ORIGINAL RESEARCH ARTICLE | Genetics inMedicine

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How do students react to analyzing their own genomes in a whole-genome sequencing course?: outcomes of a longitudinal cohort study

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Purpose: Health-care professionals need to be trained to work with whole-genome sequencing (WGS) in their practice. Our aim was to explore how students responded to a novel genome analysis course that included the option to analyze their own genomes.

Methods: This was an observational cohort study. Questionnaires were administered before (T3) and after the genome analysis course (T4), as well as 6 months later (T5). In-depth interviews were conducted at T5.

Results: All students (n = 19) opted to analyze their own genomes. At T5, 12 of 15 students stated that analyzing their own genomes had been useful. Ten reported they had applied their knowledge in the workplace. Technical WGS knowledge increased (mean of 63.8% at T3, mean of 72.5% at T4; P = 0.005). In-depth interviews suggested that analyzing their own genomes may increase students' motivation to learn and their understanding of the patient experience. Most (but not all) of the students reported low levels of WGS results–related distress and low levels of regret about their decision to analyze their own genomes.

Conclusion: Giving students the option of analyzing their own genomes may increase motivation to learn, but some students may experience personal WGS results–related distress and regret. Additional evidence is required before considering incorporating optional personal genome analysis into medical education on a large scale.

Genet Med advance online publication 29 January 2015

Key Words: genetic education; medical education; personal genomes; whole-genome sequencing

INTRODUCTION

Whole-exome sequencing (WES)/whole-genome sequencing (WGS) is now used routinely in research and clinical applications. The demand for WES/WGS exceeds the supply of appropriately trained health-care professionals.[1] Expanded genomics education must be incorporated into genetics and other clinical training programs to meet the acute need for health-care professionals capable of implementing and applying genomic medicine.[2]

One strategy that could enhance the educational experience is offering students the option to analyze their own personal genomic data in laboratory-style genome analysis courses.[3,4] Consistent with self-determination theory,[5–7] which emphasizes the importance of autonomy in learning,[8] students analyzing their own genomic data might attach more personal importance to learning, be more engaged, be more motivated, and ultimately achieve better educational outcomes than students working with third-party genomic data.[3,9–11] Despite several institutions offering personal genomic testing within the educational setting, only one—Stanford—has published results regarding students' experiences in these courses.[12,13] They used direct-to-consumer genotyping. As costs decrease, WGS will increasingly become the standard technology for clinical genomics. It is therefore critical that future genetics professionals move beyond genotyping and acquire practical experience dealing with the larger scale, scope, and complexity of the WGS data they will encounter in their future practice.

There are potential risks in offering any kind of personal genomic data for educational purposes,[14] including the potential for coercion (students might believe refusing to use their own genomes could harm their academic evaluation by course faculty or program directors); breaches of data confidentiality and privacy; inadequate information and counseling; the appearance that the institution is endorsing the genomics service by providing it free of charge or at reduced cost; and the potential for adverse psychological reactions to the personal genomic results.[10] Students could be harmed if they receive information about their health or identity that causes them stress, anxiety, and/or depression. Also, learning personal health information they find distressing could reduce, rather than increase, students' attention to course content. However, research in prenatal genetic counseling suggests helping individuals make informed decisions about pursuing personal genomic results may reduce the likelihood of negative psychological outcomes.[15–17] Informed decisions are decisions that are informed by adequate knowledge about the technology (e.g., risks, benefits, limitations, uncertainties) and that are consistent

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Submitted 17 July 2014; accepted 12 December 2014; advance online publication 29 January 2015. doi:10.1038/gim.2014.203

with the individual's values.[18,19] Courses that provide students the option of analyzing their own genomes must help them make thoughtful and careful decisions about whether personal genome analysis is right for them as individuals.[10,20]

We therefore designed a required 26-h introductory course, an advanced personal genomics course, and an accompanying sequencing protocol in which students could choose to analyze their own or an anonymous personal genome. As previously reported, we observed increases in informed decision making among this student cohort, as measured by decreased decisional conflict after the introductory course.[20] The objectives of this report are to explore the educational and psychological outcomes of the students who had the option of analyzing their own WGS data as part of their advanced genomics training.

MATERIALS AND METHODS

This was a longitudinal cohort study that took place at the Icahn School of Medicine at Mount Sinai (ISMMS) in New York between September 2012 and September 2013. The protocols for both the sequencing component and the social science research component of the course were submitted to the ISMMS institutional review board. The board determined that the primary aim of the research was to assess the students' decision making and outcomes regarding analyzing their own genomes in an educational setting and that the research (questionnaires, interviews) addressing these aims posed no greater than minimal risk and met criteria for exemption under category 2 research involving the use of educational tests or survey procedures.

