared p-value = 0.08

WES Participants Who Received Personally Impactful Results Received

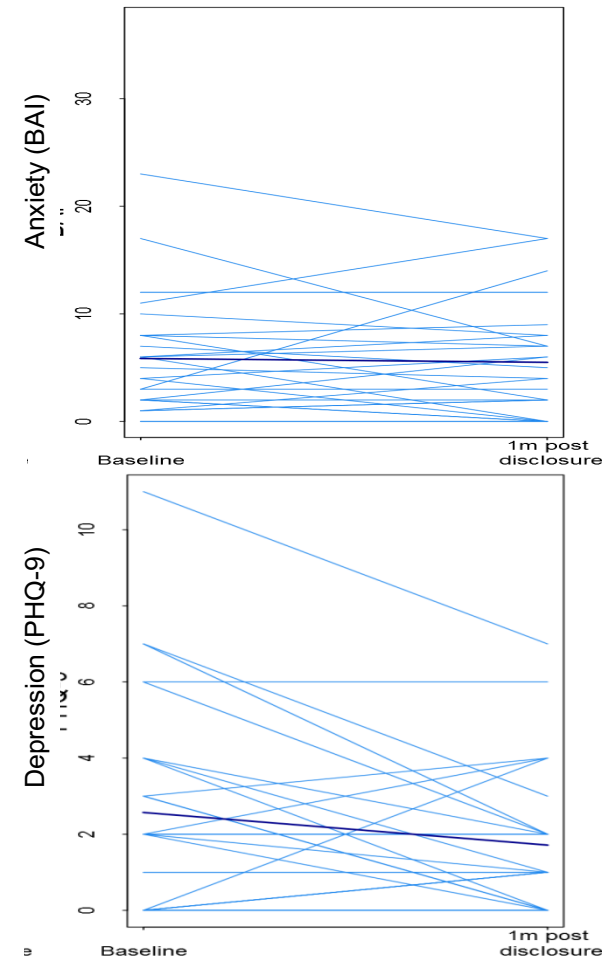
Result	N
ApoE	
E3/E4	15
E4/E4	1
Other results	
Hereditary Nonpolyposis Colorectal Cancer	1
Cardiomyopathy	2
Arrhythmia	2
Glucose-6-phosphate dehydrogenase deficiency	1
Charcot-Marie-Tooth disease (X-linked)	1
Antitrypsin alpha 1 deficiency	1
Pituitary hormone deficiency	1
Hypertriglyceridemia	1
Factor XI deficiency	1
Hemochromatosis	1
Venous thromboembolic disease	1
Von Willebrand Disease	1
Familial Mediterranean Fever	1
Age related macular degeneration	4
	35

No Difference in Anxiety or Depression in WES Participants Who Did and Did Not Receive Personally Impactful Results

+ Personally Impactful Results



- Personally Impactful Results



No difference in psychosocial and behavior measures in WES participants who did and did not receive personally impactful results

Scale	Everyone (N=44)		+ PIR		- PIR	
	Mean Change	SD	Mean Change	SD	Mean Change	SD
Health Related Behavior	0.02	0.29	0.04	0.31	0.01	0.73
Internal Health Locus of Control	-0.21	0.35	-0.22	0.33	-0.04	0.94
Sleep Behavior	-0.17	0.68	-0.08	0.85	-0.21	1.82
Stigma of Genetic Information	-0.07	0.65	0.12	0.51	-0.10	0.52

PIR: personally impactful results

Results Disclosure

“Less material than I thought would be here”

RoR269, elected to receive but did not have any personally impactful results.

“It feels like good news.”

RoR128, elected to receive but did not have any personally impactful results.

“What I was worried about I’m not worried about because now I know that I can be screened and never get it.”

RoR270, elected to receive select personally impactful results and found to have an HNPCC variant consistent with her family history of uterine cancer

Summary of Participant Study

- 73% of participants elected to receive all results
 - Opted out of subset of results based on personal or family history and experience with the disease
- Participants did not experience a significant change in anxiety or depression 1 month after receiving results
- When given the opportunity, participants can effectively determine appropriate preferences for genomic information for themselves

However, Two HHS Regulations Provide Conflicting Guidance

Clinical Laboratory Improvement Amendments of 1988 (CLIA)

- Ensures the quality of results from clinical laboratories.
- According to CMS, only allows the sharing of test results with participants if they are generated in CLIA-certified laboratories.

Health Insurance Portability and Accountability Act of 1996 (HIPAA)

- Protects personal health information (medical records and other info included in designated record set (DRS)).
- Requires the return of results requested by a participant (when part of HIPAA-covered entity), regardless of whether they were generated in a CLIA-certified laboratory.

Potential Benefits, Risks, and Costs

Evidence suggests benefits have been understated and risks overstated.

Potential benefits

- Better relationships between investigators and participants.
- More transparency and trust.
- Better recruitment and retention.

Risks

- Participants may make important clinical or life decisions based on information that subsequently proves to be wrong or is misinterpreted.
- Possible adverse psychosocial effects from receiving results with serious health implications or that have uncertain meaning.
- Legal liabilities for research institutions.

