

The American Journal of Human Genetics, Volume 95

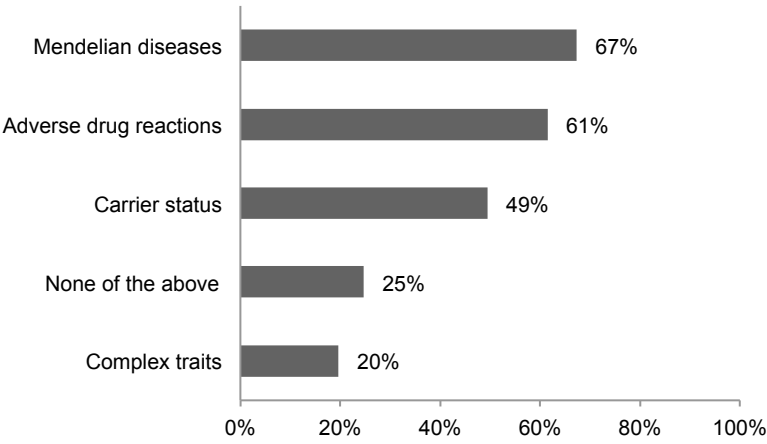
Supplemental Data

**Attitudes of Genetics Professionals
Toward the Return of Incidental Results
from Exome and Whole-Genome Sequencing**

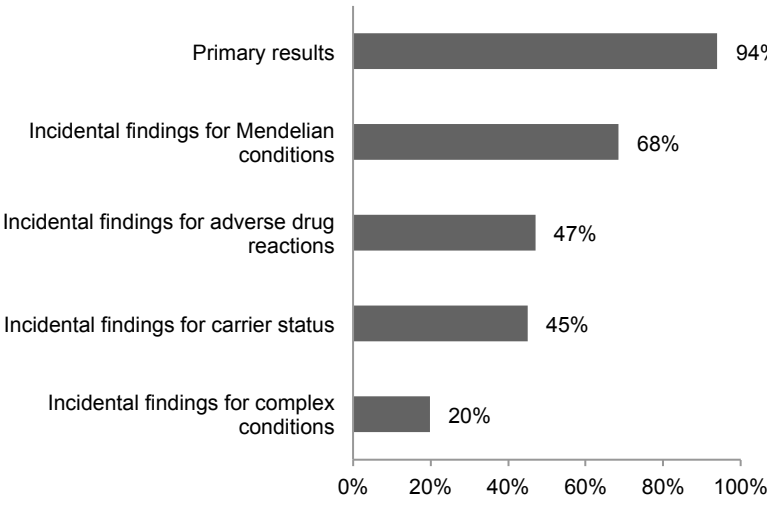
Joon-Ho Yu, Tanya M. Harrell, Seema M. Jamal, Holly K. Tabor, and Michael J. Bamshad

Figure S1.

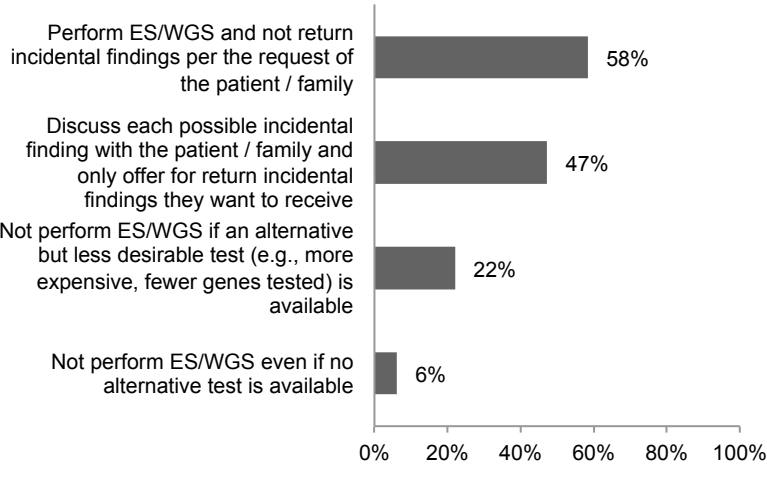
(Q10) Complete the following statement: "Health care providers have an obligation to offer return of positive incidental findings from clinical ES/WGS to patients for . . ." (n=794)



