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Decision-Making Preferences About Secondary Germline Findings That Arise From Tumor Genomic Profiling Among Patients With Advanced Cancers

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Abstract

Purpose: In patients with advanced cancers, tumor genomic profiling (TGP) can reveal secondary germline findings (SGFs) regarding inherited disease risks. This study examines the process by which patients with advanced cancers would make the decision about whether or not to learn these SGFs, and their preferences regarding specific challenging decision scenarios including whether patients should be required to receive SGFs and whether SGFs should be returned to family after a patient's death.

Patients and Methods: We conducted qualitative semi-structured interviews with 40 patients with advanced breast, bladder, colorectal, or lung cancer who had TGP. Data were collected regarding participants' perspectives about the hypothetical decision to learn their SGFs including their anticipated approach to the decision-making process, as well as their preferences about challenging decision scenarios. Data were evaluated using thematic content analysis.

Results: We identified themes regarding participants' preferred degree of decisional autonomy, perceived vital role of doctors, information needs, and anticipated process of deliberation. Although participants reported that this decision was ultimately their own, many wanted input from family and trusted others. Oncologists were expected to provide decision guidance and key clarifying information. Most participants stated that patients should be able to make a choice about receiving actionable SGFs, and a majority stated that SGFs should be available to family after a patient's death.

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Conclusion: These results provide insight into SGFs decision-making processes of patients with advanced cancers, which can allow clinicians to provide patients optimal decision support in this context. Patients with advanced cancers have specific information needs and decision-making preferences that educational and communication interventions should address to ensure that patients make informed choices about learning SGFs.

Keywords

Secondary findings; incidental findings; cancer; decision making; precision medicine

Introduction

Tumor genomic profiling (TGP) is revolutionizing cancer care. TGP involves sequencing somatic DNA to identify genetic variants indicative of tumor susceptibility to targeted therapeutics. TGP can also identify germline variants indicating that a patient has inherited disease risks, detected either in the somatic DNA or when a patient's germline DNA is directly sequenced for comparison to the somatic sequence. These germline variants are considered "secondary" findings when actively sought by researchers or clinicians (or "incidental" when not), because they arise outside of the original purpose of TGP.[1,2] Secondary germline findings (SGFs) indicating risks for various health conditions are likely to be detected in a sizable minority of patients receiving TGP; for example, presumed pathogenic germline variants have been observed in 15.7% of patients receiving TGP at our institution.[3]

Current American College of Medical Genetics and Genomics (ACMG) recommendations state that individuals undergoing clinical genomic sequencing should be allowed to opt-out of receiving SGFs.[4] This recommendation plus increasing adoption of TGP in clinical care ensures that many cancer patients will be confronted with the decision about whether to learn their SGFs. This decision is likely to be challenging, particularly for patients with advanced cancers who are currently the primary users of TGP (due to its utility for identifying eligibility for clinical trials of novel therapeutics[5,6]). These individuals must choose whether to learn information about their future disease risks and potential shared familial risks while facing a poor prognosis and the psychosocial challenges of a terminal diagnosis.[7] Although patients with varying stages of cancer have reported interest in receiving such information from TGP in real[8] and hypothetical[9–11] settings, it is unclear *how* patients decide whether to learn SGFs. Understanding the decision-making processes of patients with advanced cancers would allow clinicians to anticipate patient informational and decision support needs in this context.

This study sought to describe processes by which advanced cancer patients decide whether or not to learn SGFs arising from TGP. We analyzed qualitative data collected through an investigation of attitudes about SGFs among patients who received TGP at our institution.[12] These patients were informed about the possible incidental discovery of germline variants during the TGP consent that was conducted by their primary medical oncologist; however, because our institution did not routinely conduct secondary analyses at the time of this study, none of the patients had made a definitive decision about learning their SGFs. We examined

patients' perspectives regarding factors influential to their hypothetical decision about learning SGFs, and preferences about their role in this decision-making process. We also assessed preferences regarding specific challenging decision scenarios including whether patients should be required to receive SGFs and whether SGFs should be returned to family after a patient's death.

