Elective genomic sequencing for adults in research, clinical and commercial contexts

Elective genomic sequencing for adults

Supplemental Methods, Tables and Figures

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Supplemental Methods

Description of self-reported actions

The determination of post-disclosure actions are described in more detail below:

Participant important results (PIR): Importance was self-assessed and in response to the questionnaire items “Did you receive any results that you felt were important to you” or “which results do you feel were most important to you”. Participants could report up to 3 such results as free text items.

Discussed results (with anyone): Derived from an initial item “Have you discussed your results with anyone” followed by a select-all-that-apply item for different subgroups if the answer was “Yes” , or the union of all subgroups when the select-all item was administered to all.

Discuss w/ family and *Discuss w/ HCP*: Participants specifically reported having discussed their results with “Family member(s) (including spouse / significant other / partner)” and “Your healthcare provider (other than the [site] team)”.

1+ medical visits: Participants self-reported 1 or more “medical visits with a physician or other healthcare provider (other than the [site] team) have you had as a direct result of receiving your [site] results (in other words, visits you would not have had if you had not had personal genome sequencing)”.

Tests, medical exams, or procedures: Derived from an item “As a result of seeing your [site] results, have you had any tests, medical exams, or procedures?” or responding “Yes” to any of a set of tests or exams the participant “had because of your [site] results or follow-up care prompted by your [site] results?”.

Changed medications: Participants self-reporting “Because of your [site] results, have you made any changes to your use of medications (including prescription and non-prescription), supplements, and/or use of alternative medicine?”.

Supplemental Tables and Figures

Supplemental Table 1: Sites participating in the PeopleSeq consortium. Setting is one of Clinical, Academic, Industry or 3rd-party (where participants upload their own data). Type is one of targeted Panel, Exome and/or Genome sequencing. Kinds of results returned, approach to pre-test counseling and results disclosure and the availability of raw data shown for each site. Enrollment describes whether a site recruited participants to both pre-post surveys (PP) and catch-up (CU) or just CU.

Site	Setting	Type	Results Returned	Pre-test counseling	Results disclosure	Raw data	Enrollment
Preventative Genomics Clinic (Brigham & Women's Hospital)	C	PEG	Test dependent	Genetic counselor	Ordering HCP (MD/GC)	Upon Request	CU
Baylor College of Medicine YPO, CEO and MD/PhD	A	E	Monogenic disease findings	Investigator (MD)	Investigator (MD) with non-clinical report	None	CU
GeneDx	I	E	Monogenic disease findings	Ordering HCP	Ordering HCP	Upon Request	PP/CU
Harvard Personal Genome Project (PGP)	A	G	Variants with interpretation and lit. annotations	None	Online with semi-automated non-clinical report	VCF	PP/CU
HudsonAlpha Institute for Biotechnology	A	G	Monogenic disease findings	Genetic counselor	Investigator (MD/GC) with clinical report	None	CU
Illumina Understand Your Genome (UYG)	I	G	Monogenic disease findings, PGx	Ordering HCP	Online, clinical report sent to ordering HCP	VCF via HCP or by request	PP/CU
Invitae	I	P	Monogenic disease findings	Ordering HCP	Ordering HCP	Upon Request	CU
Mayo Clinic	C	PEG	Monogenic disease findings	Genetic counselor	Genetic Counselor	Upon Request	CU
Mount Sinai School of Medicine (MSSM)	A	G	Monogenic disease findings, PGx, polygenic risk	Investigator (GC)	Investigator (MD) with non-clinical report	BAM, VCF	CU
OpenSNP	3rd	N/A	N/A	N/A	N/A	N/A	CU
PerkinElmer	I	G	Monogenic disease findings	Ordering HCP, Genome Medical	Ordering HCP, Genome Medical	Upon request	CU
University of Vermont (UVM) (via Illumina UYG)	A	G	Monogenic disease findings, PGx	Ordering HCP	Online, clinical report sent to ordering HCP	VCF via HCP or by request	PP/CU
Genome Medical	C	PEG	Test dependent	Genetic counselor	Ordering HCP (MD/GC)	Upon Request	PP/CU
MedSeq	A	G	Monogenic disease findings	PCP or Cardiologist	PCP or Cardiologist	Upon Request	CU
Medcan	C	P	Monogenic disease findings	Genetic counselor	Genetic Counselor	Upon Request	PP/CU
Takeda	I	G	Monogenic disease findings	Via Genome Medical	Via Genome Medical	Yes, to all	CU
Genos/NantOmics	I	E	27 traits, "gene cards", variants with lit. annotations	Available for separate fee	Online	BAM, VCF	CU

Supplemental Table 2: The subset of 46 monogenic variants in participant's EGS reports (RIR) further classified by PeopleSeq researchers as clinically important. Variant description and conditions are as described in the report received by the participant. If possible, variants were linked to results self-assessed by participants as important to them (PIR). The first two participants are discussed in the main text.