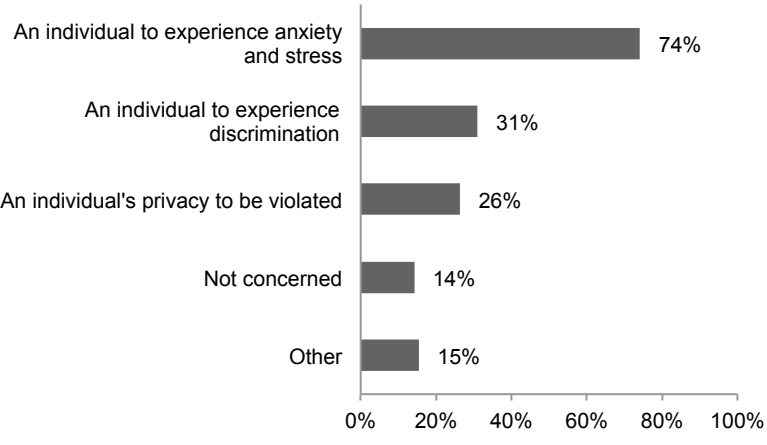
(Q24) What results from clinical ES/WGS do you typically return? (n=349)



(Q09) If a patient / family declines to receive all the incidental findings on the minimum list, would you: (n=795)



(Q08) Complete the following statement: "I am concerned that returning incidental findings from clinical ES/WGS following the ACMG recommendations may cause . . ." (n=797)



(Q07) Complete the following statement: "I think the greatest challenges to returning incidental findings from clinical ES/WGS following the ACMG recommendations are that . . ." (n=799)

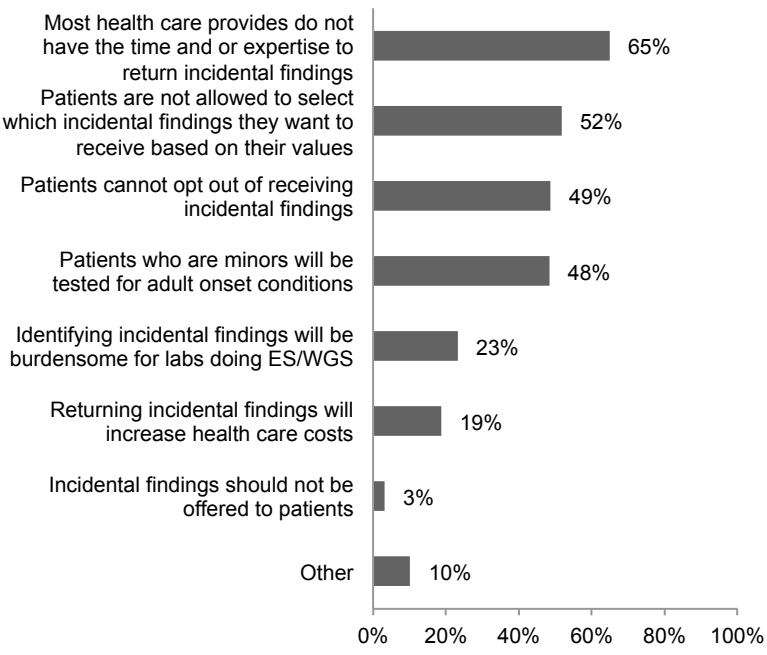


Figure S1. Additional Study Data
 Figure S1 presents additional study data of participant responses to statements and questions about physician obligation and return practice, and perceived concerns and challenges to return of incidental results. Percentages reflect the proportion of participants selecting the response category divided by the total number of respondents to the corresponding statement or question. Participants were allowed to choose more than one response such that the sum of percentages of responses per statement or question total greater than 100%.

Table S1. Survey Introduction, Definitions, and Items

Introduction: We are researchers from the University of Washington School of Medicine working on how to best return results from clinical exome / whole genome sequencing (ES/WGS) to patients and families. The purpose of this survey is to learn what you think about returning results from ES/WGS and ways to offer and return incidental findings to patients and families. The survey has three sections – Section 1 (9 questions) asks your opinion about the recent American College of Medical Genetics and Genomics (ACMG) Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing. Section 2 (11 questions) asks your opinion about returning incidental findings from ES/WGS. Section 3 (9 questions) asks for Demographic Information about you. The survey takes approximately 15 minutes to complete. This survey has been approved by the IRB of the University of Washington and all results are anonymous. We encourage you to use the comment boxes at the end of each page to help us better understand your responses and to provide feedback on the survey.

To assist you in answering the survey we provided the following definitions.

Actionable results: a result for which there is a specific clinical action to be taken for prevention or treatment of a medical conditions.