The institutional review board also determined that the sequencing was part of the educational experience and referred the course directors to the ISMMS Research Ethics Committee regarding this component of the proposed course. The research ethics committee reviewed the sequencing component, particularly focusing on confidentiality and coercion; the committee determined that their concerns regarding these ethical issues were addressed by the course design and so approved the sequencing as part of the course. The course also was reviewed and approved by the dean of the ISMMS and by the CePORTED Curriculum Committee. The course directors also consulted the medical center's general counsel and the New York State Department of Health while designing the course.

Participants were 19 students (10 male, 9 female) enrolled in an advanced genomics course. Five were genetic counseling masters students, three medical genetics residents, three MD/PhD students, three PhD students, two medical students, two junior faculty who regularly used genetics in their work, and one genetics fellow. Most of the MD and PhD students had had some prior experience with genetics or genomics research. All 19 students had previously completed an introductory course.[20] All students in the advanced course were eligible to elect to have their genome sequenced—at no financial cost to them—as part of the course, as long as they attended the first session.

Questionnaires were administered at five time points (T1–T5). Here we present the results from questionnaires administered directly before the students worked with their own genomes (T3), directly afterward (T4), and 6 months later (T5), along with in-depth interviews at T5. Nineteen students (100%) completed the T3 questionnaire, 17 (89%) completed the T4 questionnaire, and 15 (79%) completed the T5 questionnaire. Six (32%) completed the in-depth interviews at T5.

Questionnaires included a measure of technical WGS knowledge developed for this study, previously published measures of personal direct-to-consumer genomic testing knowledge, attitudes toward and the perceived usefulness of WGS,[21] self-reported understanding of WGS and types of personal WGS results received, and valid, reliable measures of depression (Center for Epidemiologic Studies Depression Scale),[22] anxiety (State-Trait Anxiety Inventory),[23] the psychological impact of personal genomic information (Multidimensional Impact of Cancer Risk Assessment (MICRA))[24], decision regret (Decision Regret Scale),[25] and satisfaction with decision.[26]

We analyzed and reported the quantitative questionnaire data using frequencies, means and SDs, paired samples *t* tests for normally distributed data, Wilcoxon signed rank tests for non-normally distributed data, and repeated measures analyses of variance with Bonferroni corrections for multiple comparisons. All quantitative data were analyzed using SPSS Statistics version 20 (IBM, Chicago, IL), except for effect sizes, which were calculated using Excel 2010 (Microsoft Corp., Redmond, WA).

Transcripts of the in-depth interviews were analyzed using thematic analysis.[27] In brief, two of the study investigators (S.C.S. and M.D.L.) read the verbatim transcripts, independently generated initial themes based on two of the transcripts, reconciled their sets of themes, and produced a single collated code book. This then was used by the two investigators to code the sections of all six of the transcripts that were relevant to the primary aims of this study, that is, the educational and psychological outcomes of the WGS. See the **Supplementary Materials and Methods** online, as well as **Supplementary Table S1** online, for further methodological details.

RESULTS

Personal WGS decisions, results, communication, and attitudes

Consistent with laboratory records, all 15 students who completed the 6-month follow-up questionnaire (T5) self-reported that they had their blood drawn for WGS and analyzed their own genome as part of the course. Six students self-reported receiving a "carrier status" result, and three reported a "variant of unknown significance" that they felt was important to them (**Supplementary Table S2** online). In the T5 questionnaire, 14 of the 15 students stated they had discussed their personal WGS results with someone, most often a sibling, mother, or friend. None reported having discussed their results with a genetic counselor (although three stated that they intended to talk to a genetic counselor in the future), and only one said they had

discussed them with an "other health professional." However, four reported that they had discussed their results with a course instructor (see **Supplementary Table S3** online). Given the course instructors included health-care providers with expertise in medical genetics and genetic counseling, as well as informatics faculty with expertise in variant interpretation, it is possible the instructors were playing a dual role for the students even though they deflected any specific questions about the students' health or family history. Students' attitudes toward WGS did not significantly differ between T3 and T4, although there were medium effect sizes for some items (**Table 1**).

