GENETEST-101:

Developing an App for Non-Genetics Providers Working with Rare Disease Patients

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National Human Genome Research Institute

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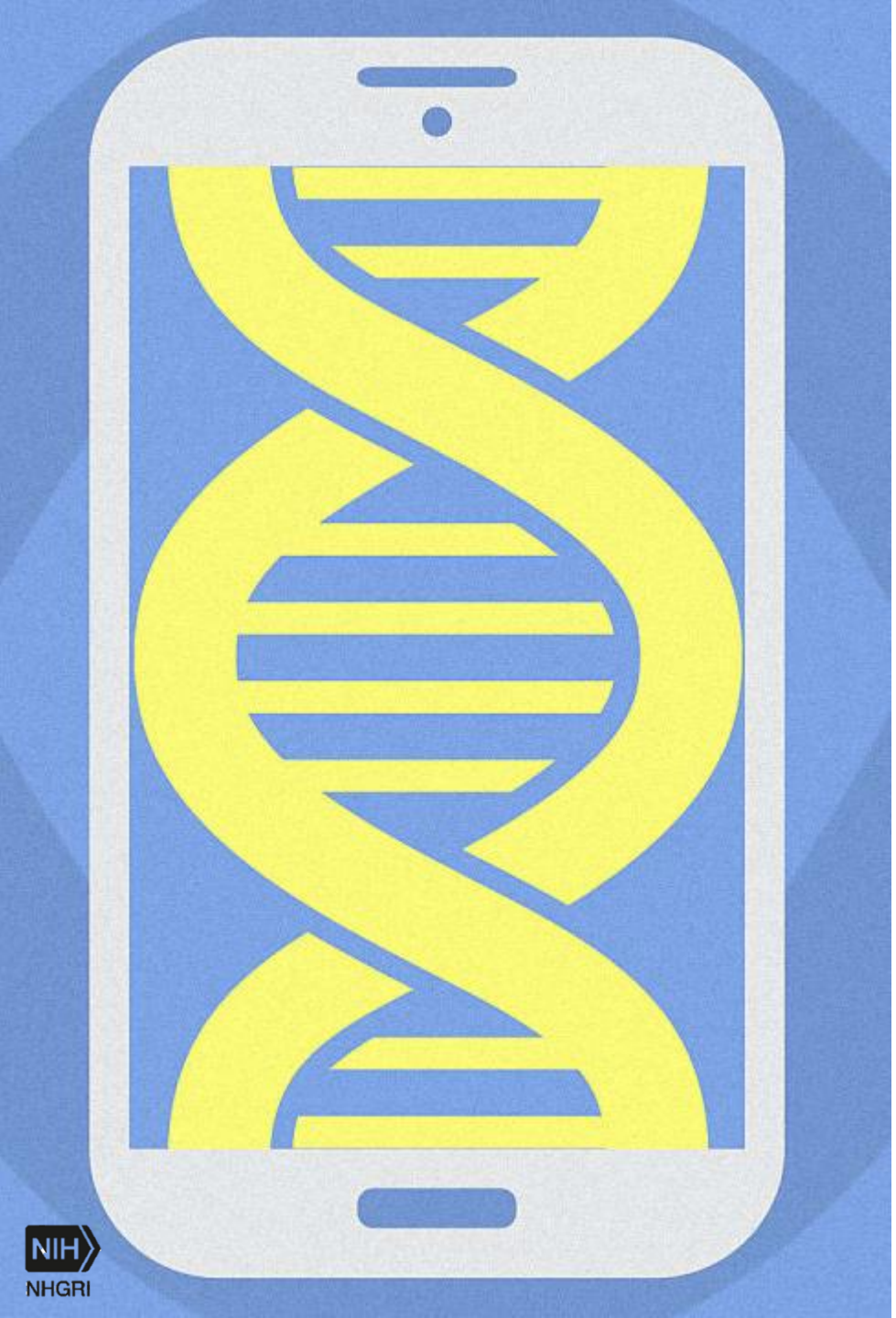
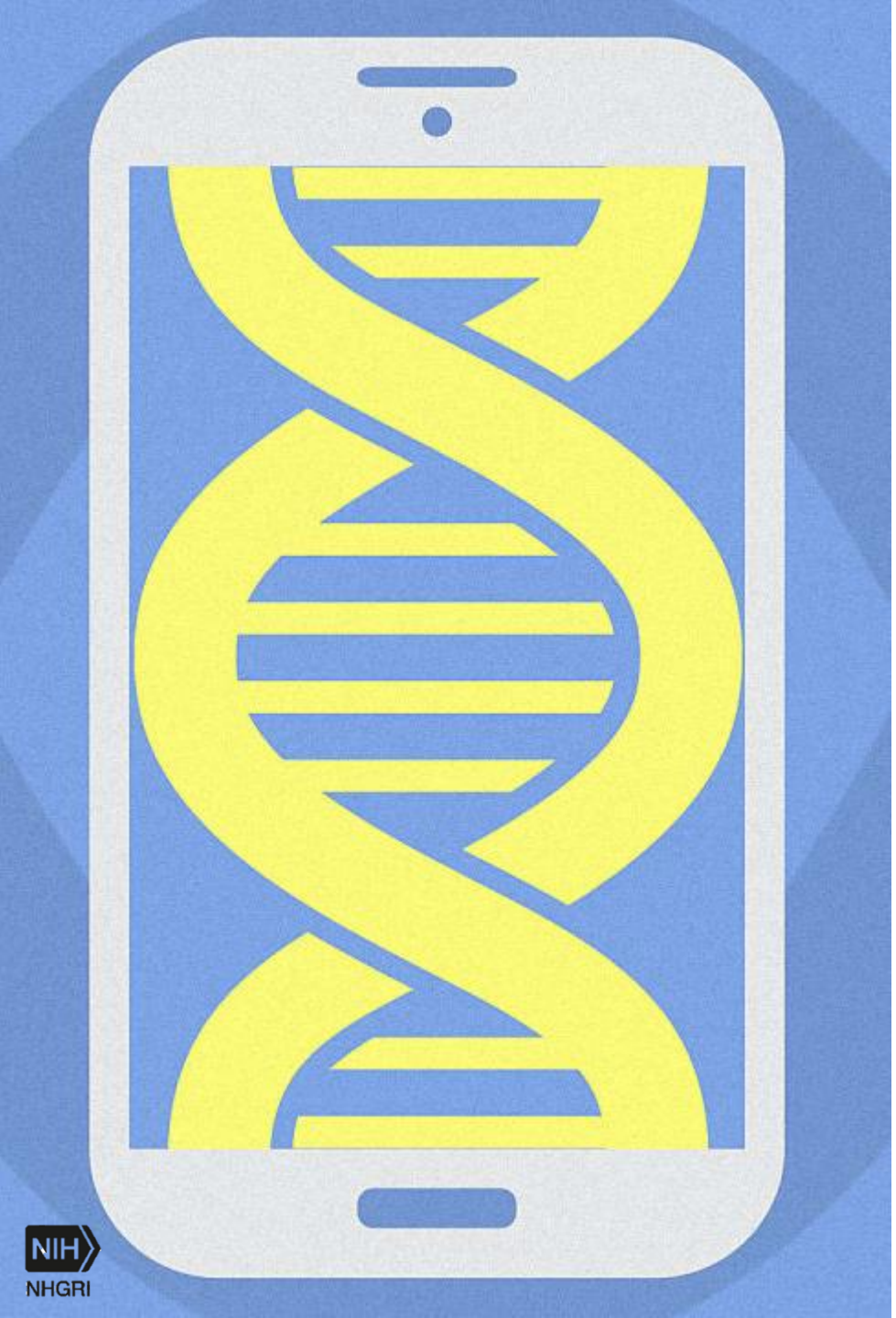


