

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

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On behalf of the ASHG Recontact Workgroup

# Acknowledgements

## ASHG POSITION STATEMENT

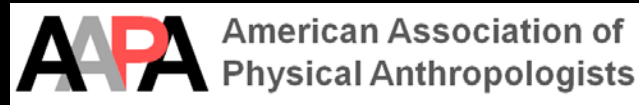
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### The Responsibility to Recontact Research Participants after Reinterpretation of Genetic and Genomic Research Results

Yvonne Bombard,<sup>1,2,3,\*</sup> Kyle B. Brothers,<sup>1,4</sup> Sara Fitzgerald-Butt,<sup>5,6</sup> Nanibaa' A. Garrison,<sup>1,7,8</sup>  
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Emmanuelle Souzeau,<sup>25,26</sup> Jason L. Vassy,<sup>20,27,28</sup> Jennifer K. Wagner,<sup>1,29</sup> and Howard P. Levy<sup>1,30,31</sup>

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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

JAMA | Original Investigation

## Prevalence of Variant Reclassification Following Hereditary Cancer Genetic Testing

Jacqueline Mersch, MS, CGC; Nichole Brown, MS, CGC; Sara Pirzadeh-Miller, MS, CGC;  
Erin Mundt, MS, CGC; Hannah C. Cox, PhD; Krystal Brown, PhD; Melissa Aston, BS;  
Lisa Esterling, PhD; Susan Manley, MS, CGC, MBA; Theodora Ross, MD, PhD

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*Open*

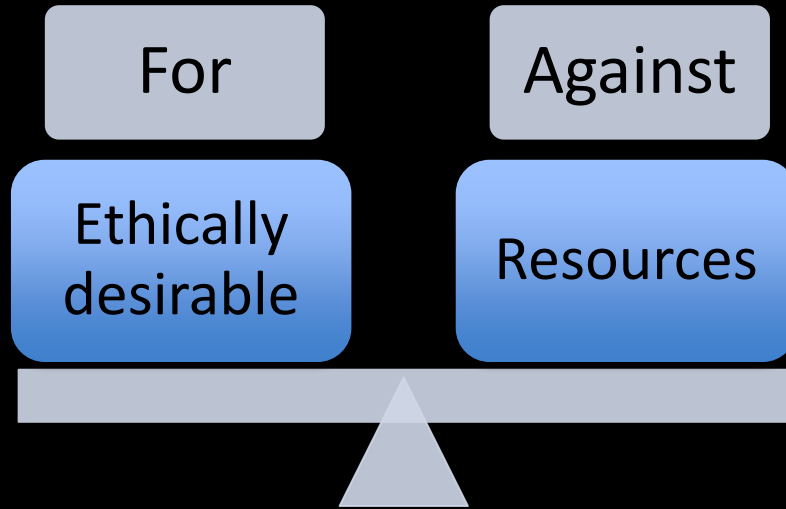
SPECIAL ARTICLE

Genetics  
in Medicine

### Communicating new knowledge on previously reported genetic variants

Samuel J. Aronson, ALM, MA<sup>1,2</sup>, Eugene H. Clark, BM<sup>1,2</sup>, Matthew Varugheese, MS<sup>1,2</sup>,  
Samantha Baxter, MS, CGC<sup>3</sup>, Lawrence J. Babb, BS<sup>1,2</sup> and Heidi L. Rehm, PhD, FACMG<sup>3,4</sup>

# Recontact: What's the debate?



Research:

- Lower desirability (different goals)?
- Higher resource costs (distract from research)?

# CSER/eMERGE RoR Statement

## ARTICLE

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### Return of Genomic Results to Research Participants: The Floor, the Ceiling, and the Choices In Between

Gail P. Jarvik,<sup>1,2,\*</sup> Laura M. Amendola,<sup>1</sup> Jonathan S. Berg,<sup>3</sup> Kyle Brothers,<sup>4,5</sup> Ellen W. Clayton,<sup>6</sup> Wendy Chung,<sup>7</sup> Barbara J. Evans,<sup>8</sup> James P. Evans,<sup>3</sup> Stephanie M. Fullerton,<sup>9</sup> Carlos J. Gallego,<sup>1</sup> Nanibaa' A. Garrison,<sup>6</sup> Stacy W. Gray,<sup>10,11</sup> Ingrid A. Holm,<sup>12,13,14</sup> Iftikhar J. Kullo,<sup>15</sup> Lisa Soleymani Lehmann,<sup>10</sup> Cathy McCarty,<sup>16</sup> Cynthia A. Prows,<sup>17</sup> Heidi L. Rehm,<sup>10</sup> Richard R. Sharp,<sup>18</sup> Joseph Salama,<sup>1</sup> Saskia Sanderson,<sup>19</sup> Sara L. Van Driest,<sup>6</sup> Marc S. Williams,<sup>20</sup> Susan M. Wolf,<sup>21</sup> Wendy A. Wolf,<sup>12,14</sup> eMERGE Act-ROR Committee and CERC Committee, CSER Act-ROR Working Group, and Wylie Burke<sup>9</sup>

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#### 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?

