# Personal Genome Sequencing Outcomes Study

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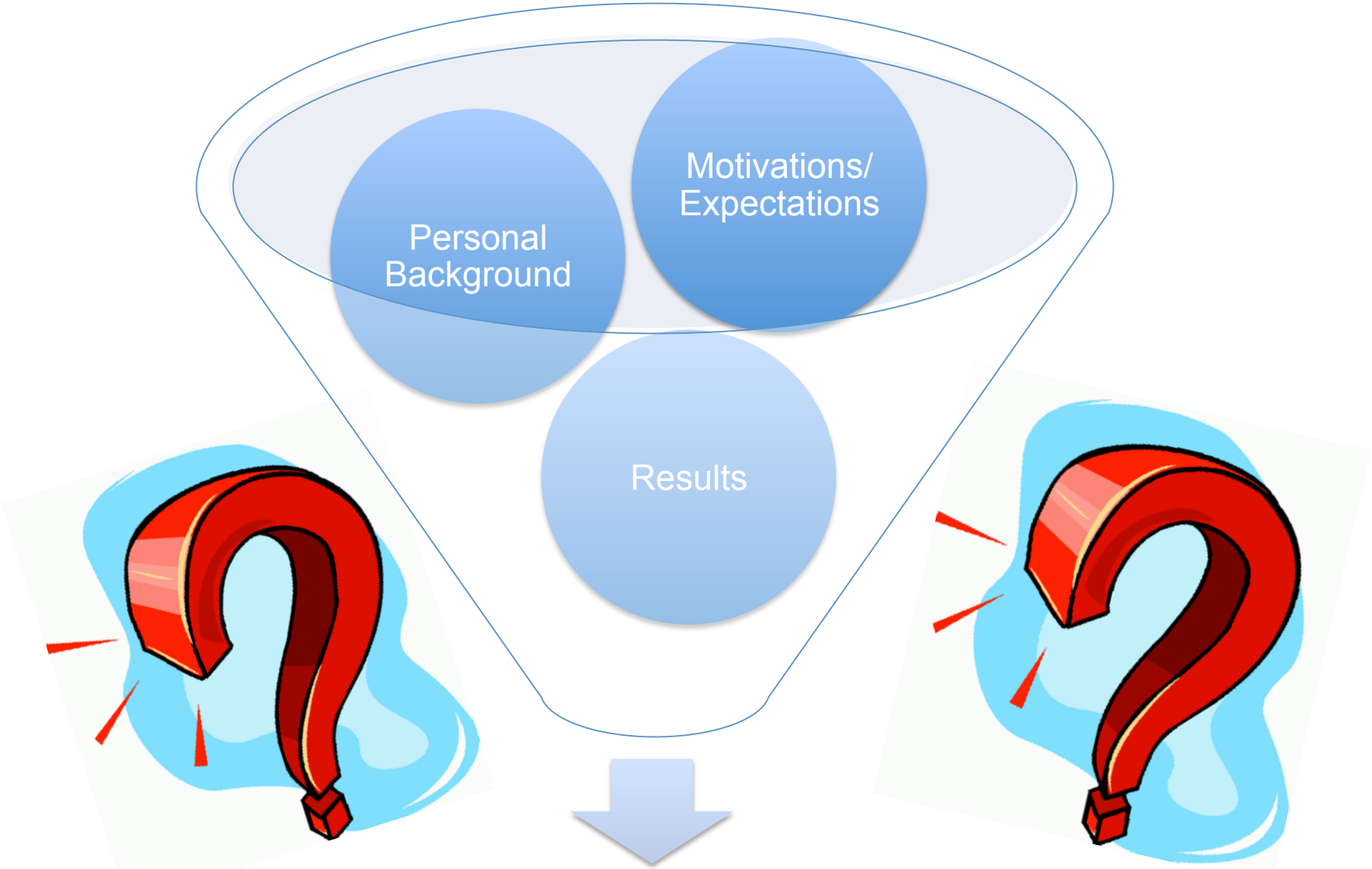
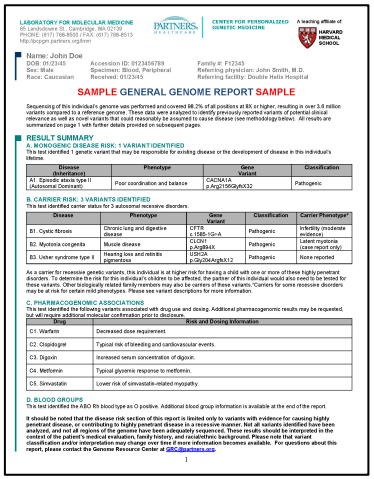