Costs

- Time, personnel and resources.
- But, practice may lead to cost savings in terms of improved participant recruitment and retention.

Ethical Considerations

- Obligation to return when reliable results suggest imminent danger (i.e., ‘duty to warn’ or ‘duty to rescue’)
- Opportunity to demonstrate the ethical principles of respect for persons, beneficence and justice.
- However, there are other mechanisms (e.g., return of aggregate results) may be more appropriate in certain circumstances—and ethical principles can be used to argue against return in some cases.

Thus, it is important to consider the benefits, risks, and costs on a study specific basis through a thoughtful decision-making process.

Guiding Principles for the Return of Results

1. Because **research results have value to many participants**, return of results should be routinely considered as a matter of reciprocity, respect, transparency and trust.
2. When assessing value of returning results, **trade-offs for all stakeholders** should be considered.
3. When results are offered, **participants can decide** whether to receive or to share their results.

Guiding Principles (cont'd)

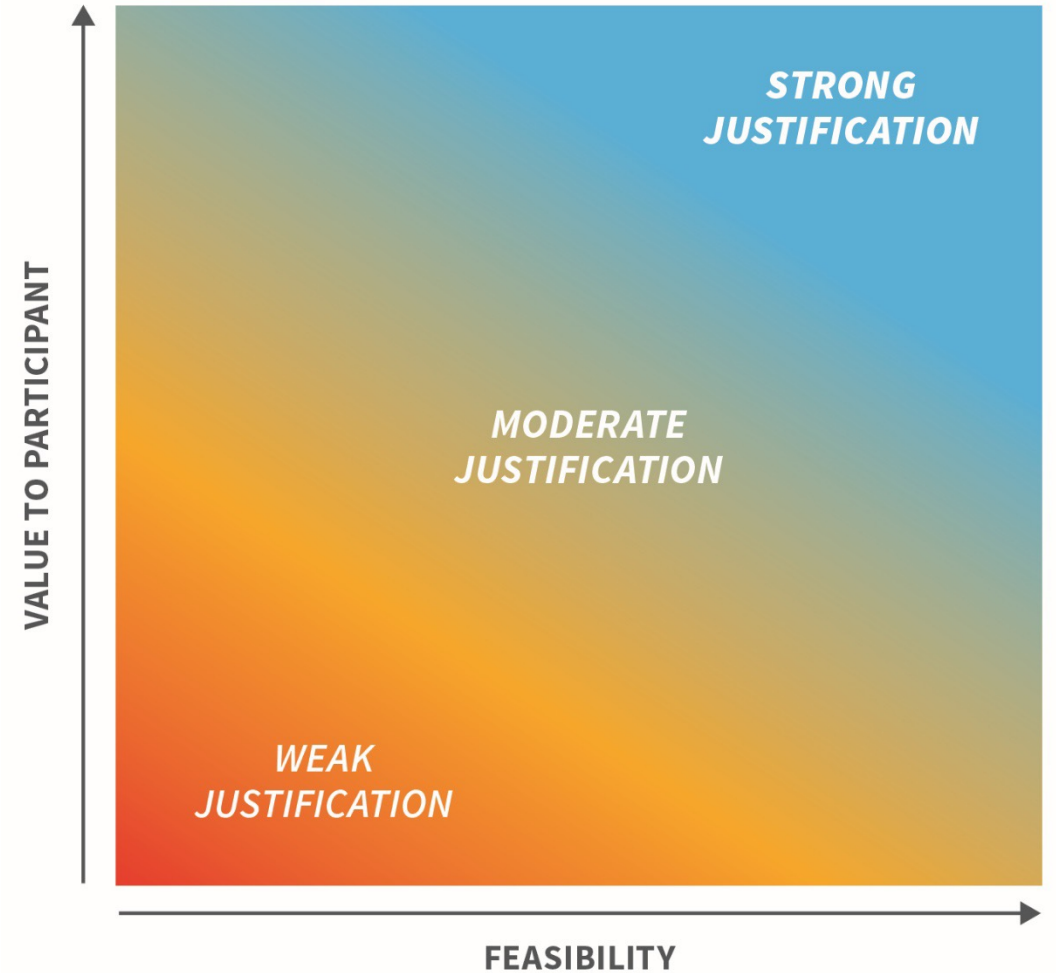
4. **Communication is key** to promote understanding of the meaning and limitations of information.
5. **Validity and reliability** of results is crucial to provide value to investigators, participants, and society.
6. **Inclusion of diverse populations is critical** to the conduct of high-quality research. Researchers should seek input from participants and communities, to accommodate the full spectrum of needs and preferences.

Decision Making on a Study-by-Study Basis

- Decisions on return will vary depending on the characteristics of the research, the nature of the results, and the interests of participants.
- Investigators should prepare for three scenarios for return:
 - Planned investigator **offer**.
 - Upon participant **request**.
 - In the event of **unanticipated findings**.