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**ACMG POLICY STATEMENT**

**Genetics  
in Medicine**



**Patient re-contact after revision of genomic test results:  
points to consider—a statement of the American College of  
Medical Genetics and Genomics (ACMG)**

Karen L. David, MD, MS<sup>1</sup>, Robert G. Best, PhD<sup>2</sup>, Leslie Manace Brenman, MD, MPhil<sup>3</sup>,  
Lynn Bush, PhD, MS<sup>4,5</sup>, Joshua L. Deignan, PhD<sup>6</sup>, David Flannery, MD<sup>7</sup>, Jodi D. Hoffman, MD<sup>8</sup>,  
Ingrid Holm, MD, MPH<sup>9</sup>, David T. Miller, MD, PhD<sup>5</sup>, James O'Leary, MBA<sup>10</sup> and  
Reed E. Pyeritz, MD, PhD<sup>11</sup> on behalf of the ACMG Social Ethical Legal Issues Committee

Volume 21 | Number 4 | April 2019

POLICY

European Journal of Human Genetics (2019) 27:169–182

**ESHG**



## Recontacting patients in clinical genetics services: recommendations of the European Society of Human Genetics

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Shane Doherty<sup>5</sup> • Naomi Hawkins<sup>7</sup> • Tanya F. Halbersma-Konings<sup>8</sup> • Leigh Jackson<sup>9</sup> • Hülya Kayserili<sup>10</sup> •  
Susan E. Kelly<sup>1</sup> • Anneke M. Lucassen<sup>6,11</sup> • Álvaro Mendes<sup>12</sup> • Emmanuelle Rial-Sebbag<sup>13</sup> • Vigdís Stefánsdóttir<sup>14</sup> •  
Peter D. Turnpenny<sup>15</sup> • Carla G. van El<sup>16</sup> • Irene M. van Langen<sup>8</sup> • Martina C. Cornel<sup>16</sup> • Francesca Forzano<sup>17</sup> •  
On behalf of the European Society of Human Genetics

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



# Workgroup Members & Process

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# 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)
  - Decedents (Wolf *et al*, 2015, doi: 10.1111/jlme.12288)
  - 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.

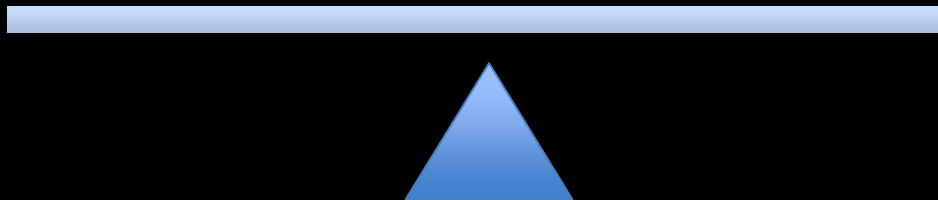
Respect for persons:

- Autonomy: ongoing informed participation
- Veracity/truthtelling: 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

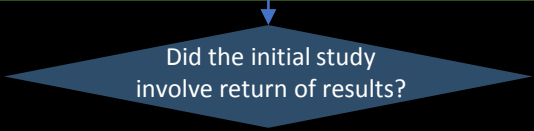
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ASHG recommends that research projects develop a plan for return (or not) of reinterpretations of results. As part of that plan, research participants should be alerted to the likelihood that interpretations of results may change over time and be given 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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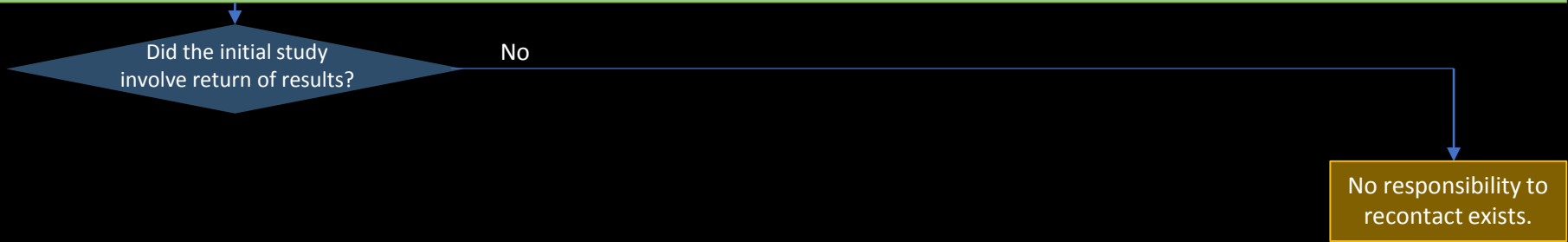


Did the initial study  
involve return of results?