**Outcomes of Genome Sequencing (Medical, Behavioral, Economic)**

# Study Design



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PARTNERS HEALTHCARE

CENTER FOR PERSONALIZED GENETIC MEDICINE

A teaching affiliate of HARVARD MEDICAL SCHOOL

Name: John Doe
DOB: 01/23/45
Sex: Male
Race: Caucasian

Accession ID: 0123456789
Specimen: Blood, Peripheral
Received: 01/23/45

Family #: F12345
Referring physician: John Smith, M.D.
Referring facility: Double Helix Hospital

**SAMPLE GENERAL GENOME REPORT SAMPLE**

Sequencing of this individual's genome was performed and covered 98.2% of all positions at 8X or higher, resulting in over 3.6 million variants compared to a reference genome. These data were analyzed to identify previously reported variants of potential clinical relevance as well as novel variants that could reasonably be assumed to cause disease (see methodology below). All results are summarized on page 1 with further details provided on subsequent pages.

**RESULT SUMMARY**

**A. MONOGENIC DISEASE RISK: 1 VARIANT IDENTIFIED**

This test identified 1 genetic variant that may be responsible for existing disease or the development of disease in this individual's lifetime.

| Disease (Inheritance) | Phenotype | Gene Variant | Classification |
|---|---|---|---|
| A1. Episodic ataxia type II (Autosomal Dominant) | Poor coordination and balance | CACNA1A p.Arg2156GlyfsX32 | Pathogenic |

**B. CARRIER RISK: 3 VARIANTS IDENTIFIED**

This test identified carrier status for 3 autosomal recessive disorders.

| Disease | Phenotype | Gene Variant | Classification | Carrier Phenotype* |
|---|---|---|---|---|
| B1. Cystic fibrosis | Chronic lung and digestive disease | CFTR c.1585-1G>A | Pathogenic | Infertility (moderate risk) |
| B2. Myotonia congenita | Muscle disease | CLCN1 p.Arg894X | Pathogenic | Latent myotonia (case report only) |
| B3. Usher syndrome type II | Hearing loss and retinitis pigmentosa | USH2A p.Gly2043AlafsX12 | Pathogenic | None reported |

As a carrier for recessive genetic variants, this individual is at higher risk for having a child with one or more of these highly penetrant disorders. To determine the risk for this individual's children to be affected, the partner of this individual would also need to be tested for these variants. Other biologically related family members may also be carriers of these variants.*Carriers for some recessive disorders may be at risk for certain mild phenotypes. Please see variant descriptions for more information.

**C. PHARMACOGENOMIC ASSOCIATIONS**

This test identified the following variants associated with drug use and dosing. Additional pharmacogenomic results may be requested, but will require additional molecular confirmation prior to disclosure.

| Drug | Risk and Dosing Information |
|---|---|
| C1. Warfarin | Decreased dose requirement. |
| C2. Clopidogrel | Typical risk of bleeding and cardiovascular events. |
| C3. Digoxin | Increased serum concentration of digoxin. |
| C4. Metformin | Typical glycemic response to metformin. |
| C5. Simvastatin | Lower risk of simvastatin-related myopathy. |

**D. BLOOD GROUPS**

This test identified the ABO Rh blood type as O positive. Additional blood group information is available at the end of the report.

It should be noted that the disease risk section of this report is limited only to variants with evidence for causing highly penetrant disease, or contributing to highly penetrant disease in a recessive manner. Not all variants identified have been analyzed, and not all regions of the genome have been adequately sequenced. These results should be interpreted in the context of the patient's medical evaluation, family history, and racial/ethnic background. Please note that variant classification and/or interpretation may change over time if more information becomes available. For questions about this report, please contact the Genome Resource Center at GRC@partners.org.