Variant as described in report				**Self-assessed as Important**
Variant	**Class**	**Zygosity**	**Condition(s)**	
HFE:c.845G>A (p.Cys282Tyr)	P	Homozygous	Hereditary Haemochromatosis	
BRCA2:c.9252_9255delAACAinsTT (p.Lys3084fs)	P	Heterozygous	Breast Cancer	
JAK2:c.1849G>T (p.Val617Phe)	P	Heterozygous	Myeloproliferative diseases	✓
SLC3A1:c.1400T>C (p.Met467Thr)	P	Homozygous	Cystinuria	✓
CHEK2:c.1100delC (p.Thr367fs)	P	Heterozygous	CHEK2-Related Cancer Susceptibility	✓
BRCA2:c.5857G>T (p.Glu1953Ter)	P	Heterozygous	BRCA2 Related Disorders	✓
FLNC Deletion (Exons 27-28)	P	Heterozygous	Neuromuscular and heart-related conditions	✓
GLA c.644A>G (p.Asn215Ser)	P	Hemizygous	Fabry Disease	✓
F5:c.1601G>A (p.Arg534Gln), F2:c.*97G>A	P	Heterozygous	Prothrombin-Related Thrombophilia, Factor V Leiden Thrombophilia	✓
HOXB13:c.251G>A (p.Gly84Glu)	Increased Risk Allele	Heterozygous	Prostate Cancer	✓
CHEK2:c.1100del (p.Thr367fs)	P	Heterozygous	Hereditary Cancer	✓
MSH2:c.792+1del	LP	Heterozygous	*	✓
BRCA2:c.5238dup (p.Asn1747Ter)	P	Heterozygous	*	✓

* Report available to PeopleSeq project included interpretation but not the associated condition

Supplemental Table 3: Fraction of individuals endorsing specific motivations as very/somewhat important vs. not important/not applicable who reported receiving results important to them (PIR). X^2 test statistic, degrees of freedom and p-value are reported for each motivation.

Motivation	**Very or somewhat important**		**Not important or NA**		
Important Results (PIR)	**Yes**	**Not sure**	**Yes**	**Not sure**	**X^2 test**
Curiosity about my genetic makeup	0.676	0.153	0.698	0.116	0.4(2) p=0.801
Interest in finding out about my personal disease risk	0.677	0.154	0.622	0.081	4.8(2) p=0.0895
Interest in finding out what I can do to improve my health	0.677	0.162	0.664	0.080	10.6(2) p=0.00495
Interest in finding out about my personal response to medications	0.664	0.167	0.696	0.114	4.1(2) p=0.13
Desire to plan for the future	0.682	0.163	0.645	0.114	10.2(2) p=0.00623
It seemed like it would be a fun, entertaining, or novel opportunity	0.656	0.154	0.708	0.151	4.4(2) p=0.112
Desire to learn about my genetic make-up without going through my physician	0.629	0.180	0.690	0.176	4.4(2) p=0.112
Other members of my family have had their genomes sequenced	0.748	0.135	0.660	0.156	5.3(2) p=0.0699
To learn more about my genetics because I lack information about my family history	0.717	0.161	0.648	0.147	11.3(2) p=0.00347
To provide disease risk information for my children (current or future)	0.687	0.145	0.653	0.167	1.2(2) p=0.556
There is a medical condition in my family that may be genetic	0.725	0.135	0.605	0.177	16.8(2) p=2.27E-4
There is a medical condition in my family that has been confirmed to be genetic	0.708	0.144	0.660	0.156	2.7(2) p=0.266
To learn more about genome sequencing as part of my professional activities	0.675	0.138	0.676	0.171	3.5(2) p=0.174
To contribute to the advancement of science	0.646	0.171	0.723	0.131	3.1(2) p=0.218
Curiosity about my ancestry	0.623	0.191	0.693	0.134	6.1(2) p=0.0465

Supplemental Table 4: Fraction of individuals endorsing specific motivations as very/somewhat important vs. not important/not applicable who reported any important results (PIR) coded as negative. X^2 test statistic, degrees of freedom and p-value are reported for each motivation.

Motivation	**Very or somewhat important**	**Not important or NA**	
Negative important results (PIR)	**Yes**	**Yes**	**X^2 test**
Curiosity about my genetic makeup	0.229	0.227	0.0(1) p=1
Interest in finding out about my personal disease risk	0.230	0.179	0.3(1) p=0.587
Interest in finding out what I can do to improve my health	0.223	0.264	0.8(1) p=0.358
Interest in finding out about my personal response to medications	0.195	0.337	21.2(1) p=4.21e-06
Desire to plan for the future	0.230	0.229	0.0(1) p=1
It seemed like it would be a fun, entertaining, or novel opportunity	0.222	0.241	0.4(1) p=0.533
Desire to learn about my genetic make-up without going through my physician	0.212	0.248	1.1(1) p=0.293
Other members of my family have had their genomes sequenced	0.232	0.230	0.0(1) p=1
To learn more about my genetics because I lack information about my family history	0.213	0.240	0.9(1) p=0.342
To provide disease risk information for my children (current or future)	0.232	0.224	0.0(1) p=0.83
There is a medical condition in my family that may be genetic	0.249	0.205	2.6(1) p=0.104
There is a medical condition in my family that has been confirmed to be genetic	0.225	0.232	0.0(1) p=0.846
To learn more about genome sequencing as part of my professional activities	0.219	0.245	0.9(1) p=0.349
To contribute to the advancement of science	0.216	0.301	4.7(1) p=0.0299
Curiosity about my ancestry	0.194	0.280	9.0(1) p=0.00264

Supplemental Table 5: The fraction of individuals reporting specific motivations as the “most important”. This item was only included in a subset of surveys (*n*=1062). Fractions do not add to one due to missing data.

Motivation	**Fraction**
Interest in finding out about my personal disease risk	0.278
Curiosity about my genetic make-up	0.110
To learn more about genome sequencing as part of my professional activities	0.073
To provide disease risk information for my children (current or future)	0.063
Other	0.059
Interest in finding out what I can do to improve my health	0.056
There is a medical condition in my family that may be genetic	0.055
To contribute to the advancement of science	0.039
Desire to plan for the future	0.019
There is a medical condition in my family that has been confirmed to be genetic	0.017
To learn more about my genetics because I lack information about my family history	0.015
Interest in finding out about my personal response to medications	0.012
It seemed like it would be a fun, entertaining, or novel opportunity	0.015
Curiosity about my ancestry	0.00657
Desire to learn about my genetic make-up without going through my physician	0.006
Other members of my family have had their genomes sequenced	0.001