Project Overview

- **Goal:** Create a tool that could be utilized by non-genetics healthcare providers as a point-of-care resource throughout the genetic testing process
- **Audience:** Pediatricians, family physicians, PAs, NPs, etc.
- App is not finalized/complete; please do not disseminate outside of ISCC-PEG at this time



Project Overview

Stage 1: Print and electronic “toolkit”

- Developed to accompany Rare Disease subgroup’s workshop at the Pediatric Academic Societies 2021 annual meeting

Stage 2: Mobile app prototype

- Adapted and expanded from original toolkit

Idea: supplemental materials to synergize with PAS workshop efforts

Premise: if you see something that suggests a rare genetic condition, what do you do?

Creation of toolkit resource: pdf + excel document

Feedback from Rare Disease Project Group + revisions

Stage 1: Toolkit Development

Training Next Generation Pediatricians in Genomics: A Case-Study Approach

Inter-Society Coordinating Committee for Practitioner Education in Genomics (ISCC-PEG)

Initial Clinical Evaluation

ID "Red flags" that suggest a patient could have a rare genetic condition and may need a referral to genetics:

- Utilize Family GENES acronym (Australian Medical Association Genetic and Rare Disease Network)
- When to Suspect a Genetic Syndrome (*American Family Physician*)

As appropriate, refer patient to a genetics professional or proceed with genetic testing:

- Find a Genetics Clinic (ACMG)
- How to Find a Disease Specialist (GARD)

Test Selection

- Genetic Testing 101: Genetic Testing Topics (MedlinePlus Genetics)
- Determine appropriate genetic test(s): Comparing Genetic Tests (Jackson Lab), Genomic Diagnosis for Pediatric Disorders (*Frontiers in Pediatrics*)
- Select genetic testing laboratory: Genetic Testing Registry (NCBI)
- Consider potential follow-up studies

Pre-test Counseling

- Explain genetic testing options and facilitate patient decision-making: Genetic Testing FAQ (NIH NHGRI), Counseling About Genetic Testing and Communication of Genetic Test Results (ACOG)
- Obtain informed consent for testing: Informed Consent and Pretest Counseling Checklist (Jackson Lab), What is Informed Consent? (MedlinePlus Genetics)
- Ethical/Legal Considerations: Genetic Information Nondiscrimination Act (Jackson Lab), Genetic Testing of Children (AMA)

Diagnostic Result

- Interpret genetic test results: Utilize variant nomenclature (Human Genome Variation Society), ACMG-AMP sequence variant interpretation recommendations (*Genetics in Medicine*), and resources such as ClinVar (NCBI) and Franklin (Genoox) to assess variant pathogenicity (particularly for variants of unknown significance)
- Explore variant clinical relevance using resources such as ClinGen (NCBI), GeneReviews (NCBI), and OMIM (Johns Hopkins)
- Consider whether follow-up genetic testing may be helpful: parental testing (de novo vs. inherited), broader testing if results are negative (such as WES/WGS)
- Refer to genetics professionals for complex or uncertain results: Find a Genetics Clinic (ACMG)

Explain Results to Family

- Contracting: Ask family about their current understanding and for any initial questions. Describe the purpose of visit: (Genetic Counseling Toolkit)
- Disclose results: Test Results (Genetic Counseling Toolkit), What Do the Results of Genetic Tests Mean? (MedlinePlus Genetics)
- Address psychosocial concerns: Caring for a Patient with a Rare Disease (GARD)
- Integrate into clinical care: Utilize GeneReviews article if available to communicate screening, management plans, genetic risks to other family members, and reproductive options

Next Steps

Connect families with rare disease resources and/or condition-specific support groups:

- Info: GARD, NORD, Genetic Alliance, MedlinePlus Genetics
- Support: Family Voices, Parent to Parent USA, Facebook Support Groups
- Research: Undiagnosed Disease Network, clinical trials/research studies

Toolkit 1-pager

Excel Resource List

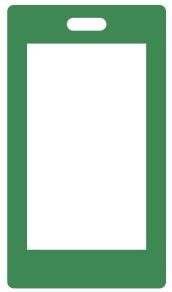
Training Next Generation Pediatricians in Genomics: A Case-Study Approach (Inter-Society Coordinating Committee for Practitioner Education in Genomics)

Resource	Organization	URL	When to use it					What is it?	Tips and Tricks
			Clinical Eval	Test Selection	Pre-test	Diagnostic Result	Explaining Results		
MedlinePlus Genetics	NIH U.S. National Library of Medicine	https://medlineplus.gov/genetics/					INFO	Patient-friendly info about genetic concepts, conditions, and testing options. Printable PDFs of all content.	This site is a good first place to go if you are unfamiliar with a particular condition or concept. Search for specific conditions to find info in patient-friendly language.
OMIM	Johns Hopkins Medicine	https://www.omim.org/					INFO	Provides info about gene variants and associated phenotypes with helpful references and links to other sources.	Use orange "Clinical Synopsis" button to view summary of associated features; this can be used to help determine differential diagnosis. List on the right side of the page links to other helpful resources.
GeneReviews	NIH U.S. National Library of Medicine	https://www.ncbi.nlm.nih.gov/books/NBK1116/					INFO	Point-of-care resource that provides expert review articles about genetic conditions, covering diagnosis, management, and genetic counseling.	Differential diagnosis section provides list of conditions with overlapping signs and symptoms. Helpful determining conditions to consider. Genetic counseling section discusses recurrence risks.
PubMed	NIH U.S. National Library of Medicine	http://www.ncbi.nlm.nih.gov/pubmed					INFO	Database of biomedical primary literature reports and manuscripts. Helpful for finding primary literature related to specific biomedical topics; helpful if other sources such as GeneReviews don't have sufficient info.	Use filters on the left side of the webpage to limit search results to recently-published papers or certain article types such as review articles.

Research toolkit adaptation options

Toolkit -> app revisions and feedback

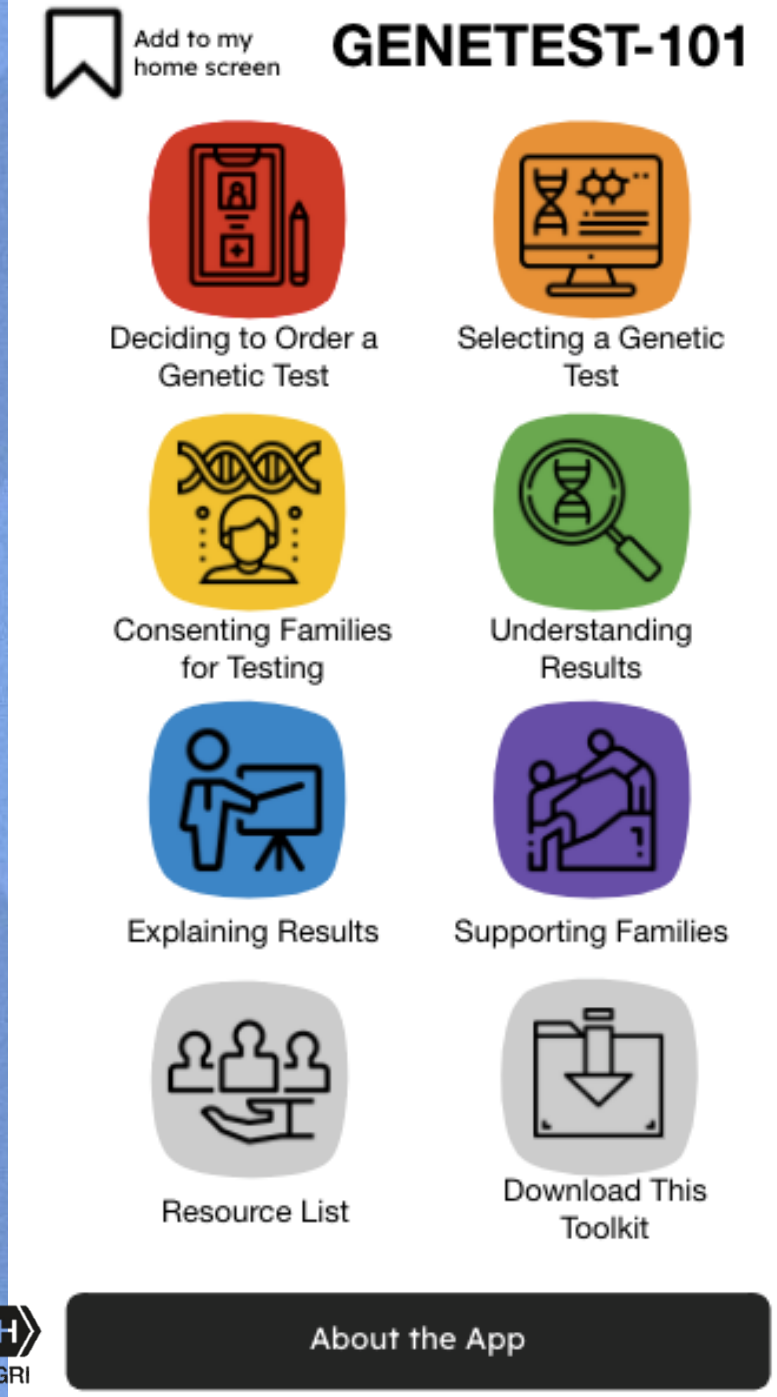
Plan and conduct formal evaluation + analysis



Further revisions based on evaluation feedback

Dissemination and determination of any next steps

Stage 2: App Development



App Development

- Created using Google slides template
- Adapted content from toolkit to address the genetic testing process
- Included instructions for users to add to phone home screen
- Converted toolkit excel database into a section called “Resource List”
- Added links to download pdf and/or excel documents

Explaining Results

The process of explaining test results can vary depending on the results themselves and the individual patient. Regardless, using patient-friendly language and addressing psychological issues that arise is an important component of results disclosure.