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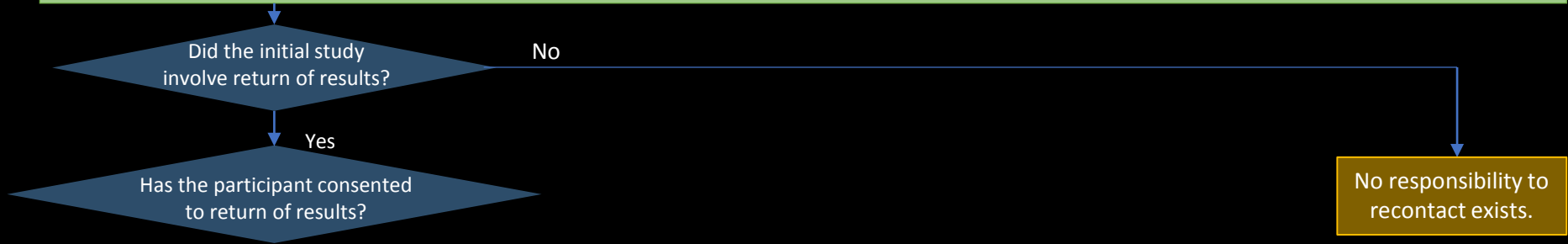
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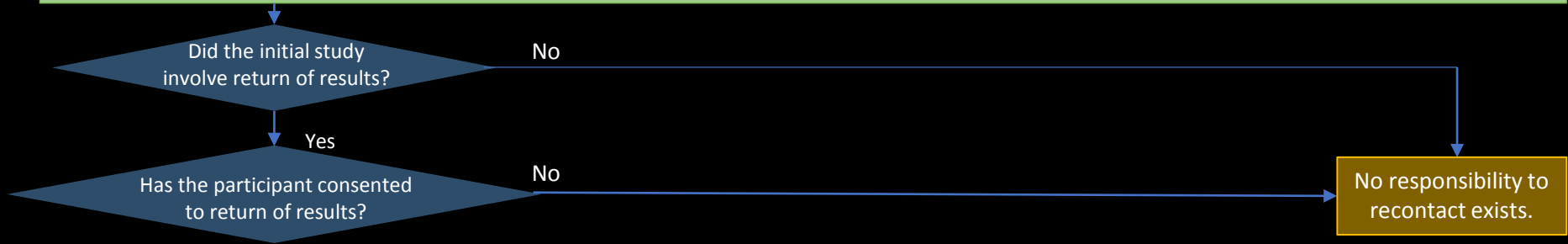
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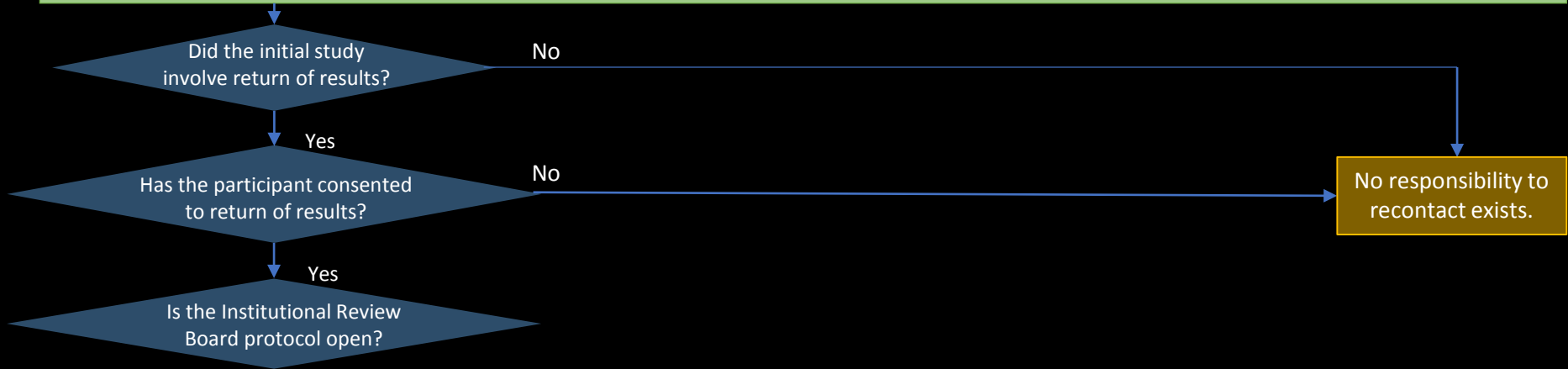