Child: a person less than 18 years of age

Health care provider: a physician, nurse, genetic counselor, and other allied health professional

Patient: a person with a medical condition who undergoes clinical sequencing

Positive result: a result that suggests an individual has a condition, is at risk of having a condition, or is a carrier of a condition

Primary result: pathogenic alterations in a gene or genes that are relevant to the diagnostic indication for which sequencing was ordered

Incidental finding: an unexpected positive result that is apparently not relevant to a diagnostic indication for which the sequencing was ordered

Items

1. Incidental findings found in the genes on the minimum list should be reported by a laboratory, regardless of the indication for which the clinical sequencing was ordered. (disagreement/agreement)^a
2. Incidental findings found in genes on the minimum list should be reported to a patient / family regardless of their preferences for receiving incidental results. (disagreement/agreement)
3. It is the responsibility of the health care professional to decide which incidental findings found on the minimum list be reported to a patient / family. (disagreement/agreement)
4. Incidental findings found in genes on the minimum list should be reported to a patient / family regardless of the age of the patient. (disagreement/agreement)
5. Patient / family preferences should be used to guide which incidental findings, if any, be reported back to them. (disagreement/agreement)
6. Please list any questions and/or comments you may have: (open response)

7. Complete the following statement: "I think the greatest challenges to returning incidental findings from clinical ES/WGS following the ACMG recommendations are that . . ." (please select all that apply)
- patients cannot opt out of receiving incidental findings
 - patients are not allowed to select which incidental findings they want to receive based on their values
 - patients who are minors will be tested for adult onset conditions
 - identifying incidental findings will be burdensome for labs doing ES/WGS
 - most health care providers do not have the time and or expertise to return incidental findings
 - returning incidental findings will increase health care costs
 - incidental findings should not be offered to patients
 - other (please specify)
8. Complete the following statement: "I am concerned that returning incidental findings from clinical ES/WGS following the ACMG recommendations may cause . . ." (please select all that apply)
- an individual to experience anxiety and stress
 - an individual to experience discrimination
 - an individual's privacy to be violated
 - not concerned
 - other (please specify)
9. If a patient / family declines to receive all the incidental findings on the minimum list, would you (please select all that apply):
- not perform ES/WGS even if no alternative test is available
 - not perform ES/WGS if an alternative but less desirable test (e.g., more expensive, fewer genes tested) is available
 - perform ES/WGS and not return incidental findings per the request of the patient / family
 - discuss each possible incidental finding with the patient / family and only offer for return incidental findings they want to receive
10. Complete the following statement: "Health care providers have an obligation to offer return of positive incidental findings from clinical ES/WGS to patients for . . ." (please select all that apply)
- Mendelian diseases
 - Carrier status
 - Adverse drug reactions
 - Complex traits
 - None of the above
11. Please list any questions and/or comments you may have: (open response)
12. For each of the following statements, please indicate your level of agreement or disagreement on a 5-point scale (1=strongly disagree; 5=strongly agree).
- Incidental findings should be offered to an adult patient who has undergone clinical ES/WGS.
 - Incidental findings should be offered to the parent(s) of a child who has a medical condition and has undergone clinical ES/WGS.
 - Incidental findings should be offered to a healthy individual (e.g., a parent of a child with a medical condition) who has undergone clinical ES/WGS.

13. For each of the following statements, please indicate your level of agreement or disagreement on a 5-point scale (1=strongly disagree; 5=strongly agree).
- Only actionable incidental findings should be offered to an adult patient who has undergone clinical ES/WGS.
 - Only actionable incidental findings should be offered to the parent(s) of a child who has a medical condition and has undergone clinical ES/WGS.
 - Only actionable incidental findings should be offered to a healthy individual (e.g., a parent of a child with a medical condition) who has undergone clinical ES/WGS.
14. For each of the following statements, please indicate your level of agreement or disagreement on a 5-point scale (1=strongly disagree; 5=strongly agree).
- Incidental findings about childhood-onset conditions should be offered to the parent(s) of a child with a medical condition who has undergone clinical ES/WGS.
 - Incidental findings about adult onset conditions should be offered to the parent(s) of a child who has a medical condition and has undergone clinical ES/WGS.
 - Incidental findings about carrier status should be offered to the parent(s) of a child with a medical condition who has undergone clinical ES/WGS.
15. Please list any questions and/or comments you may have: (open response)
16. Assuming that a healthcare provider has decided which incidental findings should be offered for return, should patients be able to choose which of these results they want? (Yes, No, Don't Know)
17. Do you think it is too difficult to allow patient / family preferences to inform a health care provider which incidental findings from ES /WGS should be offered for return? (Yes, No, Don't Know)
18. Do you think giving patients / families an option to choose which incidental findings to receive would improve care? (Yes, No, Don't Know)
19. Please list any questions and/or comments you may have: (open response)
20. Do you think an online or web-based tool would facilitate assessment of patient preferences for available incidental findings? (Yes, No, Don't Know)
21. Do you think an online or web-based tool would facilitate return of available incidental findings? (Yes, No, Don't Know)
22. Rank the following responses to the statement in order of preference (1=first choice, 4=last choice): "I think incidental findings should be communicated by . . ."
- a face-to-face meeting with a genetic counselor
 - a phone call with a genetic counselor
 - an interactive website with access to a genetic counselor by phone or online
 - a report sent in the mail
23. If interpretation of an incidental finding and discussion of medical management is done by a genetics professional, do you think an incidental finding could be communicated effectively by:
- mail
 - e-mail
 - web-based tool