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Personal Genome Sequencing (PGS)

Results reported

Survey

PGS groups

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# Harvard Personal Genome Project (PGP)

- 4611 PGP participants
  - 652 genomes
    - 197 invites
    - 123 responses
- All PGS results contributed to public database

# Illumina Understand Your Genome (UYG)

illumina®

- 529 UYG participants
  - 478 genomes
    - 362 invites
    - 121 responses
- MD orders PGS and returns results

# Mount Sinai HealthSeq Study

Icahn School of Medicine at Mount Sinai

- 40 HealthSeq participants
  - 40 genomes
    - 25 invites
    - 14 responses
- PGS results disclosed by geneticist or GC

# PGS Program Details

| PGS Group | Ordering MD | Return of Results (MD/GC) | Self Exploration | Access to Raw Data |
|---|---|---|---|---|
| UYG | + | + | + | - |
| HealthSeq | - | + | - | + |
| PGP | - | - | - | + |

# Survey

- Motivations and expectations
- Psychological state
- Risk perceptions
- Health status
- Health and wellness behaviors
- Healthcare utilization
- Insurance behaviors and intentions
- Sociodemographics
- Perceived utility of PGS
- Comprehension and use of results
- Genomic knowledge

# Demographics of Respondents

| Characteristics | Number of Respondents (%) Total N=258 |
|---|---|
| Mean Age | 53y |
| Male | 67% |
| Caucasian | 85% |
| Doctorate or Professional Degree | 77% |
| Household Income ≥ $100,000 | 76% |
| Married | 67% |
| Has Child(ren) | 66% |
| Healthcare Provider or Clinical Researcher | 24% |

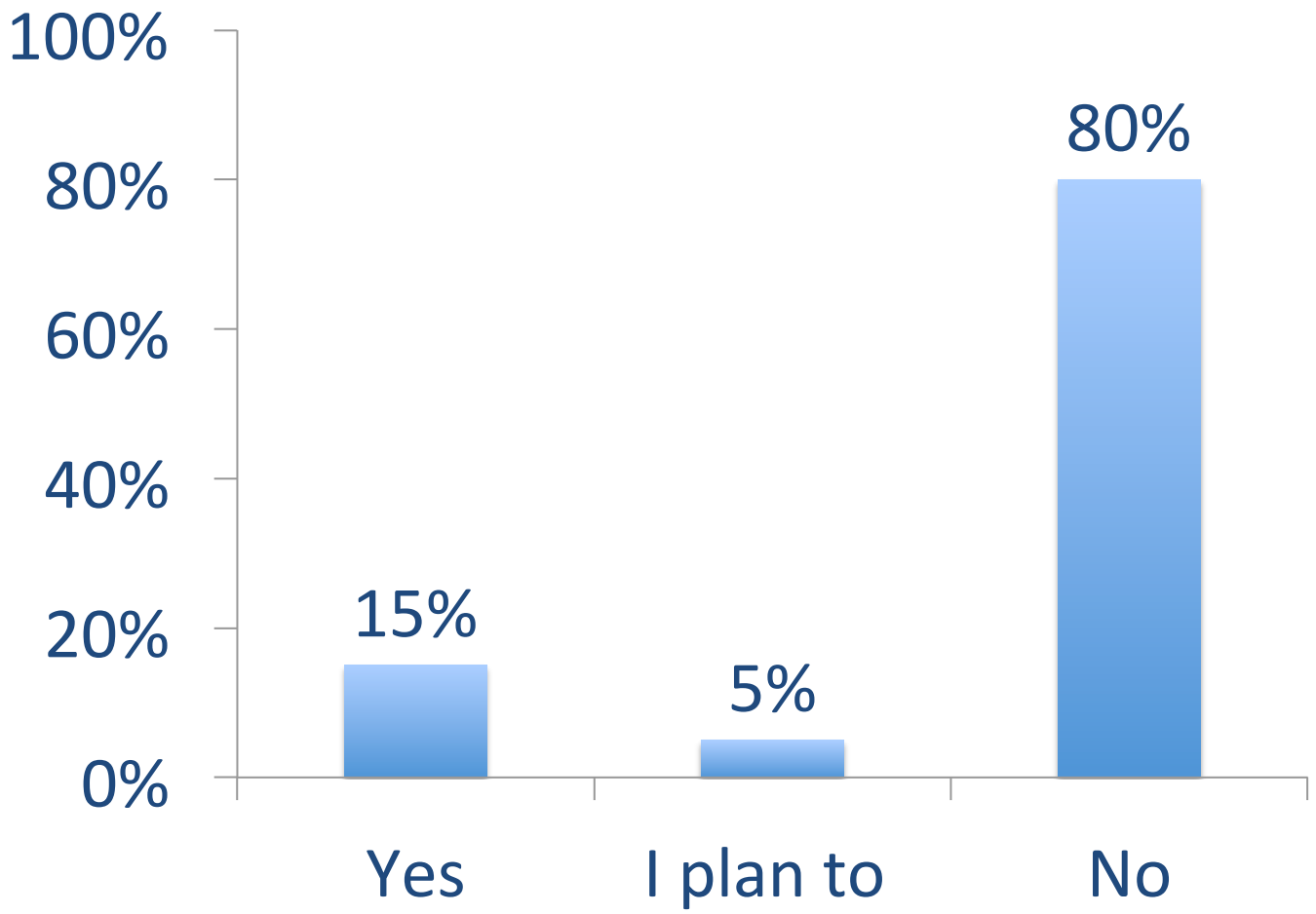
# How important were certain factors in participants' decision to pursue PGS?