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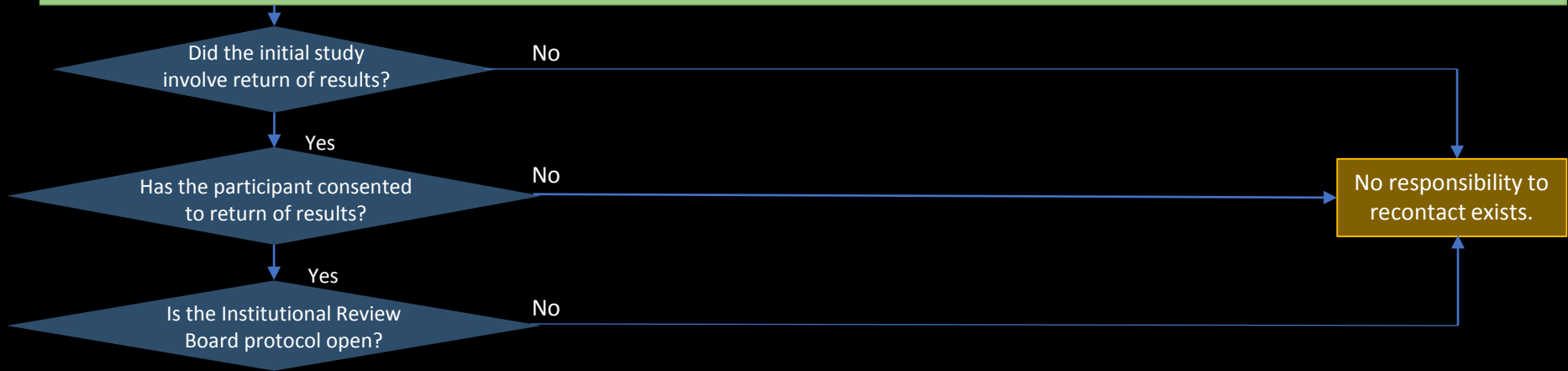
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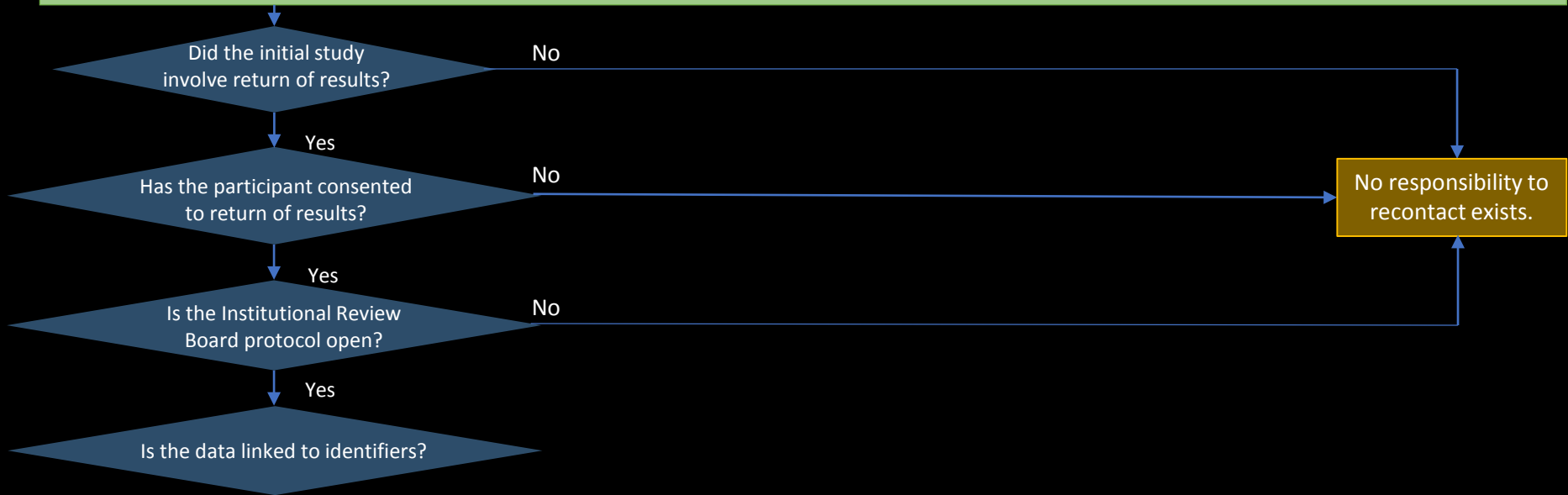
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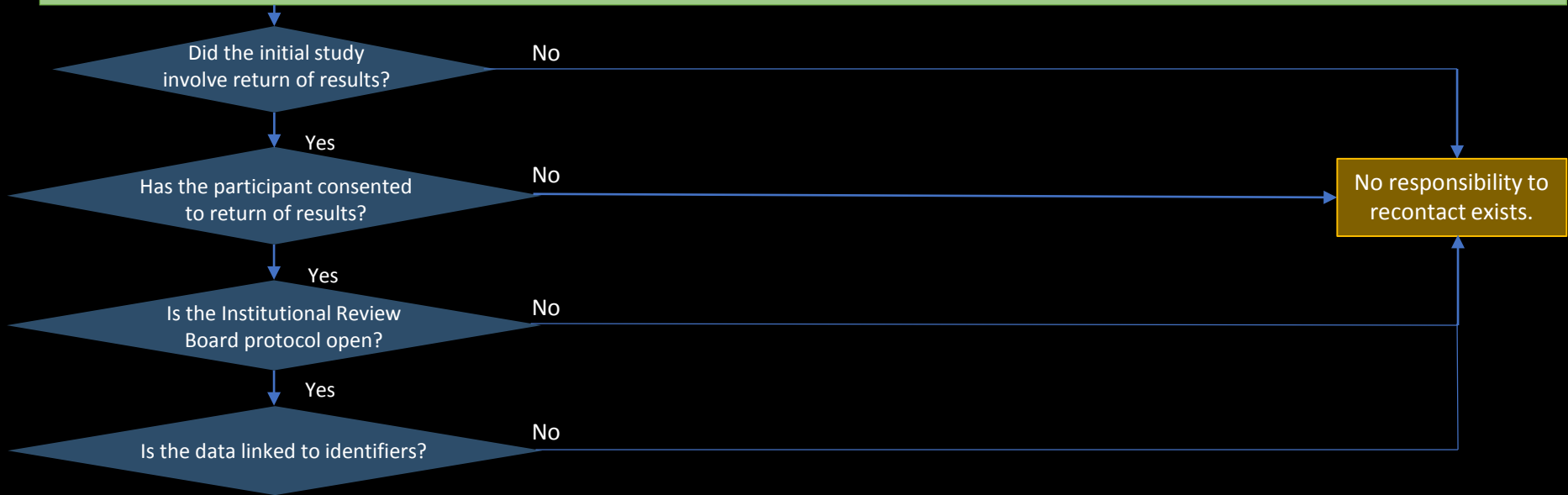
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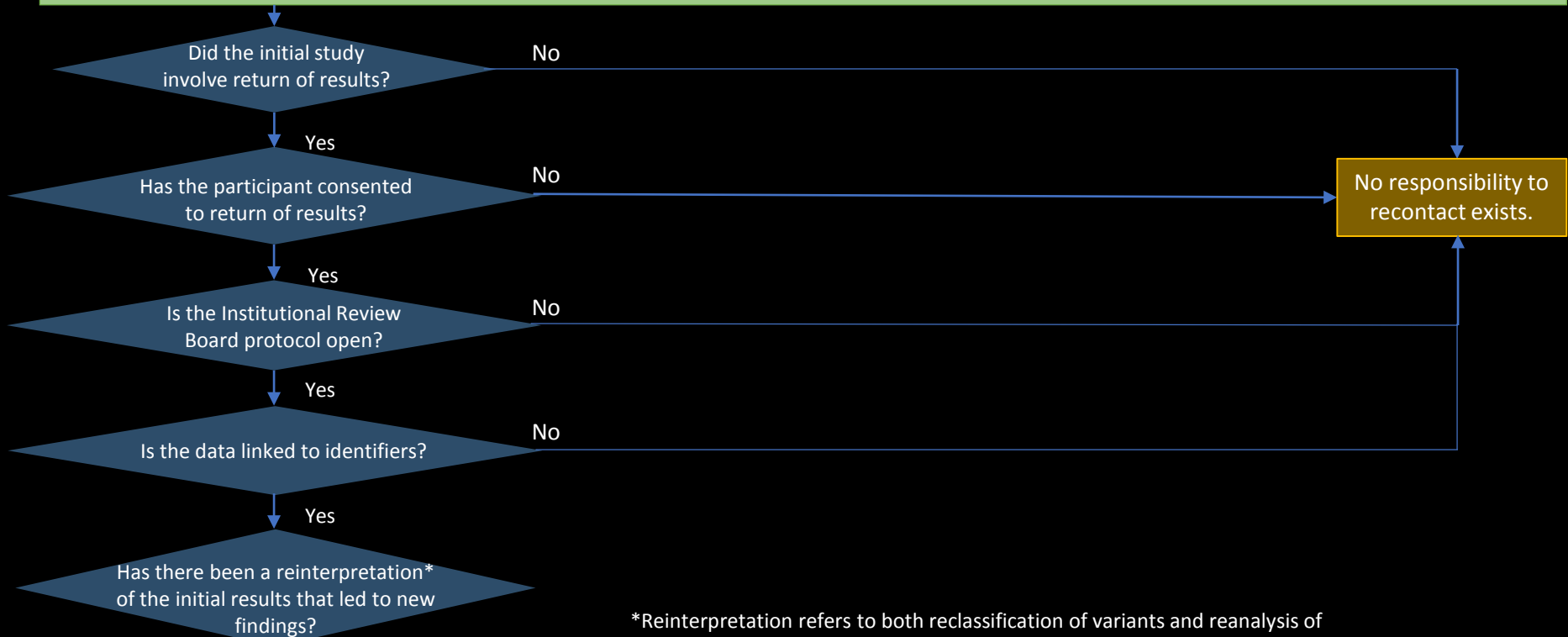