Methods

Study methods are described in detail elsewhere.[12] In brief, we recruited 40 adults diagnosed with advanced breast, bladder, colorectal, or lung cancer who had undergone TGP with an institutional somatic sequencing panel (MSK-IMPACT[13,14]). The Memorial Sloan Kettering Cancer Center Institutional Review Board approved this study.

Individual semi-structured interviews[15–18] were conducted with participants in person or via telephone based on participant preference. All participants provided informed consent before the interview. Interviews lasted approximately 45 minutes, and were audio-recorded and transcribed. Demographic data were collected in the interview and abstracted from medical records. Participants received $25 for their contribution.

Transcripts were analyzed through thematic content analysis, an inductive qualitative data analysis method that seeks to identify recurring conceptual patterns directly from the data through intensive reading, coding, and interpretation.[16,17,19–21] We used four coders to achieve analyst triangulation[22] and iterative rounds of consensus analysis to ensure trustworthiness of the findings.[23] ATLAS.ti was used to facilitate analysis.[24] We selected illustrative participant quotations from the interviews to support our findings, and computed descriptive statistics for demographic data.

Results

As shown in Table 1, study participants predominantly were diagnosed with stage IV cancer (92.5%), White/Caucasian (85%), college graduates (57.5%), married/partnered (87.5%), and had at least one child (70%).

Participants described how they would approach the decision if their doctor were to present the option of learning SGFs. We categorized participant responses into four key themes and relevant sub-themes, described below and indicated by italicized text; illustrative quotations appear in Table 2.

Theme 1: Degree of decisional autonomy.

As participants considered how they would decide whether to learn SGFs, a spectrum emerged regarding participants' preferred degree of decisional control and autonomy from close others. The close others that participants referred to primarily were significant others, close biological family (e.g., siblings, children), and occasionally friends. One group of participants expressed a preference for the *patient as an autonomous decision maker.* These participants reported that they would prefer to make the SGFs decision on their own, neither needing nor desiring input from others. Influential factors for this perspective included a

view that the decision was “my choice” because it involved highly personal information fundamentally related to “my body,” and a desire to avoid burdening others, particularly family, with potentially distressing information.

A second group of participants preferred that *close others play a consultative role in the decision-making process.* These participants anticipated communicating with close others about the option to learn SGFs and would consider their advice and opinions, but would ultimately make the final decision on their own. Some in this group noted that their families’ views were highly valued, but would not be determinative in their decision-making.

Finally, a smaller group preferred that *close others serve as active partners in decision-making.* These participants wanted their close others, particularly spouses/partners, to engage as full collaborators in the SGFs decision. Participants noted that as with other important life decisions, their spouses/partners would naturally be involved in this process. Others explained that their family should be actively involved in this decision because SGFs may have direct health-related implications for them.

Participants who anticipated involving others in their decision-making further described their *process of selecting close others for communication* about the option of learning SGFs. Many participants would seek the perspectives of individuals (e.g., siblings, children) possessing medical or scientific expertise. Participants also considered the intimacy of the relationship, as well as the individual’s level of involvement in their overall healthcare. Finally, several participants deemed important the ability or appropriateness of the individual to participate in a discussion about this issue, which could be dependent upon the individual’s age, cognitive ability, or capacity to cope emotionally with learning negative or upsetting information.

Theme 2: Vital role of doctors.

Participants perceived their doctors (i.e., oncologists) as a vital influence on their decision-making. Several participants indicated that they would deeply value speaking with their doctor about the prospect of learning SGFs. The importance placed on this consultation and the doctor’s personal opinion was due in part to the *nature and quality of the doctor-patient relationship*. For example, several participants reported great trust in their doctors, based on a foundation of past experiences and certainty that their doctors will act in their best interests. Their decision to learn SGFs was contextualized within an established, trusting relational dynamic; consequently, these participants indicated that they would be strongly inclined to learn SGFs if their doctor offered. Similarly, a few participants described how they generally feel comfortable discussing important issues with their doctor. Doctors were also seen as experts who would serve as the *primary source of relevant and valuable information* necessary for the decision. Several participants anticipated that their doctors would possess expertise regarding a range of issues relevant to SGFs, and could thus help them to acquire all essential information.