Explaining positive results

Explaining negative results

Explaining uncertain results

Using patient-friendly language

Addressing psychosocial concerns

View resource list

Explaining Negative Results

While for some patients and families negative results may be a relief, for others it may mean that they are still without an explanation for their symptoms. In those cases, guidelines for explaining positive results can be helpful for framing the disclosure. Other key points to keep in mind include:

- A negative result does not guarantee that there is no genetic cause of the features seen.
- Follow up testing may be indicated, depending on the patient's features and what testing was previously performed.
- In the future, reanalysis or retesting may be able to provide a genetic explanation. Likelihood of this depends on the overall likelihood of a single genetic cause for the patient's symptoms.

PREVIOUS: Explaining positive results

NEXT: Explaining uncertain results

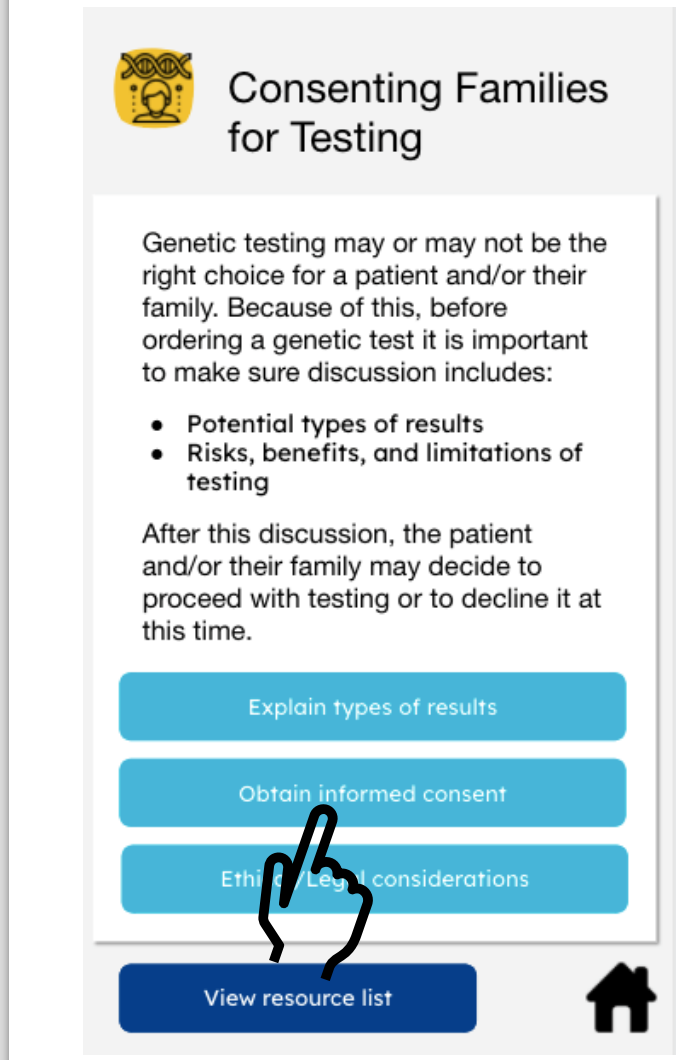
Further Evaluation of Variants of Uncertain Significance, cont.

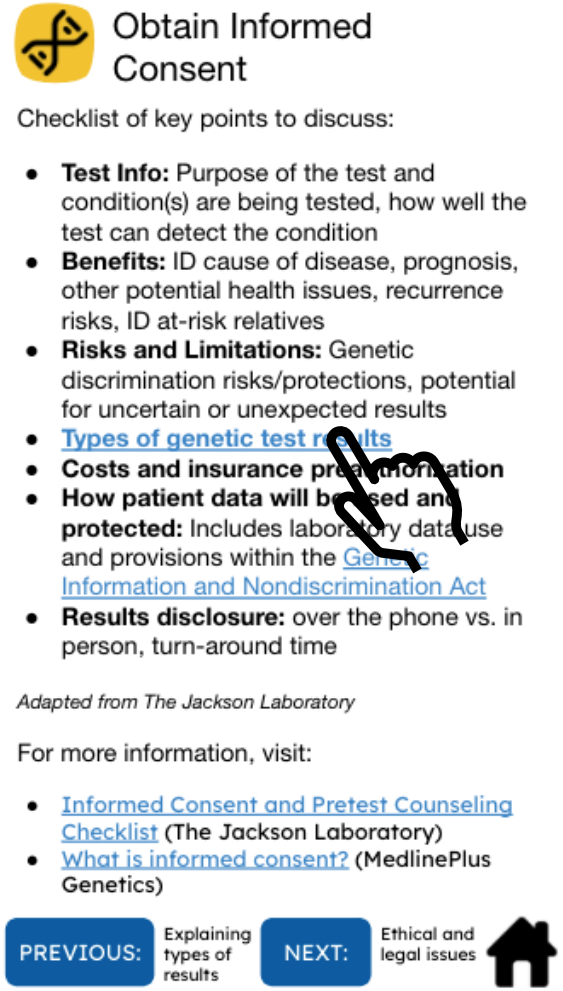
Follow-up Testing: If test results were negative and the patient's symptoms strongly suggest an underlying genetic cause, broader testing can be considered. This may involved a chromosomal microarray (CMA) to investigate deletions and duplications across the genome. It may involve whole exome or whole genome sequencing to investigate sequence changes in a broader, less targeted fashion.