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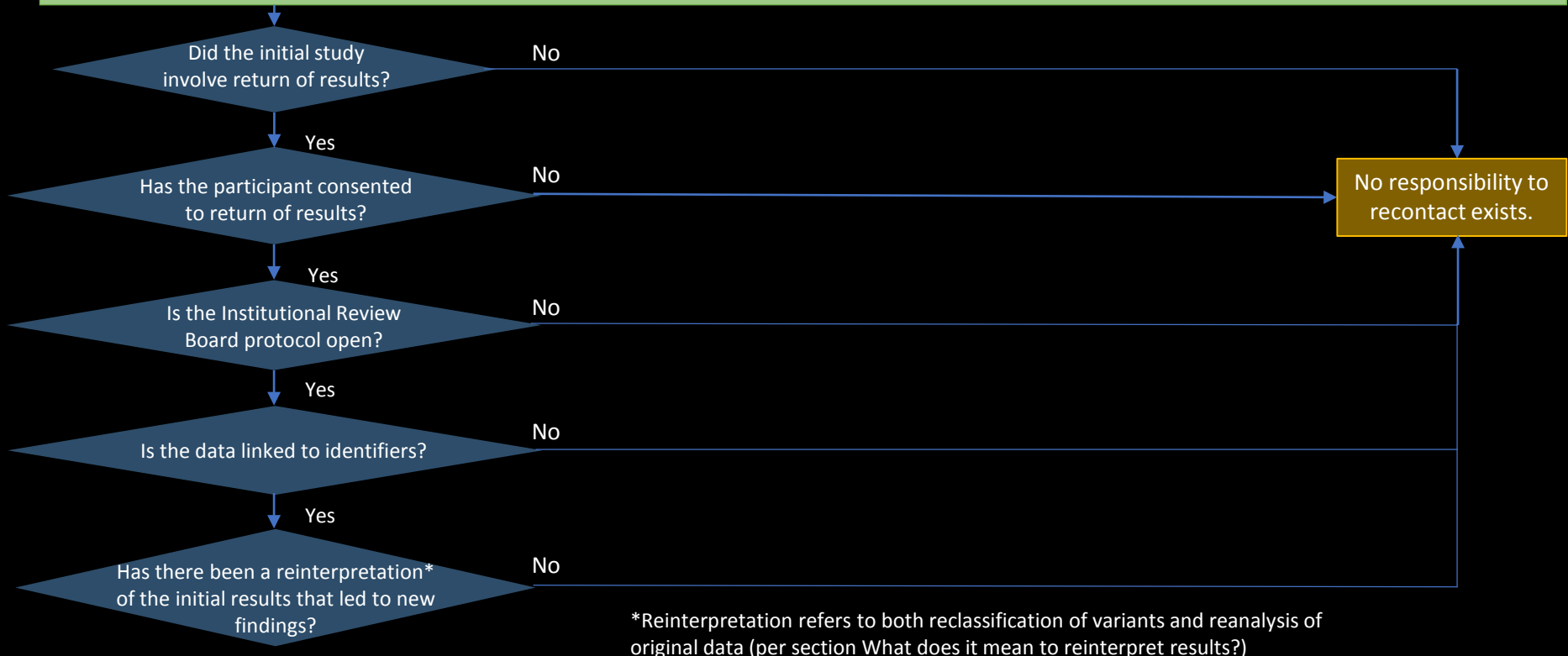
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\*Reinterpretation refers to both reclassification of variants and reanalysis of original data (per section What does it mean to reinterpret results?)