Theme 3: Information needs.

Participants described a typology of information that they would require to make an educated decision about learning SGFs. This included: 1) an explanation of whether SGFs

would provide a *clinical benefit* to the patient, their family, or other cancer patients, and whether these benefits would outweigh any possible harms; 2) *assistance in interpreting the meaning* of SGFs, such as the degree of certainty of the results and meaning of specific mutations; 3) *degree of scientific uncertainty* of SGFs and confidence in their applicability to health decisions; 4) description of the *testing procedure* in terms of the invasiveness of sample acquisition; 5) information about *who will have access* to the findings (e.g., insurers, healthcare providers); and 6) *negative implications or harms* of learning SGFs for the patient and family, including any unanticipated consequences. Many participants stated that they would ask questions about these issues in order to feel adequately informed; yet, a minority doubted that they would have any specific questions if presented with this decision due primarily to placing a high innate value on SGFs.

Theme 4: Process of deliberation.

Two preferences emerged among participants regarding the necessity to engage in an extensive decision-making process. A majority anticipated proceeding through a *deliberative decision-making process* characterized by weighing potential benefits against harms to determine their interest in learning SGFs (a detailed description of these perceived benefits and harms is provided elsewhere[12]). Participants described procedural aspects of their deliberation, expressing a preference for *taking time to decide,* during which they would consider the option on their own and seek out information regarding the value of SGFs. These participants also expressed a *desire to consult others* for their perspectives, including family, friends, and healthcare providers. Furthermore, a few participants expressed a preference for *conducting independent research* to learn more about receiving SGFs and the meaning of potential mutations.

A minority of the sample articulated *no need to engage in an extensive deliberation* to determine their interest in SGFs. These participants reported that there was virtually no decision to make because they were already certain of their interest. Several factors informed this perspective. First, these individuals perceived a *high value and utility of information*, including knowledge in general and knowledge related to their present or future health. Second, many expressed a characteristic *preference for quick decisions,* thus they would immediately respond to a doctor's offer to learn SGFs without further contemplation. Finally, some described a *sense of urgency* regarding learning SGFs, stating that it would be necessary to gain and act upon this information quickly in order to directly benefit their present health.

Preferences regarding decision scenarios.

During the interview, participants were presented with challenging scenarios and asked to describe their preferences for how clinicians should handle these situations. Participants' opinions were quantified and are presented with illustrative quotes in Table 3. First, in response to debate regarding the disclosure of SGFs,[25–28] we asked participants whether findings involving diseases that have effective medical interventions or medication side effects (i.e., actionable SGFs) should always be returned to patients. Most participants (28/40; 70%) stated that patients should be able to choose whether to receive this

information, whereas a minority (12/40; 30%) stated that such information should always be disclosed to patients.

Participants were also asked to decide whether they believed that if actionable SGFs were detected after a patient's death, these findings should be made available to a patient's family/significant other. The vast majority (36/40; 90%) reported that such information should be made available after a patient's death. This perspective was motivated predominantly by perceived family health benefits. A subset of participants (16/23; 69.5%) further expressed a belief that patients should be required to provide consent for this disclosure prior to their death, such as at the time of agreeing to TGP, while fewer (7/23; 30.5%) deemed patient consent unnecessary. Only a few participants were unsure about whether actionable SGFs should be available to a patient's family after death (2/40; 5%), or stated that such information should not be made available (2/40; 5%). Preferences against disclosure were due to concerns about negative emotional implications of such information for families.