24. What results from clinical ES/WGS do you typically return? (please select all that apply)

- a. Primary results
- b. Incidental findings for Mendelian conditions
- c. Incidental findings for complex conditions
- d. Incidental findings for carrier status
- e. Incidental findings for adverse drug reactions
- f. Not applicable

25. Please list any questions and/or comments you may have: (open response)

26. In what country do you live?

- a. US (please specific state below)
- b. Other (please specific country below)

Please specify state or country (open response)

27. Sex

- a. Male
- b. Female
- c. Other

28. Age

29. US respondents only: How do you typically identify yourself on the U.S. census? Are you Hispanic/Latino?

- a. No
- b. Yes

30. US respondents only: How do you typically identify yourself on the U.S. census? (Please check all that apply)

- a. American Indian or Alaska Native
- b. Asian
- c. Black, African American
- d. Native Hawaiian or Other Pacific Islander
- e. White
- f. Other

31. Please indicate your profession: (choose the one that fits best)

- a. Human Geneticist
- b. Clinical Geneticist
- c. Medical Geneticist
- d. Population Geneticist
- e. Genetic Epidemiologist
- f. ELSI Researcher
- g. Nurse Practitioner
- h. Student or Trainee
- i. Other (please specify)

32. Please indicate the extent of your work in the following areas: (all of the time, most of the time, sometimes, rarely, never)

- a. Basic science research
- b. Clinical genetics research
- c. Patient care
- d. ELSI (ethical, legal, social implications) research
- e. Other

33. Please choose all of your post-baccalaureate degrees:

- a. Master of Arts (M.A.)
- b. Master of Science (M.S.)
- c. Master of Public Health (M.P.H.)
- d. Doctor of Medicine or Osteopathic Medicine (M.D./D.O.)
- e. Juris Doctor (J.D.)
- f. Doctor of Philosophy (Ph.D.)
- g. Other (please specify)

34. Which of the following best describes your work environment?

- a. Academic
- b. Private
- c. Government

35. If you have additional comments, please use the space provided. (open response)

^a Disagreement/Agreement were measured using labeled 1-5 Likert-scale like response categories, arranged horizontally on the page where 1=Strongly disagree; 2=Disagree; 3=Neither agree nor disagree; 4=Agree; 5=Strongly Agree.

Table S2. Participant characteristics

Variables and response categories	n	Percent (%)
Gender (n=752)		
male	312	41
female	439	58
other	1	<0.1
Race (n=609)		
American Indian and Alaska Native	3	0.5
Asian	49	8
Black or African American	11	1.8
Native Hawaiian and Other Pacific Islander	1	0.2
White	547	89.8
other	10	1.6
more than one	8	1
Ethnicity (n=616)		
Hispanic	27	4
Non-hispanic	589	96
Age (n=631)		
mean (range)	46.2	(23 to 85)
36 and under	169	27
37-45	151	24
46-56	161	26
57 and over	150	24
Country of residence (n=756)		
United States	611	81
other	145	19
Work environment (n=753)		
academic	547	73
private	123	16
government	47	6
other	36	5
Profession (n=753)		
human geneticist	142	19
clinical geneticist	184	24
medical geneticist	29	4
population geneticist	20	3
genetic epidemiologist	45	6
genetic counselor	167	22
ELSI researcher	26	4
nurse practitioner	3	<0.1
student or trainee	36	5
Other	101	13
Types of work (n=750)		

basic science research	504	67
clinical genetics research	596	79
patient care	477	64
ELSI (ethical, legal, social implications) research	370	49
other	62	8
Highest level of education (n=742)		
baccalaureate or less	5	<0.1
masters	184	25
professional doctorate	157	21
PhD	310	42
MD/PhD	86	12

Note: Sample size (n) varies between variables because individuals were allowed to skip questions.