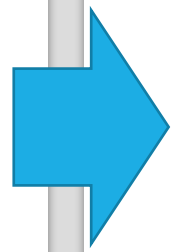
If test results are uncertain, complex, or you are unsure if follow-up testing should be conducted, referral to a genetics professional may be indicated.

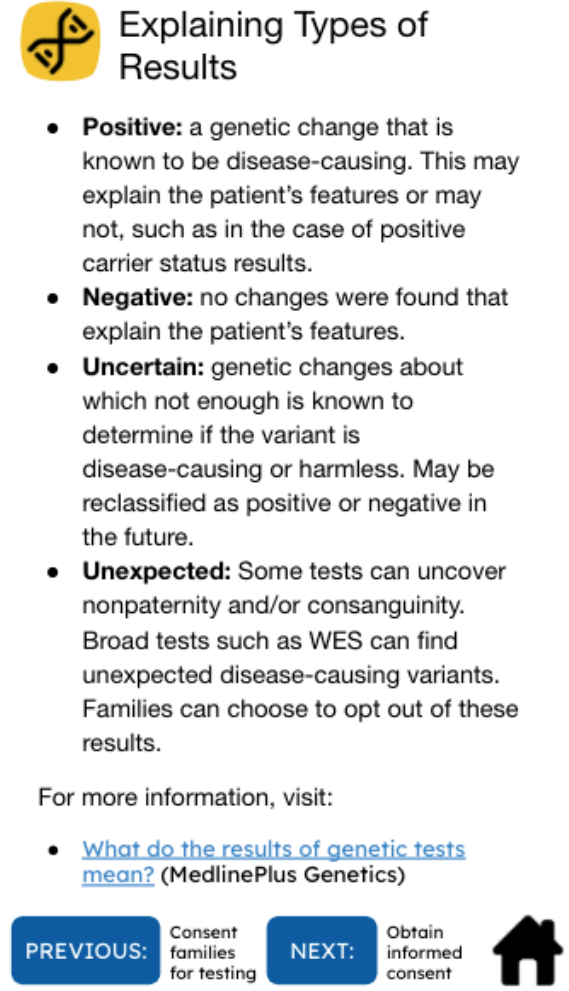
PREVIOUS: Evaluate VUSs 2/2

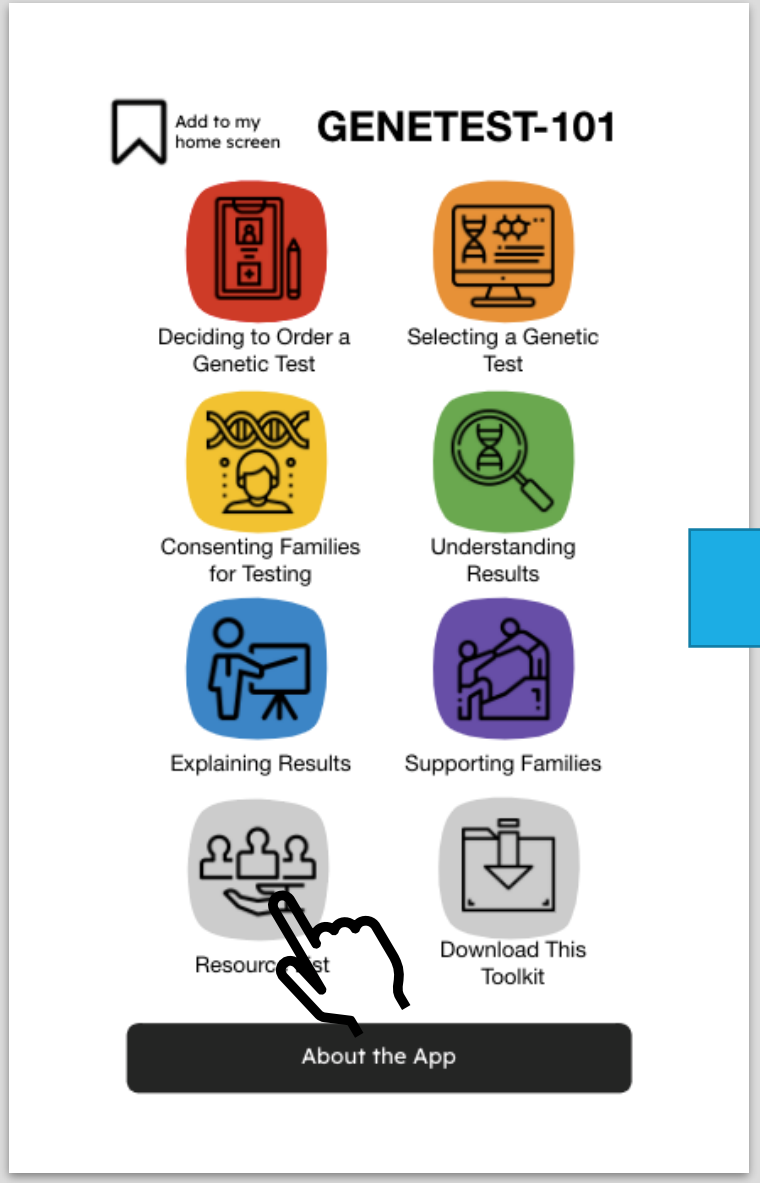
NEXT: Explaining results

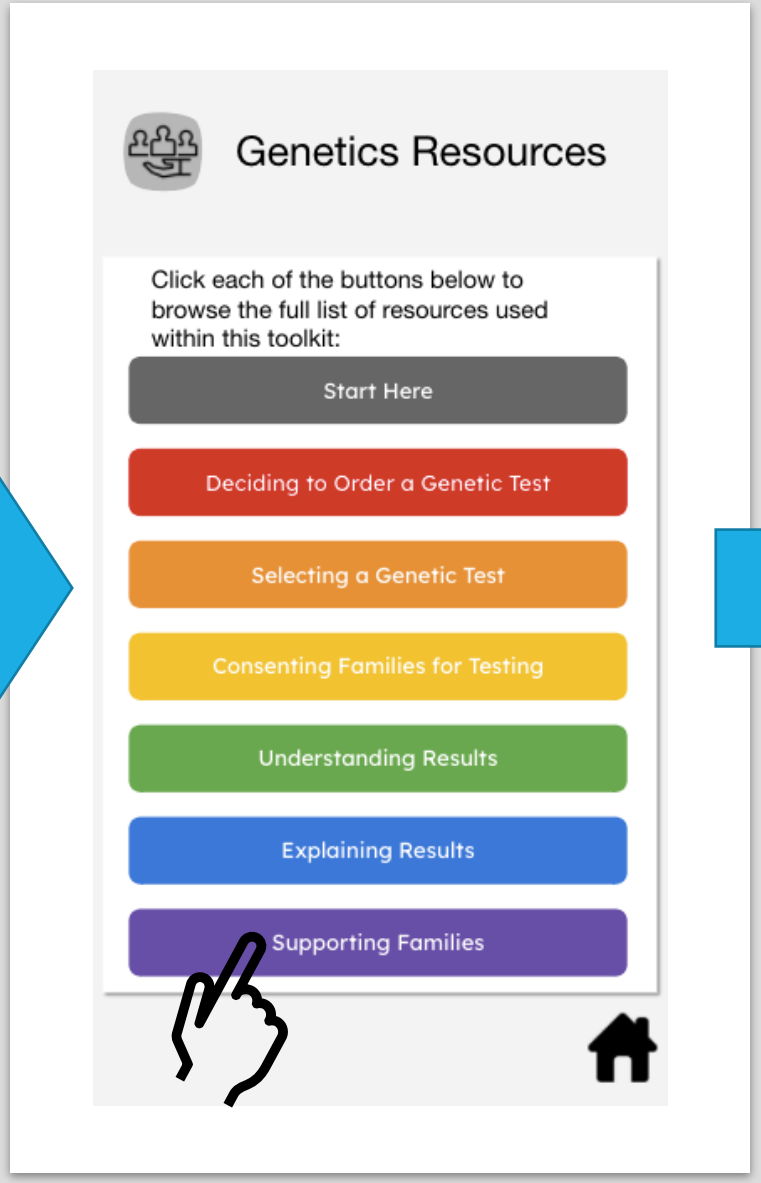

Consenting Families for Testing
Genetic testing may or may not be the right choice for a patient and/or their family. Because of this, before ordering a genetic test it is important to make sure discussion includes:
Potential types of results
Risks, benefits, and limitations of testing
After this discussion, the patient and/or their family may decide to proceed with testing or to decline it at this time.
Explain types of results
Obtain informed consent
Ethical/Legal considerations
View resource list

