Exploring the Responsibility to Recontact: Research Participants With Reinterpreted Genomics Results

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On behalf of the ASHG Recontact Workgroup
Acknowledgements
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What’s the Problem?

• As per your research plan, you release VUS results to asymptomatic participants.
• You happen to discover that a previously released VUS has now been reclassified as pathogenic.
• What should you do now?
Prevalence of VUS reclassification is high

Prevalence of Variant Reclassification Following Hereditary Cancer Genetic Testing

Communicating new knowledge on previously reported genetic variants

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Recontact: What’s the debate?

For

Ethically desirable

Against

Resources

Research:
• Lower desirability (different goals)?
• Higher resource costs (distract from research)?
Minimally...

- Researchers should offer actionable results
- No duty to hunt
- Limited to period of active funding
- Participants must be identifiable & may opt out
After RoR, is there a duty to recontact?

Clinical setting: ACMG & ESHG  but  Research setting: no policy exists
**Workgroup Members & Process**

**ASHG POSITION STATEMENT**

The Responsibility to Recontact Research Participants after Reinterpretation of Genetic and Genomic Research Results

Yvonne Bombard,1,2,3,* Kyle B. Brothers,1,4 Sara Fitzgerald-Butt,5,6 Nanibaa’ A. Garrison,1,7,8 Leila Jamal,1,5,9 Cynthia A. James,5,10 Gail P. Jarvik,11,12 Jennifer B. McCormick,1,13 Tanya N. Nelson,14,15,16,17,18 Kelly E. Ormond,1,19 Heidi L. Rehm,20,21,22 Julie Richer,14,23,24 Emmanuelle Souzeau,25,26 Jason L. Vassy,20,27,28 Jennifer K. Wagner,1,29 and Howard P. Levy1,30,31

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- **Oct 2017**: ASHG BOD approved proposal
- **Dec 2017**: WG convened
- **Jan-Oct 2018**: WG drafted statement
- **Nov 2018**: ASHG BOD approval
- **Dec 2018**: Partner Org’s Endorsements
Approach

Scope:

• Research settings, recognizing clinical cross-over exists
• Applies **only** in cases in which there was return of results
• Exclusions:
  – Purely clinical (ACMG, ESHG)
  – Pediatrics & transition to adulthood
  – Initial return of results (Jarvik *et al*)
Approach

Word choice:

- “Recommend” & “desirable”
- No “duty” or “obligation”
- “Responsibility” only for clarification:
  - “No responsibility...” in certain settings
  - “Any responsibility...” is subject to limitations
Framework

Proactive, grounded in ethical principles.

Respect for persons:
- Autonomy: ongoing informed participation
- Veracity/truth telling: notify participant of new “truths”

Beneficence & Justice:

Benefits to individual participants

Risk of not achieving research goals
Framework

Practicability:
• Maximize individual engagement & benefit
• Preserve research goals of scientific knowledge & societal benefit
• Individual risk may not be justified if research goals aren’t met

Inherently subjective ➔ IRBs & Advisory Boards
Recommended Pathway for Considering Recontacting Participants after Reinterpretation of Genetic and Genomic Research Results

ASHG recommends that research projects develop a plan for return (or not) of reinterpretations of results. As part of that plan, research participants should be alerted to the likelihood that interpretations of results may change over time and be given the opportunity to provide informed consent regarding the plan for return of results, including initial and reinterpreted results. ASHG strongly recommends that there is no responsibility for researchers to hunt or scan genetic or genomic data or literature for changes in variant interpretation.
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Did the initial study involve return of results?

No

No responsibility to recontact exists.
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1. Did the initial study involve return of results?
   - No
   - Yes

2. Has the participant consented to return of results?
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Did the initial study involve return of results?

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Has the participant consented to return of results?

No

Is the Institutional Review Board protocol open?

Yes

No responsibility to recontact exists.

Yes

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- Did the initial study involve return of results? No
- Has the participant consented to return of results? No
- Is the Institutional Review Board protocol open? No
- Is the data linked to identifiers? No responsibility to recontact exists.
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3. Is the Institutional Review Board protocol open?
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   - Yes

4. Is the data linked to identifiers?
   - No
   - Yes

5. Has there been a reinterpretation* of the initial results that led to new findings?
   - No responsibility to recontact exists.

*Reinterpretation refers to both reclassification of variants and reanalysis of original data (per section What does it mean to reinterpret results?)
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**Flowchart Diagram**

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Do the new findings involve a change from or to P/LP?

Yes
Recommended Pathway for Considering Recontacting Participants after Reinterpretation of Genetic and Genomic Research Results

Do the new findings involve a change from or to P/LP?

- Yes
  - Recontact may be desirable, if sufficient resources exist.
- No
Do the new findings involve a change from or to P/LP?

Yes

Are the new findings related to the phenotype under study or reasonably expected to affect participant’s medical management?

Yes

Recontact may be desirable, if sufficient resources exist.

No
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1. Do the new findings involve a change from or to P/LP?
   - No
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   \[\text{Yes} \rightarrow \text{Are the new findings related to the phenotype under study or reasonably expected to affect participant's medical management?} \]
   \[\text{No} \rightarrow \text{Recontact is advised, rather than strongly recommended.} \]
   \[\text{Yes} \rightarrow \text{Recontact may be desirable, if sufficient resources exist.} \]
2. Are the new findings related to the phenotype under study or reasonably expected to affect participant’s medical management?
   - No
   - Yes
   \[\text{No} \rightarrow \text{Recontact is advised, rather than strongly recommended.} \]
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3. Does the research project have active funding?  
   - Yes

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No

Yes

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Recontact is advised, rather than strongly recommended.

ASHG strongly recommends that researchers attempt recontact to offer updated results within 6 months of identifying the reinterpreted variant. Attempts to recontact should be documented and limited to a "good faith effort" to reach the participant within the limits of existing constraints. Use similar individuals and communication methods for recontacting as for initial return of results.

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