Participants were similarly asked to decide whether they believed that SGFs regarding diseases without effective medical interventions or that indicate one is a healthy carrier for recessive diseases (i.e., non-actionable SGFs) should be made available to a patient's family after a patient's death. Again, a majority stated that such information should be made available (3¾0; 82.5%), due largely to the potential for family health benefits. Most participants who provided an opinion regarding consent reported that patients should be required to consent to the disclosure of this information to their families (11/12; 92%). Fewer (6/40; 15%) stated that non-actionable SGFs should not be made available to family after a patient's death, due to concerns about negative emotional reactions and the limited ability to intervene on such diseases. One participant was unsure (2.5%). Finally, when comparing the preferences of participants regarding the return of actionable versus non-actionable SGFs to family after a patient's death, 22.5% (9/40) were discordant in their preferences across these scenarios.

Discussion

This study clarifies advanced cancer patients' decision-making processes regarding SGFs from TGP. Given the personal nature of genetic risk information, participants viewed the decision to learn SGFs as ultimately their own. However, consistent with other medical decision contexts,[29–33] variability existed in participants' preferences for involving others including spouses/partners, children, or siblings in their decision-making. Consequently, when presenting the option of learning SGFs, clinicians must allow patients to solicit input from close others and help navigate challenges inherent in decision-making with multiple individuals.[34] Additional research should investigate how such interpersonal influences may shape, hinder, or support patients' SGFs decision-making.

Participants anticipated that their doctors (i.e., oncologists) would serve as the primary source of guidance for this decision. Participants placed great trust in their oncologists, acknowledging the influence of their expertise and personal opinions on their decision-making. Participants anticipated that they would have extensive questions about the benefits, harms, interpretation, and process of obtaining SGFs, and would expect their oncologists to

provide answers. However, past research demonstrates that this may not be feasible, because many oncologists have limited experience with germline testing and express concerns about their ability to address challenges presented by SGFs.[8] Several approaches may help bridge this gap between patient expectations and oncologist preparedness, including oncologist-targeted communication training, novel patient education materials, or referral to genetic counselors to address patients' questions. Future research should evaluate which of these approaches are most effective at achieving the delicate balance between meeting patients' information needs and practical challenges of cancer care delivery (e.g., time demands, workforce limitations). Research should also examine how different models of patient education (e.g., oncologist-led, genetics professional-led) influence patients' SGFs decisions, and how patients weigh the opinions of different care providers in this context.

Many participants anticipated a preference to undergo a thoughtful deliberation about the prospect of learning SGFs. Conversely, a minority believed that they would make an immediate decision guided by their personal values and beliefs. Research suggests that adopting a more intuitive decision-making approach can yield similar outcomes to deliberative decision-making,[35] although both approaches have benefits and drawbacks.[36] It is noteworthy that some participants' preferences for a quick decision were motivated by beliefs that SGFs would provide clinical utility or necessitate urgent action for them to reap health benefits. These expectations may be inaccurate for many advanced cancer patients, because the information revealed will not change their prognosis or clinical management. Accordingly, clinicians must ensure that all patients, including those immediately enthusiastic or accepting of SGFs, accurately understand the limitations of this risk information.

These results also provide insight into advanced cancer patients' preferences regarding challenging scenarios involving the return of SGFs. Consistent with ACMG recommendations[4] and expert opinions,[37] most participants stated that patients should choose whether they want to receive actionable SGFs from TGP. Participants acknowledged that some individuals may not want this information, and that clinicians should honor such preferences. Additionally, participants expressed diverse opinions regarding management of SGFs after a patient's death. Participants generally were more supportive of the return of actionable SGFs to family after a patient's death than non-actionable SGFs; although, in both instances, a majority supported sharing this information with family largely due to perceived family health benefits. The observation that 22.5% of participants held discordant views about the appropriateness of sharing actionable versus non-actionable SGFs with family after a patient's death highlights the importance of distinguishing the different categories of risk information that can be revealed through TGP (e.g.,[38]) when educating patients and eliciting their preferences.[8,39] Participants' general approval of obtaining patient consent at the time of TGP to ensure preference-concordant management of SGFs following death reinforces current ethical recommendations.[40]

This study has notable strengths. The qualitative design enabled an in-depth analysis of the decision-making preferences of a sample of advanced cancer patients diverse in diagnosis, gender, and health status. However, the majority was well-educated (85% reporting at least some college); decision-making preferences and processes of these individuals may differ

from those with lower formal education. Additional limitations include that this sample was racially and ethnically homogenous, recruited from one institution, and assessed at a time when the decision about learning SGFs was hypothetical in nature. Thus, findings may not be generalizable to the broader population of advanced cancer patients treated in other care settings who are navigating this decision in real time. Future work should examine decision-making processes of more diverse patients, and evaluate how different approaches to presenting patients with the option of learning SGFs (e.g., education and consent led by oncologists versus genetics professionals, presentation during a medical oncology visit versus a separate visit) ultimately influence patient decision-making.