Educational outcomes

Questionnaire results. At T5, 12 of the 15 students agreed that analyzing their own genome as part of the course had been useful. Ten said they had applied the knowledge gained during the course in their work (**Table 2**). As **Table 3** shows, objectively-assessed technical WGS knowledge increased from T3 to T4, with a large effect size ($a = -2.80$; $P = 0.005$; $r = 0.70$). Self-reported understanding of WGS did not differ significantly between T3 and T4, but it was higher at T5 than at T4 ($P = 0.003$) and T3 ($P = 0.002$). Objectively-assessed knowledge

Table 1 Students' attitudes toward whole-genome sequencing before (T3) and after (T4) working with their own personal genomes

Attitude question	T3 (n = 19)	T4[a] (n = 17)	T3–T4[b]
How useful do you think the results from whole-genome sequencing will be to a physician?			
Useful/very useful	10 (52.6%)	7 (41.1%)	$z = -1.40$, $P = 0.16$, $r = 0.34$
Mean (SD)	3.41 (0.94)	3.12 (0.99)	
Median	Useful	Not sure	
How useful do you think the results from whole-genome sequencing information will be to patients themselves?			
Useful/very useful	9 (47.4%)	6 (35.3%)	$z = -0.51$, $P = 0.61$, $r = 0.12$
Mean (SD)	3.29 (1.05)	3.12 (0.99)	
Median	Not sure	Not sure	
Whole-genome sequencing is useful for patients.			
Agree/strongly agree	14 (73.7%)	9 (52.9%)	$z = -1.23$, $P = 0.22$, $r = 0.30$
Mean (SD)	3.71 (0.92)	3.35 (0.79)	
Median	Agree	Agree	
Physicians have a professional responsibility to help individuals understand the results they receive from whole-genome sequencing, even if the physician has not ordered the test.			
Agree/strongly agree	8 (42.1%)	6 (35.3%)	$z = -1.13$, $P = 0.26$, $r = 0.27$
Mean (SD)	3.00 (1.32)	2.71 (1.21)	
Median	Neither	Disagree	
Physicians have enough knowledge to help individuals interpret results of whole-genome sequencing.			
Agree/strongly agree	0 (0%)	0 (0%)	$z = -1.34$, $P = 0.18$, $r = 0.32$
Mean (SD)	1.59 (0.51)	1.41 (0.62)	
Median	Disagree	Strongly disagree	
Most people can accurately interpret whole-genome sequencing results.			
Agree/strongly agree	0 (0%)	0 (0%)	$z = -1.00$, $P = 0.32$, $r = 0.24$
Mean (SD)	1.35 (0.49)	1.24 (0.44)	
Median	Strongly disagree	Strongly disagree	
I know enough about genetics to understand whole-genome sequencing results.			
Agree/strongly agree	7 (36.8%)	6 (35.3%)	$z = -1.73$, $P = 0.083$, $r = 0.42$
Mean (SD)	3.35 (1.06)	2.94 (0.97)	
Median	Neither	Neither	
I understand the risks and benefits of getting personal whole-genome sequencing done.			
Agree/strongly agree	18 (94.7%)	17 (100.0%)	$z = -0.38$, $P = 0.71$, $r = 0.09$
Mean (SD)	4.24 (0.56)	4.29 (0.47)	
Median	Agree	Agree	

[a]Data are missing for two students at T4. [b]Differences assessed using the Wilcoxon signed rank test.

Table 2 Students' reports (*n* = 15) of whether and how the whole-genome sequencing course was useful, reported in the 6-month follow-up (T5) questionnaire

	Responses at 6-month follow-up (T5)
Perceived value of the WGS course	
I think analyzing my own genome as part of this WGS course was useful.	
Strongly disagree	1 (6.7%)
Disagree	1 (6.7%)
Neither agree nor disagree	1 (6.7%)
Agree	7 (46.7%)
Strongly agree	5 (33.3%)
Application of WGS knowledge	
Have you applied the knowledge that you gained during the WGS course in any of your medical practice or other work since the course?	
No	5 (33.3%)
Yes	10 (66.7%)
If yes, can you explain how?	
	Planning new projects for my research in studying XXXXX genomics (participant 3)
	The means by which we learned to analyze our whole genomes in the course have been translated into analyzing high-throughput sequencing data in a research laboratory setting. (participant 4)
	Better understanding of bioinformatics and next-gen sequencing analyses (participant 6)
	I have begun to apply that knowledge in my practice and hope to have more opportunities to do so in the future. (participant 7)
	I have become more involved in analyzing variants from whole-genome/exome sequencing in a clinical setting. (participant 8)
	I expect to spend a portion of my time in my new job working with patients and research subjects who are pursuing [WGS]. (participant 12)
	I think this experience has given me a more realistic perspective of the utility of WGS/WES. During job interviews and in my career I now have a more conservative view on the use of these techs until more info is known. (participant 14)
	I have been asked [to help classify] variants at my job. (participant 15)
	Related seq analysis for chip-seq (participant 20)

WGS, whole-genome sequencing.

about direct-to-consumer personal genomics did not differ between T3 and T4 (see **Supplementary Table S4** online).