| Motivations (very/somewhat important) | Percentage of Participants (N=258) |
|---|---|
| Personal interest in genetics in general | 99% |
| Curiosity about my genetic make-up | 98% |
| Desire to participate in research to help others | 92% |
| Interest in finding out things to do to improve my health | 81% |
| Interest in learning about my personal response to medications | 81% |
| It seemed fun and entertaining | 77% |
| Desire to plan for the future | 69% |
| Interest in my ancestry | 66% |
| Interest in finding out about personal disease risk | 41% |
| Concern about family history of a possible or confirmed genetic condition | 21% |

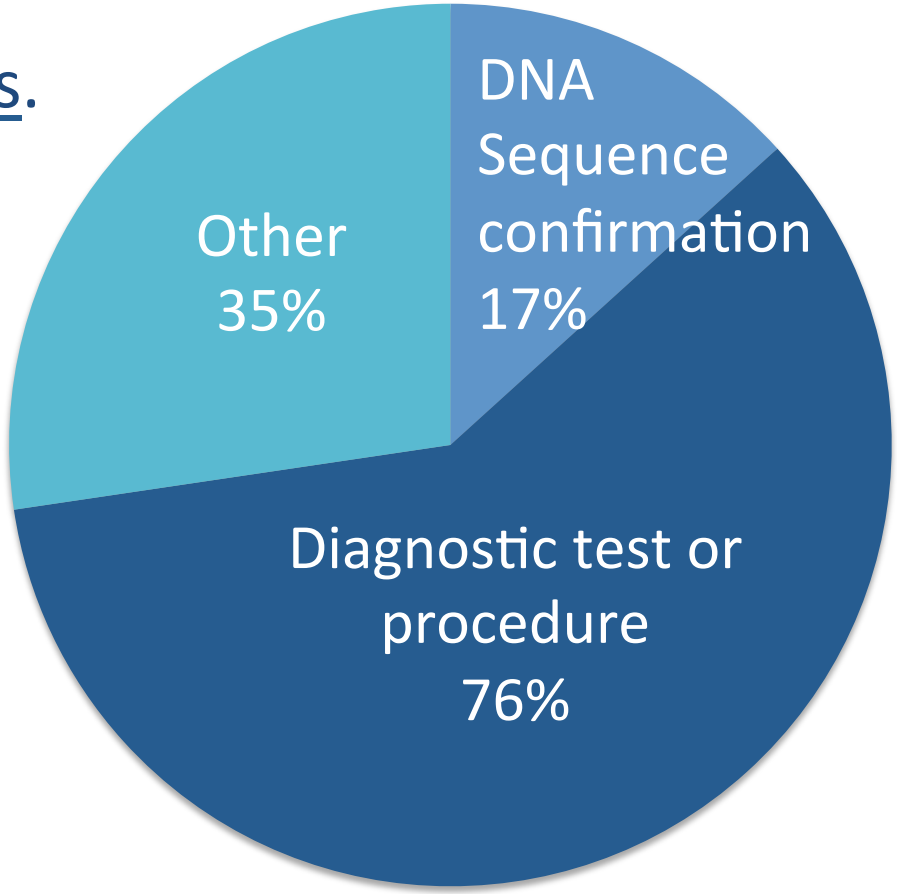
Those 21% of respondents were *more* likely than others to report learning something from PGS that would improve their health (p=0.003).