Feasibility and value framework

The justification for return becomes stronger as the potential **value** of the result to participants and the **feasibility** of return increase.



Need to Harmonize Federal Regulations

- HIPAA/CLIA conflict cause variable interpretation and action across IRBs and research sites.
- FDA regulations are unclear regarding how return of results impacts the IDE process.
- Regulatory conflicts create:
 - Inconsistent and inequitable access for participants.
 - Dilemmas for laboratories, investigators, and institutions.
- Example: How to frame request for new sample, when needed for CLIA confirmation

NAM Recommendations

Include Plans in Study Protocols

Investigators

- Should include plans in protocols that describe whether results will be returned and, if so, when and how.

Research sponsors and funding agencies

- Should require that applications for funding consistently address the issue.

Institutions and IRBs

- Should develop policies to support the review of plans to return research results.

Incorporate Participant Needs and Preferences

Investigators

- **Should seek information** (e.g., reviewing published literature, leveraging experiences from similar studies, consulting institutional advisory boards, and/or engaging community and participant groups).

Research institutions and sponsors

- **Should facilitate investigator access to relevant community and participant groups.**

Sponsors

- **Should engage community and participant representatives in the development of policy and guidance related to the return of individual research results.**

Considerations for Special Populations

Children and adults who lack decision-making capacity

- Plan for return should be addressed in consent process and approved by the parents or legally authorized representative (LAR).
- Older children and adults with limited capacity should be asked for their assent when possible.

Deceased

- When relevant, investigators should elicit participants' preferences for sharing their results with relatives following their death.
- If no prior direction, no standard practice.

Ensure the High Quality of Individual Research Results

Institutions and their IRBs

Should permit investigators to return individual research results **only if:**

- Testing is conducted in a **CLIA-certified laboratory**; or
- Results are not intended for clinical decision making and testing is conducted under the **externally accountable QMS** for research laboratories; or,
- Results are not intended for clinical decision making and the **IRB determines** that:
 - **Potential benefits** are sufficiently high and **risks of harm** are sufficiently low;
 - **Quality** of analysis is sufficient to provide confidence in results; and
 - Information will be provided to the participant(s) **regarding limits on test validity and interpretation.**

Ensure Transparency in the Consent Process

Investigators should communicate in clear language to research participants

- Which individual research results participants can **access** (incl. under HIPAA) and which, if any, will be **offered**.
- If results will be **offered**, consent should state:
 - **Risks and benefits** associated with receiving results.
 - Conditions under which researchers will alert participants of **urgent results**.
 - **Time and process** by which results will be communicated.
 - Whether results will be placed in a medical record and/or communicated to the participant's clinician.
 - When relevant, the participant's option to have results shared with family members if participant becomes incapacitated or deceased.

Implement Effective Communication Strategies

Investigators and institutions

- Should communicate results to **convey the key messages** and to foster participants' understanding.
- This includes ensuring modes of communication are appropriate for participants with different needs, capabilities, resources, and backgrounds.

Returning results will require investigators to **communicate the limits of test validity** and interpretation.

Example of Successful Communication Practices for the Return of Research Results in Environmental Health

Growing Up Female

- Pilot study on feasibility of measuring biomarkers of exposure to perfluorochemicals (PFCs) and other compounds in blood and urine, girls 6-8 years.
 - Consent process informed participants that elevated blood sugar, insulin, blood pressure, and cholesterol would be reported to their parents and that “the investigators will tell you about significant new findings developed during the course of the research and new information that may affect your health, welfare, or willingness to stay in this study” (p.2).
 - During data collection, CDC alerted investigators that there were elevated perfluorooctanoic acid (PFOA) levels among a cohort of participants.
 - **Investigators searched the literature and sought advice** from environmental health research organizations.
 - The **communication plan** included presentations, an informational packet, a visual depiction of results, a summary of study findings, a glossary, FAQs, contact information, press release.
 - PI and a family physician presented a study update, including a comparison of the cohort’s PFOA results with national data and data from other cohorts. Families then received the individual reports for their children.
 - The PI and other researchers facilitated one-on-one or small group discussions of the results.
- (Hernick et al., 2011)

Expand the Evidence-Base

Sponsors and funding agencies

- Should support additional research to **better understand the benefits and harms** of return of individual research results, as well as participant needs, preferences and values, and to **enable the development of best practices** and guidance.

Revise and Harmonize Current Regulations

Regulators

- Should revise and harmonize the relevant regulations in a way that **respects the interests of participants** and **balances the competing considerations of safety, quality, and burdens** on the research enterprise.

Final thoughts

The NAM recommendations:

- Promote a **process-oriented approach** to returning individual research results that considers the value to the participant, the risks and feasibility of return, and the quality of the research laboratory.
- Permit an increase in the return of individual research results over time as stakeholders develop the necessary expertise, infrastructure, policies, and resources.

The initial investments will likely be significant, but ultimately the return on those investments in terms of **increased participant trust and engagement** with the research enterprise and higher quality standards for research laboratories will be worthwhile.

Free PDF of NAM report available at
nationalacademies.org/ReturnofResults