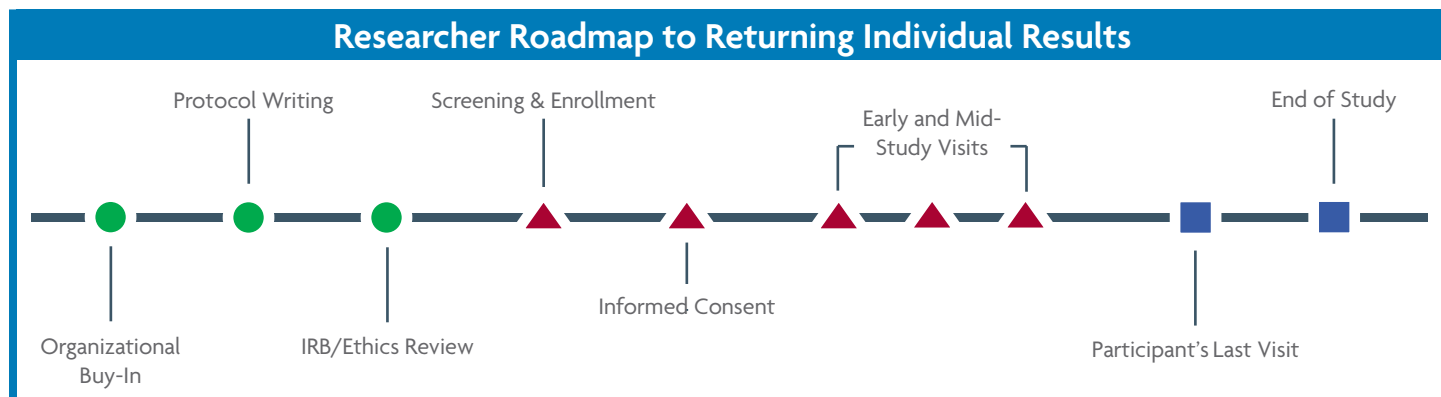


## Supporting Participant Decision-Making in Genetic Testing Studies

*This case study shares an example of how one institution created an educational tool to support decision making for potential participants in a genetic testing study.*



*The roadmap above shows steps for researchers to consider when planning to return individual results to participants. This case study focuses on the pre-study part of the timeline illustrated by the green circles.*

### Jamie's Story

While in her mid-20s, Jamie was diagnosed with Multiple Sclerosis (MS). With time, her symptoms changed. Unable to explain her condition, her neurologist questioned the diagnosis. As her symptoms continued to wax and wane, it became difficult not to have a diagnosis or possible treatment options.

At the age of 49, 14 years ago, Jamie had an opportunity to participate in a genetic study that she felt would help put the pieces of this medical puzzle together. The study investigated whether people would change their behaviors if they knew they were genetically at higher risk for certain diseases.

Jamie was motivated to participate because of her MS symptoms, and even though Alzheimer's disease (AD) was also being tested, her family history of AD simply wasn't on her radar screen. As an interventional genetic study, Jamie should have received interactive genetic counseling before, during, and after the study. Surprisingly, Jamie received her results electronically while alone, without having any counseling to support or advise her.

Jamie's results showed that she had two copies of the Apolipoprotein E4 (apoE4) allele, the most prevalent genetic risk factor of AD. At that time, it was estimated that she had a 91% lifetime risk of succumbing to the disease.

Jamie was faced with a torrent of emotions at receiving this news as she watched her father suffer in the late stages of his own battle with AD.

Jamie felt especially upset that she received this information without any prior preparation or support from the researchers. She contacted the principal investigator (PI) to describe her experience. She shared that she was anxious and upset about her results. The PI's response was unsympathetic, explaining that Jamie should be appreciative that she could now prepare for and take measures to prevent the onset of AD.

Unsatisfied with the answer and the lack of empathy displayed by the PI, Jamie sought recourse from the IRB, the ethics review board with oversight responsibilities for the study. The IRB informed her that she signed the consent form and that the researchers had met their obligation of informing her of the risks; none of her rights had been violated. Later, Jamie was diagnosed with PTSD and even contemplated suicide.

After reading the book "To Test or Not to Test," written by Doris Zallen, Jamie realized that she was not alone. She knew she had to take action so that other individuals would be spared her experience. Jamie is now an advocate for patients and study participants to ensure that institutions have policies and procedures in place to support participants through the process of enrolling in genetic studies and receiving their research results.

## Background

Genetic testing can indicate whether or not people will develop a disorder, such as Huntington's disease, or if they are at an increased risk for a future health problem, such as Alzheimer's disease. Obtaining, revealing, and sharing such genetic information has become an important element in clinical trials and in clinical practice. Direct-to-consumer companies (such as "23 and me," "Ancestry.com," and others) have increased public knowledge and access to testing.