# Post-Disclosure Medical Actions

# Have your results prompted you to make an appointment with any healthcare provider(s)?



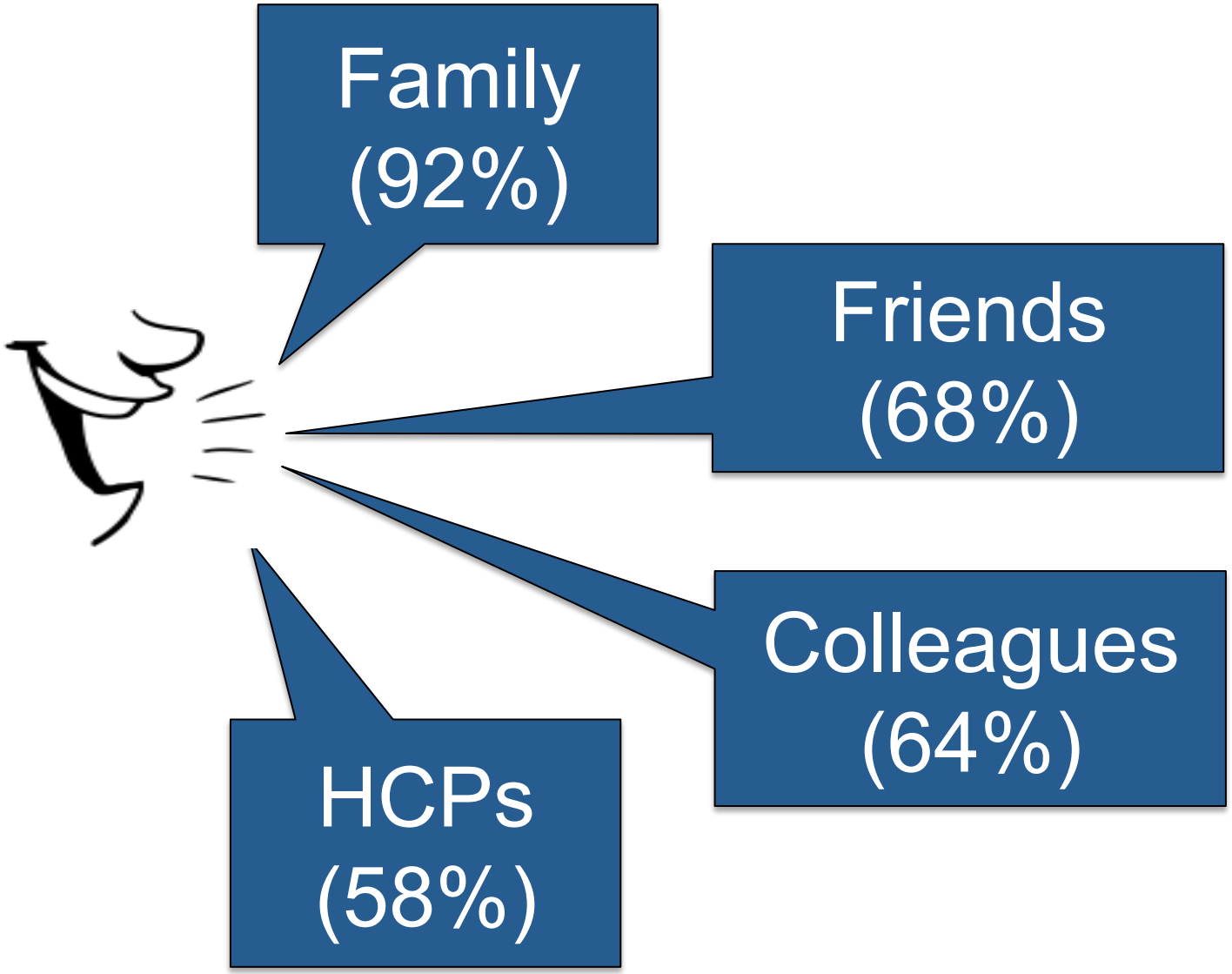
**12%** of respondents reported *having* a medical exam or procedure based on their sequencing results.