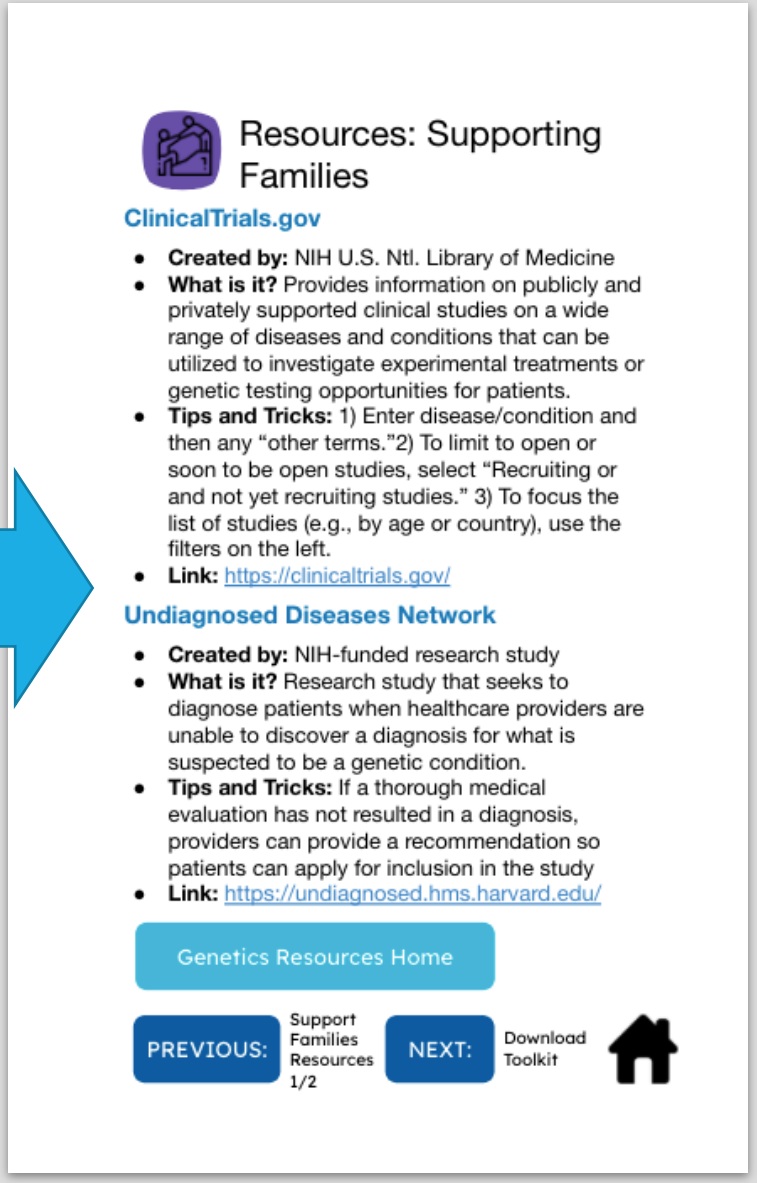

Obtain Informed Consent
Checklist of key points to discuss:
Test Info: Purpose of the test and condition(s) are being tested, how well the test can detect the condition
Benefits: ID cause of disease, prognosis, other potential health issues, recurrence risks, ID at-risk relatives
Risks and Limitations: Genetic discrimination risks/protections, potential for uncertain or unexpected results
Types of genetic test results
Costs and insurance pre-authorization
How patient data will be used and protected: Includes laboratory data use and provisions within the Genetic Information and Nondiscrimination Act
Results disclosure: over the phone vs. in person, turn-around time
Adapted from The Jackson Laboratory
For more information, visit:
Informed Consent and Pretest Counseling Checklist (The Jackson Laboratory)
What is informed consent? (MedlinePlus Genetics)
PREVIOUS: Explaining types of results
NEXT: Ethical and legal issues

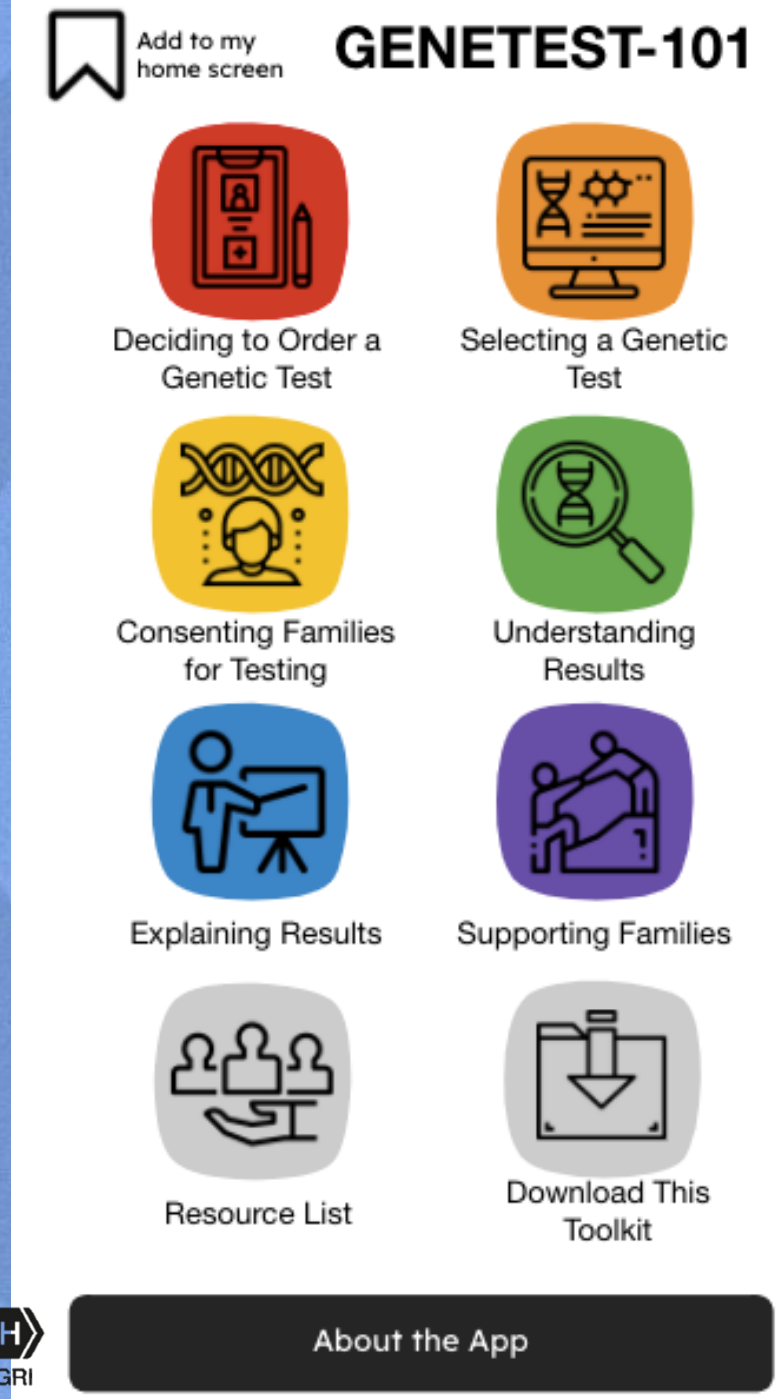



Explaining Types of Results
Positive: a genetic change that is known to be disease-causing. This may explain the patient's features or may not, such as in the case of positive carrier status results.
Negative: no changes were found that explain the patient's features.
Uncertain: genetic changes about which not enough is known to determine if the variant is disease-causing or harmless. May be reclassified as positive or negative in the future.
Unexpected: Some tests can uncover nonpaternity and/or consanguinity. Broad tests such as WES can find unexpected disease-causing variants. Families can choose to opt out of these results.
For more information, visit:
What do the results of genetic tests mean? (MedlinePlus Genetics)
PREVIOUS: Consent families for testing
NEXT: Obtain informed consent


Add to my home screen
GENETEST-101
Deciding to Order a Genetic Test
Selecting a Genetic Test
Consenting Families for Testing
Understanding Results
Explaining Results
Supporting Families
Download This Toolkit
About the App