Genetic testing in research raises unique challenges for researchers and clinicians, including:

- Who should be informed of any genetic findings?
- Since genes are shared within families, do family members have a right to the genetic information?
- Are there potential advantages of having this information for future health monitoring or preventive measures?
- Are there potential psychological harms of having this information if there are no preventive measures or treatments currently available?
- Is there a possibility that genetic information could become known to outsiders such as insurance companies and employers?

The "approach" section below outlines the process one institution piloted and then implemented to support participant decision-making in order to mitigate potential harms such as those illustrated in Jamie's story.

## Approach

It is important to ensure that potential research participants and patients are well informed prior to any decision about genetic testing. Pre-testing counseling is a time-intensive activity requiring the commitment of study personnel. Doris Zallen (Virginia Tech) and Michael Ekstract (Breakneck Turtles Productions), with support from the Commonwealth of Virginia's Alzheimer's and Related Diseases Research Award Fund, led a team to create an educational tool that could serve as a supplement to in-person components and help facilitate these interactions.

After learning of Jamie's difficult experience, as well as similar reports from others, they opted to focus the tool on Apolipoprotein-E (apoE) genetic testing for the risk of Alzheimer's disease.

### Creating an Interactive Decision-Making Tool: A Four-Step Process

#### 1. *The Baseline: Information Collection*

Zallen's book drew on hundreds of interviews conducted with experts in genetic testing and with individuals concerned about a variety of genetic problems for themselves or their families. Four key questions to help inform an individual's decision about having - or not having - genetic testing were identified:

1. Does my family history put me at higher risk for Alzheimer's disease than others?
2. Will the genetic test give me useful information?
3. Is this the right time in my life to take this test?
4. Will the advantages of testing outweigh the disadvantages?

**These four questions formed the template for the educational tool.**

## 2. Tool Development

The team began by developing a prototype to test both their assumptions and the tool's usefulness. Each of the questions in the template addresses a different aspect of the decision process and requires a different mode of presentation. For example, in addition to text, visual displays were needed to make statistical information clear. Video vignettes were created to help users consider the advantages and disadvantages of participating in genetic testing. As each section of the tool was developed, focus groups of individuals considering apoE-genetic testing were convened to review material and provide feedback. Special attention was given to evaluating the video vignettes. A panel of genetic professionals and physicians also provided input.

## 3. Validation

The prototype tool was next studied to assess its usefulness. Over 1,200 people, reached through a variety of Alzheimer's disease-related organizations, reviewed the prototype and provided feedback. Of these, 93% said they found it "helpful" or "very helpful" and would recommend it to others. This tool also changed the way people thought about having apoE testing, with 35% responding that they were more likely to get tested, and 20% less likely. Respondents also appreciated that the information was clear and unbiased, and that it broke a complex decision into manageable parts.

## 4. Revision

While the content of the prototype was highly praised, the team did receive useful feedback about the user interface and several presentation elements. They made design and structural changes to improve the user experience. For example, they simplified the layout and created a sequential path through the site. They added text descriptions to the video vignettes so that people who preferred reading over watching videos could more easily access the information. The resulting site is both more attractive and easier to use.

## Outcomes

Though this case was specifically about genetic risk for Alzheimer's disease, it is applicable to other situations in which genetic information is either directly sought or a secondary finding in a clinical study.

It may not be necessary to follow the exact process detailed above, but there are key takeaways that all researchers using genetic tests should bear in mind to support and empower potential participants in their decision-making process.

**This tool is now freely available at**  
[www.genetestornot.org](http://www.genetestornot.org)

### References:

DT Zallen, *To Test or Not to Test: A Guide to Genetic Screening and Risk* (New Brunswick, NJ and London, Rutgers University Press, 2008)

M Ekstract, GI Holtzman, KY Kim, SM Willis, and DT Zallen, "Evaluation of a Web-based decision aid for people considering the APOE genetic test for Alzheimer's risk", *Genetics in Medicine* 19: 676-682 (2017)

## Key Takeaways

### Listen and understand

Begin by learning from the community of potential participants so you can prepare materials that relate to their needs and priorities.

### Empower participants with information

Collate information about each relevant test and each disease area. Ensure you present value-laden information neutrally.

### Be cognizant of your consent process

Allow potential participants adequate time to access resources. Remind them again before the release of any personal genetic information.

### Set up a support structure for participants

Offer multiple modes of accessible support for participants, including online discussions, phone consultations, and in-person meetings.