*Respondents could select more than one option

# Results Sharing

# With whom have you discussed your results?



# With whom have you discussed your results?


**Social network services:** 8%

**Health/disease-based social network services:** 7%

CureTogether
Open Source Health Research

patientslikeme

# Conclusions

- Personal interest in genetics and curiosity about one's genetic make-up were key motivators
- PGS results motivated some respondents to take medically-related actions
- Respondents with family history concerns more likely to report receiving useful health insight
- Respondents shared their PGS results primarily with family, but also with friends, colleagues, and HCPs, as well as on social networks

# Limitations

- Variety of PGS groups with different program features
- Variable length of time since return of results
- Population is early adopters of PGS

# Future Directions

- We plan to compare PGS groups to explore how attitudes vary between different result disclosure models and over time

- Future groups to be surveyed include:

Baylor College of Medicine

UNLV
UNIVERSITY OF NEVADA LAS VEGAS

MedSeq™

Institute for Systems Biology
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# The PeopleSeq Study Collaborators

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Daiva Nielsen, PhD

**Illumina Understand Your Genome**

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**The Harvard Personal Genome Project**

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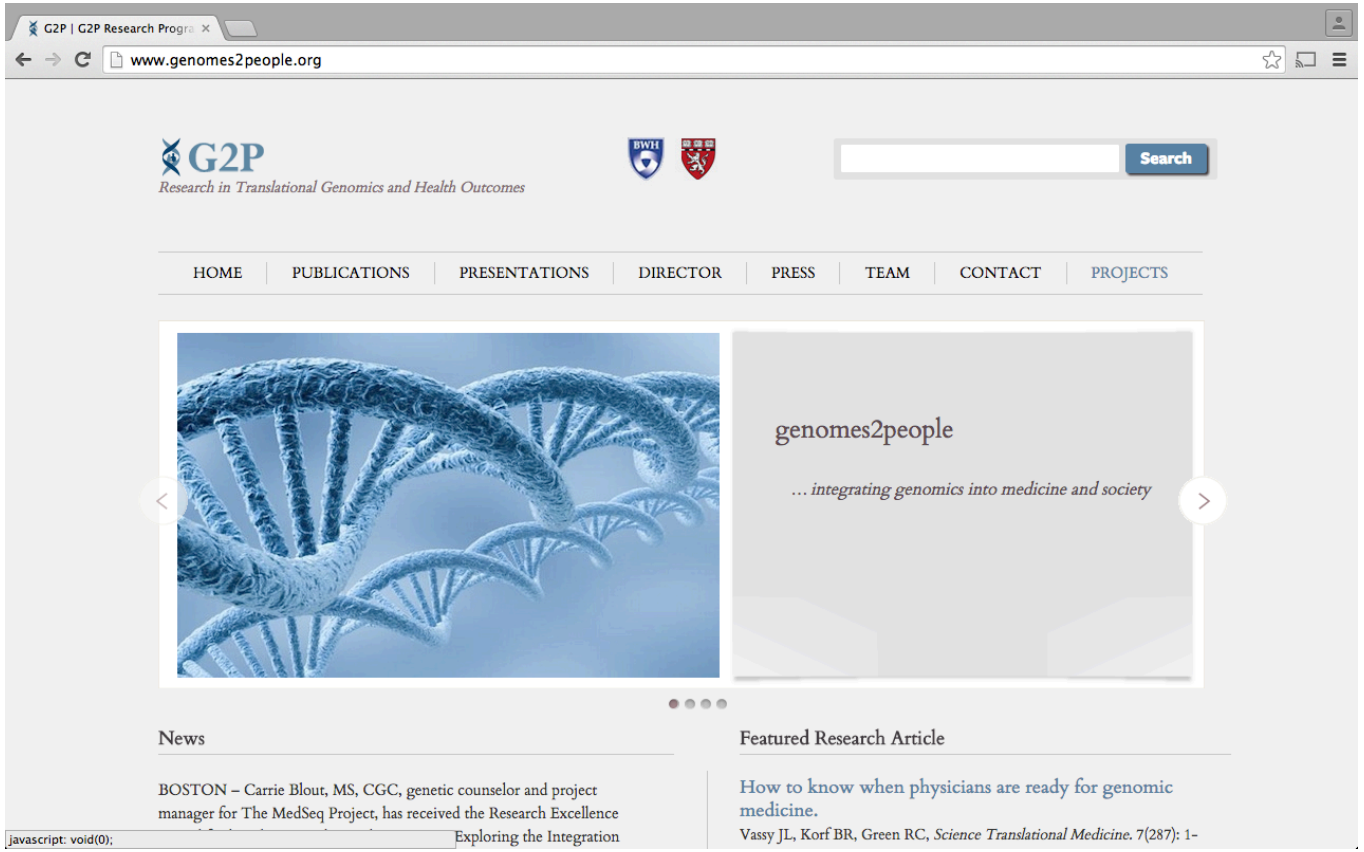
G2P GENOMES *to People*

# Questions?

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