In-depth interview results

Theme 1: Increased motivation to learn. There was a strong theme running through the in-depth interviews of students who felt the personal genome analysis increased their motivation to learn; in five of the six interviews, the students said they were more "involved," "interested," "persistent," "engaged," "excited," and/or put in more "effort" because they were analyzing their own genome. For example, one student stated, "if I was using a dummy genome, I wouldn't have had a motivation to keep digging for stuff" (participant 15). See **Table 4** for an extended quote.

Related to this, several students said they were more motivated to work outside of class because it was their own genome, for example, "If something came up in class that means something, you're going to put a lot more of your time into figuring out what it is. I think I did a fair amount of research . . . in the evenings, like as soon as I left class. I was like, 'I have to look this up more'" (participant 14).

One student said the personal connection was important: "For me, the main reason was that I felt it would better motivate me to learn and understand what the results meant if it was my own sequence. I just felt that having a personal connection . . . when you have an emotional attachment to something, you learn, you take it in better, you're more likely to remember it, so I felt that it would help me learn better" (participant 3).

Some said that although they felt they would have learned as much if they had analyzed someone else's genome, it wouldn't have been as enjoyable or interesting, for example, "I think the knowledge would be the same, but I don't think I would've enjoyed the class as much" (participant 14), and "I mean, the same questions could have been asked but being able to address the same questions looking at my own genome made it particularly interesting" (participant 7).

Theme 2: Increased understanding of the patient experience. Two students talked about how the experience of analyzing their own genomes gave them insights into the patient experience. Participant 14 said, "I think that it is important, also,

Table 3 Students' technical understanding and self-reported understanding of whole-genome sequencing before (T3) and after (T4) working with their own genome sequence data in an advanced course and in the 6-month follow-up (T5) questionnaire[a]

	Before (T3)	After (T4)	Follow-up (T5)	T3–T4 Significance	T4–T5 Significance	T3–T5 Significance
Technical understanding of WGS[b] (possible range: 0 [low knowledge] to 100 [high knowledge])	63.8 (17.31), 15–85	72.5 (8.17), 55–85	N/A	$z = -2.80$, $P = 0.005$, $r = 0.70$[c]	N/A	N/A
Self-reported understanding of WGS[d] (possible range: 1–5)	3.61 (0.63), 2.67–5.00	3.80 (0.50), 3.00–5.00	4.13 (0.53), 3.00–5.00	$P = 0.27$	$P = 0.003$	$P = 0.002$
How would you describe your current understanding of genetics?	3.89 (0.74), 2–5	4.12 (0.60), 3–5	4.47 (0.64), 3–5	$P = 0.57$	$P = 0.31$	$P = 0.037$
How would you rate your knowledge of genetics compared with others?	4.11 (0.81), 2–5	4.06 (0.56), 3–5	4.40 (0.74), 3–5	$P = 0.99$	$P = 0.16$	$P = 0.41$
How would you describe your current understanding of WGS?	3.68 (0.58), 3–5	3.82 (0.64), 3–5	4.27 (0.70), 3–5	$P = 0.12$	$P = 0.25$	$P = 0.037$
How would you rate your knowledge of WGS compared with others?	3.95 (0.91), 2–5	4.24 (0.66), 3–5	4.33 (0.62), 3–5	$P = 0.50$	$P = 0.99$	$P = 0.52$
How confident are you in your ability to analyze and interpret WGS data?	3.26 (0.87), 2–5	3.47 (0.72), 3–5	3.67 (0.62), 3–5	$P = 0.99$	$P = 0.25$	$P = 0.50$

Data are mean (SD), range unless otherwise indicated.

[a]A total of 19 students answered the T3 questionnaire, and 17 students answered the T4 questionnaire. One student did not answer the technical knowledge questions. Thus, for the technical knowledge questions there was a final sample size of $n = 16$ and for the self-reported understanding of WGS questions a final sample size of $n = 17$.

[b]The technical understanding scores are calculated based on 18 of the 20 WGS test questions developed by course directors (two questions were excluded because they were ambiguous). For 17 of the questions, correct responses were given a score of 1 and incorrect responses were given a score of 0; for one of the questions (question 10), students could obtain up to three points. Thus total possible raw scores ranged from 0 to 20. Total scores were created by calculating the mean of each student's total number of correct responses and multiplying the mean by 100 to give a total score for each student, with possible range from 0% (indicating low knowledge) to 100% (indicating high knowledge).

[c]The test of significance comparing technical understanding of WGS at T3 and T4 was the Wilcoxon signed ranks test.