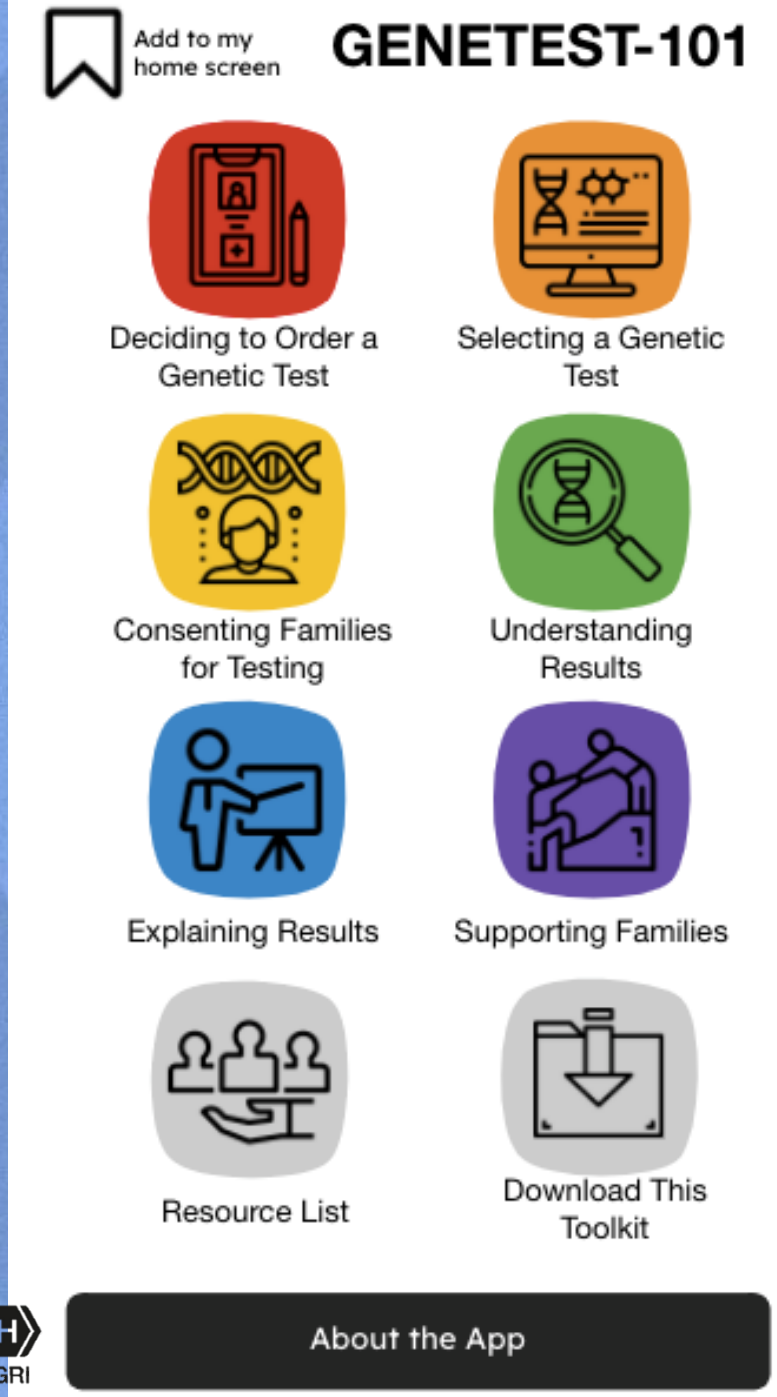

Genetics Resources
Click each of the buttons below to browse the full list of resources used within this toolkit:
Start Here
Deciding to Order a Genetic Test
Selecting a Genetic Test
Consenting Families for Testing
Understanding Results
Explaining Results
Supporting Families


Resources: Supporting Families
ClinicalTrials.gov
Created by: NIH U.S. Ntl. Library of Medicine
What is it? Provides information on publicly and privately supported clinical studies on a wide range of diseases and conditions that can be utilized to investigate experimental treatments or genetic testing opportunities for patients.
Tips and Tricks: 1) Enter disease/condition and then any "other terms."2) To limit to open or soon to be open studies, select "Recruiting or and not yet recruiting studies." 3) To focus the list of studies (e.g., by age or country), use the filters on the left.
Link: https://clinicaltrials.gov/
Undiagnosed Diseases Network
Created by: NIH-funded research study
What is it? Research study that seeks to diagnose patients when healthcare providers are unable to discover a diagnosis for what is suspected to be a genetic condition.
Tips and Tricks: If a thorough medical evaluation has not resulted in a diagnosis, providers can provide a recommendation so patients can apply for inclusion in the study
Link: https://undiagnosed.hms.harvard.edu/
Genetics Resources Home
PREVIOUS:
Support Families Resources 1/2
NEXT:
Download Toolkit



Next Steps

- Finalize prototype
- Evaluation + Data Analysis
  - Goal: Evaluate if app is (1) usable and if it is (2) useful for target audience(s)
  - Usability testing: survey with tasks/scenarios to complete + validated usability scale
  - Open-ended questions for further feedback
- Further Revisions
- Dissemination
  - Determination of long-term “home” for resource
  - Based on evaluation and feedback, determination of any other longer-term development or revisions



Feedback and Questions

A gigantic thank you to my mentor Michelle Snyder, ISCC-PEG Rare Disease Project Group members including Dr. Sabrina Malone-Jenkins, Rachel Palmquist, Kristen Fishler, Dr. Leah Burke, Janine Lewis, and ISCC-PEG Co-chairs Dr. Rich Haspel and Dr. Donna Messersmith for all their help and guidance throughout this project.

Feedback? Visit **tinyurl.com/genetestfeedback** (link in chat) to view the app and provide feedback.

- App name suggestions? GENEKIT, GENETEST-ED, GT-PRO, GENETEST-TOOL, GENETEST-APP
- Evaluation questions & approach
- Missing/extraneous content?
- Anything else!