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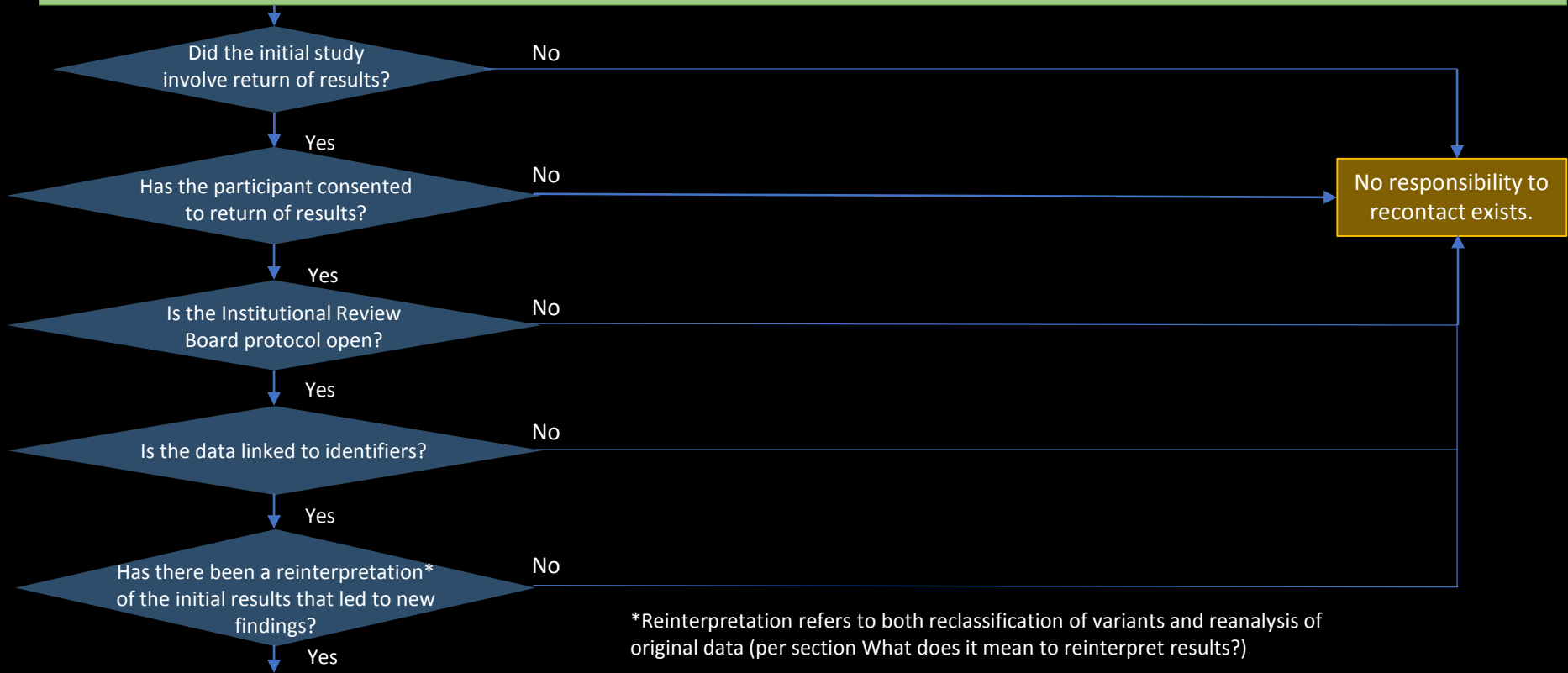
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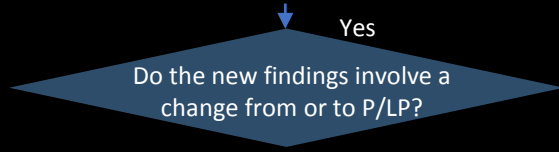