[d]The self-reported understanding of WGS scale scores are calculated based on the three self-report questions that ask students to self-report their understanding of WGS, their understanding of genetics, and their confidence in their ability to analyze and interpret WGS data. The minimum possible score was 1.0 (indicating low knowledge); the maximum possible score was 5.0 (indicating high knowledge). Possible scores for each of the individual items assessing self-reported understanding of WGS ranged from 1 (indicating low knowledge) to 5 (indicating high knowledge). The test of significance comparing self-reported understanding of the WGS scale was a repeated measures analysis of variance with Bonferroni corrections for multiple comparisons; missing values were imputed.

WGS, whole-genome sequencing.

to get that emotional aspect of it, especially if you're working in a career with patients, because I think it helps you to relate to your patients. I think, informationally, you would get the same, but in terms of clinically, in relating to patients, it's better to do your own." See **Table 4** for additional quotes.

Psychological outcomes

Questionnaire results. The mean MICRA score was 15.60 (0 indicates no emotional impact and 110 indicates high adverse emotional impact of results) (**Table 5**). In addition, all students except one (participant 10) scored <30, well below the MICRA midpoint (**Supplementary Figure S1a** online). Similarly, all but two (participants 10 and 14) scored zero on the MICRA Distress subscale (**Supplementary Figure S1b** online), and the mean score was 1.47 (possible range of 0–30) (**Table 5**), suggesting most students were experiencing no WGS results–related distress at the 6-month follow-up. The pattern was similar for the MICRA Uncertainty subscale, with a mean score of 4.20 (**Table 5** and **Supplementary Figure S1c** online). MICRA Positive Outcomes subscale scores were more mixed (**Table 5** and **Supplementary Figure S1d** online).

Decision Regret Scale scores were low overall. The mean (SD) score on the Decision Regret Scale was 14.50 (21.27) (**Supplementary Table S5** online), and all but one student (participant 10) scored ≤20 (possible range of 0–100). One student (participant 10) scored 70 on the Decision Regret Scale, suggesting they experienced higher levels of regret (**Supplementary Figure S2** online). In bivariate correlation analyses, decision regret at T5 was associated with decisional conflict at T2 ($r = 0.62$; $P = 0.014$) and T3 ($r = 0.59$; $P = 0.028$), but not at T1, and with anxiety at T3 ($r = 0.59$; $P = 0.034$) but not at T4 or T5.

On the Satisfaction With Decision scale, the mean score was 3.92 (1.36) (1 = low satisfaction, 5 = high satisfaction). Thus, while there was some variation in individual scores (see **Supplementary Figure S2** online), this indicates quite high satisfaction with the decision regarding analyzing their own genomes overall (see **Supplementary Table S5** online).

Overall, the students had low levels of depression. Center for Epidemiologic Studies Depression Scale scores were low and did not change significantly over time (**Table 5**). Mean State-Trait Anxiety Inventory anxiety scores also indicated low levels of anxiety overall and no significant changes over time (**Table 5**). See **Supplementary Figures S3 and S4** online for individual depression and anxiety scores, respectively.

Table 4 Sample quotes from the 6-month follow-up (T5) in-depth telephone interviews