Table S3. Summary of Non-Response Bias Analysis

a. Comparison of demographic characteristics between genetic counselor survey respondents and National Society of Genetic Counselors' 2012 Professional Status Survey

Variable	Response Categories	χ^2 (df)	p-value
gender	female male	2.910179641 (1)	0.08802207
age	20-29 30-39 40-49 50-59 60-69	5.588422392 (4)	0.232065723
race	American Indian Alaska Native Asian Black or African American Native Hawaiian Other Pacific Islander White Other	1.344855506 (5)	0.939249108
education	masters professional doctorate doctorate of philosophy other	0.552197193 (3)	0.907283053
work environment	academic private government other	68.04333776 (3)	1.11984x10 ⁻¹⁴

b. Comparison of demographic characteristics between medical/clinical geneticists survey respondents and the 2003 survey of American Board of Medical Genetics certified geneticists

Variable	Response Categories	χ^2 (df)	p-value
gender	female male	2.507109005 (1)	0.113333672
education	masters professional doctorate doctorate of philosophy professional doctorate + doctorate of philosophy	1.667692308 (3)	0.644140258
work environment	academic other	5.718365655 (1)	0.01678835
age ^a	mean	t=-0.5080 (240)	0.6119

^a age was compared using a two sample t-test of means assuming unequal variance

c. Comparison of demographic characteristics between the overall sample of survey respondents and the 1989 survey of members of the American Society of Human Genetics

Variable	Response Categories	χ^2 (df)	p-value
education	masters professional doctorate doctorate of philosophy professional doctorate + doctorate of philosophy	44.38090767 (3)	1.25262X10 ⁻⁹
work environment	academic	2.504331879 (1)	0.113533625

	private + government		
age ^a	mean	t=8.5318 (1023)	<0.0001

^a age was compared using a two sample t-test of means assuming unequal variance

d. Comparison of demographic characteristics between survey respondents and non-respondents from recruitment lists

Variable	Response Categories	χ^2 (df)	p-value
education	masters professional doctorate doctorate of philosophy professional doctorate + doctorate of philosophy	9.567269208 (3)	0.022626393
geographic region (U.S. only) ^b	Region 1 (northeast) Region 2 (midwest) Region 3 (south) Region 4 (west)	3.117667298 (3)	0.373836588

^b geographic regions based on U.S. Census Regions

Table S4. Comments from respondents who do not return primary results and commented on question 24

Participant ID	Comment	Profession
2811225062	Do not always adhere to list. return a narrower range. And we allow opt-out while still performing sequencing.	ELSI researcher
2798833899	Our pediatric genetic center has chosen to not offer WES at this time. There is discussion of developing an in-house test which would blind both the laboratory staff and the clinicians to non-relevant incidental findings (non-actionable or adult onset).	Genetic counselor
2795200267	I have not yet ordered ES or WGS for any patient, in part because of my concerns over handling of incidental findings and, even more, variants of unknown significance.	Clinical geneticist
2793203463	Not currently offering ES/WGS.	lab geneticist
2792704744	I have reported primary results from research exome sequencing.	Genetic counselor
2792632571	24 no personal experience to date. Think I'd do all but "complex conditions"	Clinical geneticist
2787081831	I have not done an ES/EGS study but am engaged in returning genetic results.	Human Geneticist
2780192592	The physician I work with has ordered clinical ES/WGS on multiple individuals; however, we have not received results at this time.	Genetic counselor
2775754836	Because we are not a CLIA-approved lab, our consents say that no results will be returned to subjects.	Human Geneticist
2775139367	I don't return any as they are currently for research only	Genetic epidemiologist
2770498755	We are returning results from GWAS.	Human Geneticist
2770445650	First patients for WES underway at present. Prior consent has established what incidental findings will be returned.	Clinical geneticist
2770169486	Have not ordered this test often enough to have a "typical" approach; rarely approved by insurance.	Genetic counselor
2770063644	Haven't encountered this problem yet.	Clinical geneticist
2770004273	All we have done so far is with anonymous samples, de-identified. Or with explicit research consent detailing we will not routinely return incidental findings.	physician with advanced genetics training
2769963895	Answer to 24 is "None"	Population geneticist
2769948439	We are not doing this at my hospital at present.	Genetic counselor