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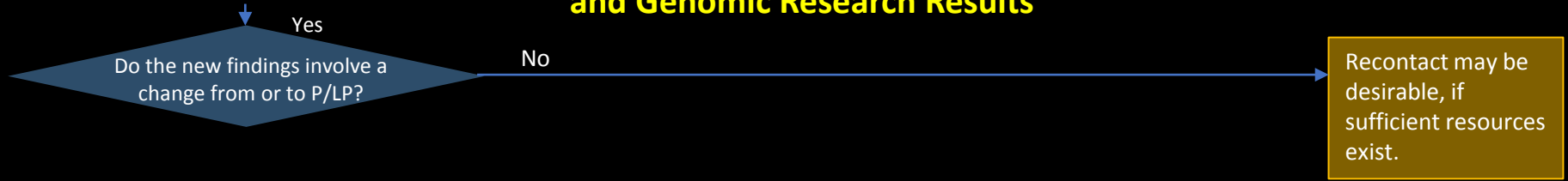
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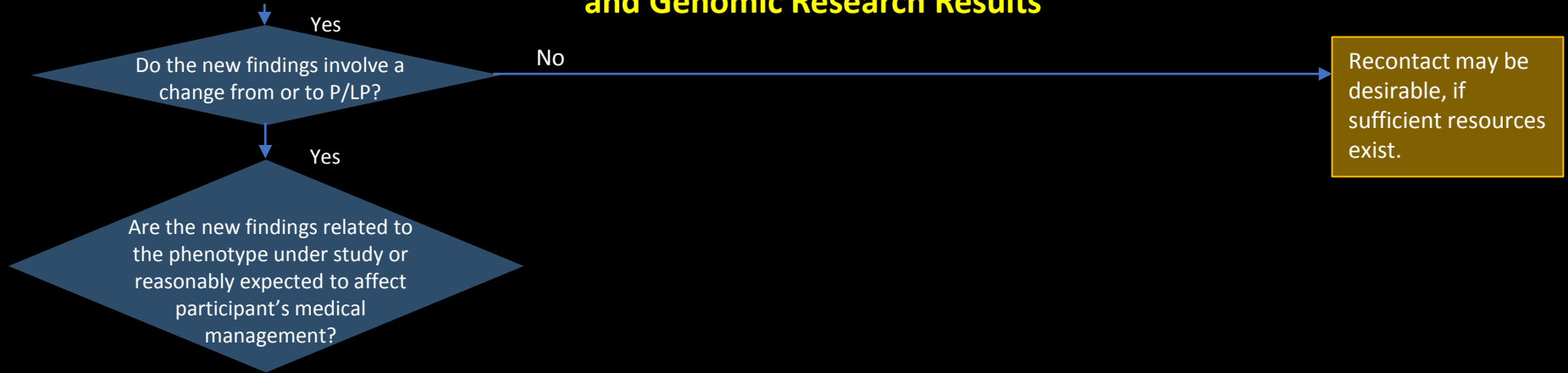
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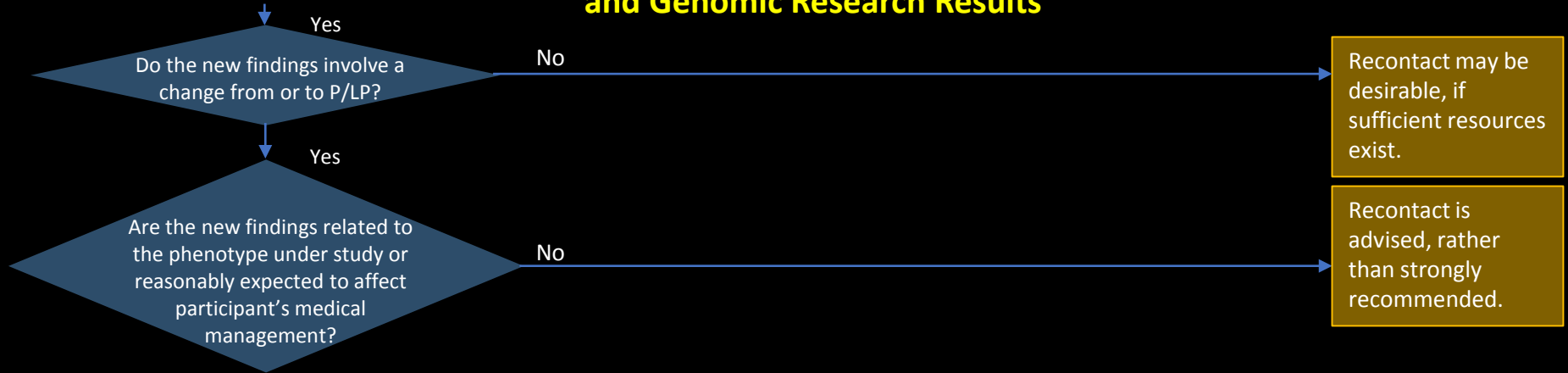
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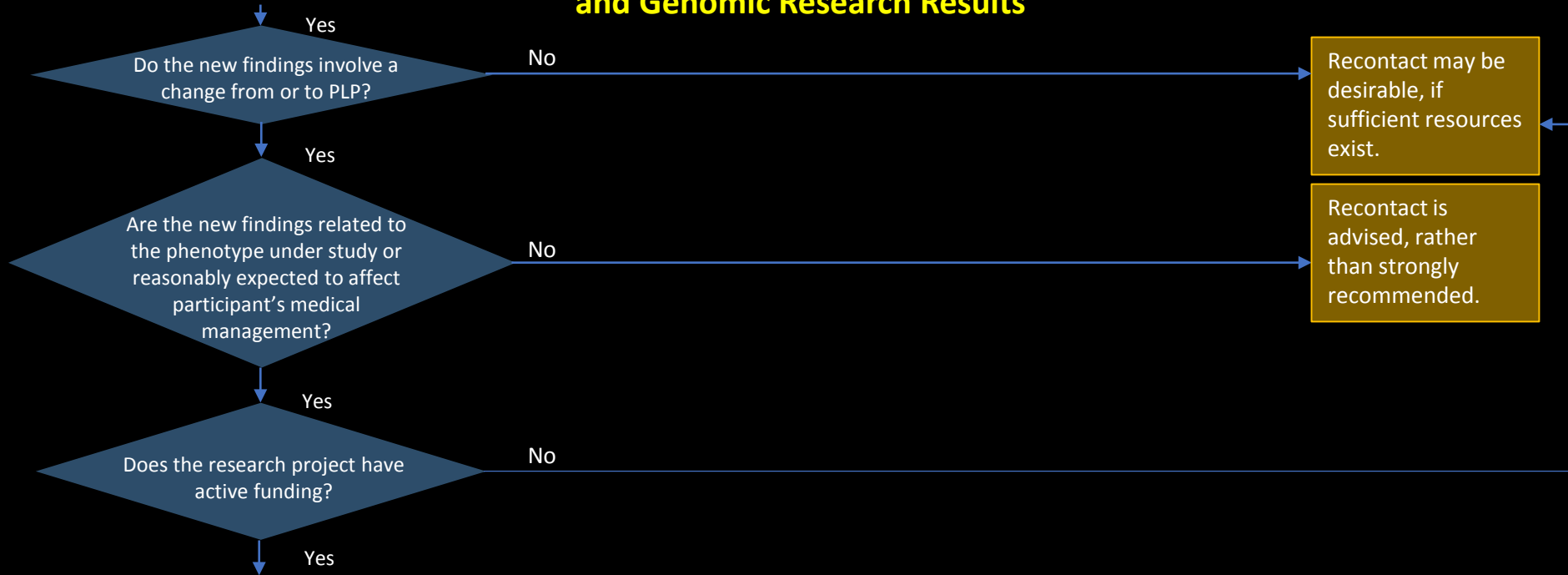
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ASHG strongly recommends that researchers attempt recontact to offer updated results within 6 months of identifying the reinterpreted variant. Attempts to recontact should be documented and limited to a "good faith effort" to reach the participant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



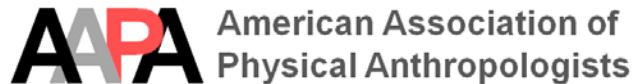
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