Themes	Example quotes
Educational outcomes	
Increased motivation to learn	"I think I would have not been engaged as much or not been as interested, if I was not doing my own. . . . Yeah, I think just because [sigh] analyzing it was very difficult, and I think sometimes we, as a class, or at least me, got frustrated that we didn't know the codes or we couldn't find what we wanted to find. I think I was much more persistent about it because it was my own. Even though it was hard, I was like, 'No, I really wanna look this up, so I'm going to figure out how to do it.' I think, if I was doing someone else's genome, I wouldn't really care what the results were, so I may not have put in as much effort in the analysis, because I think it was really difficult to do. I think, in a group setting, it's hard, too, because we all needed help, like all the time. [Laughter] . . . I think, definitely, I was more motivated because I did my own." (participant 14)
Increased understanding of the patient experience	"Because I do think it's important to experience that in order to be able to understand how patients will react to their own information. . . . Then in terms of experiencing how it is to look at some of your own data, I also realized what a significant impact some information can have. . . . You are theoretically aware of, but I think if you have never experienced that situation, it's hard to know how patients might feel. Not everybody feels the same way, obviously, but I think that taught me a little bit more about how some patients might react." (participant 10)
Psychological outcomes	
No negative emotional impact	"I guess I did see that I had an increased risk for diabetes and that sort of thing. . . . I didn't really pay too much attention to it. . . . That was something that we were doing in class. I don't know if we were all looking at that specifically, or it was something one of the instructors had us look up or I incidentally found it. I honestly don't remember. It wasn't something that I was actively searching for. Like I said, I'm not concerned about it." (participant 15)
Negative emotional impact	"I actually found an interesting variant, that, apparently, is associated with decreased white matter in the brain. Basically, the only papers it's been—or GWA studies—it's been found in, has to do with schizophrenia. I thought that was kind of interesting. Again, not something that's like positive in any way, but I was like, 'Oh, did I really wanna know this? Probably not.' [Laughter] I think, if I had found something like that, that was more clinically significant, I think it would've been—I don't know—hard to deal with. Thankfully, I didn't find anything that intense. . . . My initial reaction was like, 'Maybe I should have an MRI.' [Laughter] . . . Finding things, especially that are of unknown clinical significance or kind of just variants, I think it kind of makes you feel powerless, because there's no way to get more information, [because] it's just not out there. There's really nothing you can do about it, especially if it's not something that necessarily causes a medical problem, or if it did, it may not be something you can do anything about it anyway. Like something in terms of mental health, I mean, until you have symptoms, there's nothing you could do . . . it made me feel kind of like powerless, like I couldn't do anything about it. . . ." (participant 14)
	"When I looked at that, and I found a variant which was in the Brugada syndrome, I did start freaking out. . . . Then the whole family issue comes into play . . . and then all of a sudden your thoughts start going crazy. You think about all the implications that this could have. . . . Then I dug deeper, and I looked up the information, looked up the literature, and searched this polymorphism. It was actually downgraded to just a polymorphism, not a pathologic mutation. I mean, at that point I calmed down, and I was okay with it. Even though . . . the carrier frequency is low, but I think it's fine. At that point, I stopped looking at my genome. . . ." (participant 10)

When asked to provide open-ended comments at the end of the T4 and T5 questionnaires, most students were positive about the course and/or made pragmatic suggestions regarding course content or structure. One student (participant 10) reported that they felt in retrospect they should not have sequenced their own genome. Another student (participant 14) suggested that more caution needed to be taken regarding privacy (**Supplementary Tables S6 and S7** online).

In-depth interview results

Theme 3: No negative emotional impact. For four of the six interviewed students, there seemed to be no negative emotional impact of analyzing their own genomes: "I don't think—I wouldn't say that it's had an emotional impact on me" (participant 3). See **Table 4** for additional quotes.

Theme 4: Negative emotional impact. Two students talked about some negative emotional impact of a personal result they discovered. Participant 14 talked about how finding a rare variant of unknown significance that seemed to be associated with schizophrenia led them to feel "powerless" but that the impact on them was not as "intense" as it might have been had it been "more clinically significant" (**Table 4**).

Participant 10 talked about the impact on them of finding a rare variant that seemed to be associated with Brugada syndrome, saying they "did start freaking out," they "couldn't deal with it," and "it did scare me." The student described reanalyzing their genome after the course had finished to view a new visualization, not realizing new results would also be displayed. At this point they found the variant: the discovery caused them significant distress, but this subsided within 24 h once they had investigated the variant and determined it to be benign. This student described how they had been uncertain about whether to analyze their own genome at the outset, and that while some family and colleagues had been supportive of them doing so, others had not (**Table 4**).

DISCUSSION

This is, to our knowledge, the first study to explore the potential value—both benefits and risks—of incorporating personal WGS analysis into an advanced genomics course. All of the students elected to analyze their own personal genomes. We were

Table 5 Students' psychological well-being and impact of their whole-genome sequencing results before (T3) and after (T4) working with their own genome sequence data in an advanced course and at 6-month follow-up (T5)

	Before (T3), *n* = 19	After (T4), *n* = 17	Follow-up (T5), *n* = 15	T3–T4 Significance	T4–T5 Significance	T3–T5 Significance
Multidimensional impact of WGS results						
Overall MICRA Scale (possible range: 0–110)[a]	N/A	N/A	15.60 (15.44), 2–66	N/A	N/A	N/A
MICRA Distress subscale (possible range: 0–30)	N/A	N/A	1.47 (4.91), 0–19	N/A	N/A	N/A
MICRA Uncertainty subscale (possible range: 0–40)	N/A	N/A	4.20 (7.15), 0–27	N/A	N/A	N/A
MICRA Positive subscale (possible range: 0–20)	N/A	N/A	9.93 (6.63), 0–20	N/A	N/A	N/A
Psychological well-being						
Depression, CES-D[b] (possible range: 0–60)	10.41 (10.04), 0–35	9.63 (7.61), 0–28	10.67 (10.10), 2–42	$z = 0.67$, $P = 0.50$, $r = 0.16$	$z = 0.79$, $P = 0.43$, $r = 0.20$	$z = 1.58$, $P = 0.11$, $r = 0.41$
Anxiety, STAI[c] (possible range: 20–80)	37.71 (11.64), 20–58	34.44 (11.83), 20–59	34.40 (13.54), 20–71	$t(13) = 1.49$, $P = 0.16$, $r = 0.38$	$t(11) = -1.00$, $P = 0.34$, $r = 0.29$	$t(12) = 1.09$, $P = 0.30$, $r = 0.30$

Data are mean (SD), range unless otherwise indicated. When asked at T5 whether taking the course had any impact on family members, 14 of the 15 students said "no," while one said "not sure."

[a]Of the five students who answered the two MICRA questions about children, four said they "never" and one said they "sometimes" worried about the possibility of their children getting a disease. Four said they "never" and one said they "sometimes" felt guilty about possibly passing on a disease risk to their children.

[b]Depression was measured using the Center for Epidemiologic Studies Depression Scale (CES-D), which is a 20-item measure with possible scores ranging from 0–60 (0 = low depression, 60 = high depression). For depression, changes over time were examined using the Wilcoxon signed rank test (nonparametric version of a paired samples *t* test). We also conducted repeated measures analysis of variances. For depression, the overall results were $F = 1.85$, $P = 0.19$ (T3–T4 $P = 0.44$, T4–T5 $P = 0.30$, T3–T5 $P = 0.11$).

[c]Anxiety was measured using the State-Trait Anxiety Inventory (STAI; state part, Y form version), which is a 20-item measure with possible scores ranging from 20–80 (20 = low anxiety, 80 = high anxiety). For anxiety, changes over time were examined using paired samples *t* tests. We also conducted repeated measures analysis of variances. For anxiety, the overall results were $F = 1.44$, $P = 0.26$ (T3–T4 $P = 0.14$, T4–T5 $P = 0.52$, T3–T5 $P = 0.35$).

WGS, whole-genome sequencing.

initially surprised at the 100% uptake rate, but with hindsight we recognize that self-selection was probably at play: except for the genetic counseling master's students, for whom the course content—but not the personal WGS—was part of the core curricula, these students all voluntarily elected to take the course. Anyone who was sure they did not want to analyze their own genome probably would not elect to take the class in the first place. Also, the fact that WGS was offered free of charge was probably another significant factor; personal WGS is not yet widely available, so it may have been difficult to turn down this "opportunity."

In the questionnaires, most students reported that the process had been useful, and two-thirds reported that they had already applied what they had learned in the workplace. Technical understanding of WGS increased from before to after the course. In the interviews students expressed a strong belief that working with their own genomes had increased their motivation to learn and their persistence in mastering the analytic skills needed to work with WGS data. Some also felt they had greater empathy or understanding of the patient experience. These findings are somewhat consistent with the previous studies by the group from Stanford[12,13] and build on their results by expanding what is known in this area, from genotyping to WGS. In the questionnaire study, Stanford students who analyzed their own direct-to-consumer genetic testing data showed increases in technical knowledge, whereas those who analyzed a third-party genome did not.[12] In the interview study, Stanford students generally found the experience to be beneficial (although some expressed skepticism about their results).[13]

In our study, most—but not all—students reported low levels of psychological distress, uncertainty, and regret about their decision to analyze their own genomes on the quantitative measures and no increases in anxiety or depression. The in-depth interviews shed further light on the students' feelings about analyzing their own genomes. All interviewed students talked about the positive outcomes of having analyzed their own genomes, particularly regarding the educational impact. When WGS results–related distress was apparent, it seemed to have been preceded by experiencing conflict around the decision regarding whether to analyze their own genome in the first place and compounded by discovery of a variant of unknown significance several months after completing the course. This suggests that the positive educational benefits of personal WGS might be eroded by student distress if they discover unexpected results via the sequencing, particularly if they were conflicted about analyzing their own genomes in the first place.

While we believe students should "own" their raw data, we also recognize this raises questions about what responsibilities medical schools and universities have to students who may continue analyzing their raw data for perhaps many years after the course. These questions include what responsibilities institutions have to students regarding providing clinical follow-up of any variants found, whether they have financial responsibility for that follow-up, and whether they are responsible for

helping students deal with any distress experienced if variants are identified after the course. This course emphasized to students that the sequencing was being performed for educational, not clinical, purposes. Therefore, personal results arising from the sequencing during or after the course were not to be viewed as "clinically actionable," and any students wishing to follow up clinically on any of their sequencing results needed to do this through existing clinical channels. Although ISMMS provided optional genetic counseling during the course, it did not take financial responsibility for any other counseling or clinical follow-up the students may have wished to seek during or after the course. The role of the course faculty was to teach the students how to interpret a genome. Therefore instructors answered questions about the process of variant interpretation but deflected questions about the interpretation of a variant in the context of a student's particular health or family history. The latter is a clinical, not educational, question and needs be addressed in a clinical context. This distinction can be difficult to maintain, especially for clinical faculty, but it was important to ensure this course was an educational and not a clinical experience.

A limitation of our study is the lack of randomization and a control group. Though having a comparison group of students who had elected not to analyze their own genomes may have been helpful, this would still have been subject to confounding effects. In the only study to compare students who did and did not analyze their own genetic data,[12] those who did not analyze their own genetic data were not randomly assigned, but rather chose not to do so. Although students who analyzed their own genetic data showed greater improvements in knowledge than students who did not, this could be due to confounding factors; for example, motivation to obtain one's personal genetic data could be positively correlated with general motivation to learn about genomics. Only a randomized controlled trial study design will be able to tease out the factors influencing learning.

Another limitation of our study is that the primary knowledge measure was developed specifically for this study. Consensus on what domains of knowledge are necessary for future healthcare providers and other users of personal genomics, and how best to measure these domains, is lacking. Achieving this consensus and then developing new measures of knowledge about WGS that assess the agreed-upon important domains of understanding would be valuable and advance this field.

Further limitations were the small sample size and low interview uptake. However, constraining the class size seemed appropriate in this study, the first proof-of-principle study of its kind. Having a relatively small, single class made it arguably easier to monitor students' well-being, at least for the duration of the course, and give them the support needed if they requested it. Of course, WGS is now less costly by comparison to historical costs, but it is still not "cheap"; therefore, cost was also a consideration. This course is complex and resource-intensive, and the first iteration was especially so. We constrained the size to that which the faculty were confident they had the financial and human resources to accommodate. As WGS becomes more widespread, analysis tools improve, and costs decrease further, however, the cost and complexity will be less of a limiting factor, both in expanding this course at ISMMS and replicating it elsewhere. These trends make us confident this course, and hands-on genomics training more generally, can be scaled up in the future.

This course represents just one point on a spectrum of potential designs targeting different groups and incorporating different kinds of genomic data into laboratory exercises. An alternative design would incorporate the genome and experience of one of the many individuals who have obtained and publicly shared their genomes. This would be more scalable and less costly but might be less effective in motivating students to engage with the course content.

The class heterogeneity had both benefits and limitations. The heterogeneity was valuable because there was student representation from across the continuum of skills needed to interpret and work with WGS data. The mixed nature of the class does, however, pose challenges to interpretation: Students from different training backgrounds (e.g., matriculating students vs. residents) may have different reactions to analyzing their own genomes. Ideally, subgroup differences would be explored, but the small sample size, combined with considerations regarding protecting students' identities and privacy, prevented us from doing this here.

Larger studies with randomization built into the study design are undoubtedly needed before the benefits and risks of offering personal genome analysis to enhance learning and motivation can be truly determined. Large studies with greater numbers of students from specific training backgrounds will have the further advantage of allowing comparisons in experiences and learning between students from different fields. Our study is, however, a first, important step along the path of understanding the pros and cons of giving students the choice to analyze their own or somebody else's genome as they learn about WGS. Our hope is that our methods and results reported here will be valuable to those running or considering running similar courses at other institutions, help link studies to increase power and comparisons across student subgroups, and ultimately contribute to debates on how best to train future health professionals in genomic medicine.

Conclusion

Giving students the option of analyzing their own genomes may increase motivation to learn and awareness of the patient experience. Distress caused by personal WGS results may occur in some students. Appropriate safeguards need to be in place to mitigate these negative outcomes. This includes ensuring students have sufficient knowledge of the risks, benefits, uncertainties, and limitations of analyzing their own genomes before they make their decisions and emphasizing to them that they only do so if it is consistent with their personal values and situations. Additional evidence is required before optional personal genomes should be incorporated into medical education curricula on a larger scale.

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/gim

ACKNOWLEDGMENTS

The authors thank Jo Waller for her advice regarding the qualitative analyses and the PAPG students for their participation in this project. This work was supported in part through the computational resources and staff expertise provided by the Department of Scientific Computing at the Icahn School of Medicine at Mount Sinai.

DISCLOSURE

The authors thank Jo Waller for her advice regarding the qualitative analyses and the PAPG students for their participation in this project. This work was supported in part through the computational resources and staff expertise provided by the Department of Scientific Computing at the Icahn School of Medicine at Mount Sinai.

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