In conclusion, this study provides important insight into how advanced cancer patients approach the decision to learn SGFs, and can inform how developing precision oncology programs manage the reporting of germline variants from TGP (see Table 4 for suggestions). A paternalistic model of care in which patients lack a choice about receiving SGFs is inconsistent with patient preferences. Rather, precision oncology programs should establish models that empower patients to make informed decisions about whether to learn SGFs. Patients' preferences for involvement in this decision can be accommodated in both opt-in and opt-out models (although these models will likely differ in the resources necessary to support patient deliberation and in the number of patients who select receipt of SGFs).[41,42] It is also clear that although most patients will likely want to retain decisional control in this context, some will desire time and space to include family and other influential figures in their decision-making. Patients with advanced cancers likely have specific information needs, and possible misperceptions, about the implications and utility of SGFs. Oncologists will be the primary resources to which patients turn for clarity and guidance, and must be prepared to meet these demands. Whereas the TGP decision may be time-sensitive due to treatment implications, patients may benefit from efforts to ensure that the SGFs decision can be pursued on a different temporal schedule aligning with their preferences for information-seeking and deliberation. Thus, educational and communication interventions targeted to patients, their families, and oncologists are needed to provide clear information contextualizing the meaning of SGFs in the advanced cancer setting, assist the weighing of benefits and harms, and allow patients to explore and express their preferences regarding specific categories of SGFs and management of this information in the event of their death. Such interventions would enable provision of optimal decision support that matches patients' needs and preferences in this era of precision cancer care.

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References

1. Wolf SM, Lawrenz FP, Nelson CA, et al.: Managing incidental findings in human subjects research: Analysis and recommendations. J Law Med Ethics 36:219–48, 211, 2008 [PubMed: 18547191]

2. Presidential Commission for the Study of Bioethical Issues: Anticipate and communicate: Ethical management of incidental and secondary findings in the clinical, research and direct-to-consumer contexts Washington, DC, 2013

3. Schrader KA, Cheng DT, Joseph V, et al.: Germline variants in targeted tumor sequencing using matched normal DNA. JAMA Oncol 2:104–11, 2016 [PubMed: 26556299]

4. ACMG Board of Directors: ACMG policy statement: Updated recommendations regarding analysis and reporting of secondary findings in clinical genome-scale sequencing. Genet Med 17:68–69, 2015 [PubMed: 25356965]

5. Tripathy D, Harnden K, Blackwell K, et al.: Next generation sequencing and tumor mutation profiling: Are we ready for routine use in the oncology clinic? BMC Med 12, 2014

6. Parsons DW, Roy A, Plon SE, et al.: Clinical tumor sequencing: An incidental casualty of the American College of Medical Genetics and Genomics recommendations for reporting of incidental findings. J Clin Oncol 32:2203–5, 2014 [PubMed: 24958819]

7. Taylor-Ford M: Clinical considerations for working with patients with advanced cancer. J Clin Psychol Med Settings 21:201–213, 2014 [PubMed: 24916664]

8. Gray SW, Park ER, Najita J, et al.: Oncologists' and cancer patients' views on whole-exome sequencing and incidental findings: Results from the CanSeq study. Genet Med 18:1011–1019, 2016 [PubMed: 26866579]

9. Gray SW, Hicks-Courant K, Lathan CS, et al.: Attitudes of patients with cancer about personalized medicine and somatic genetic testing. J Oncol Pract 8:329–35, 2 p following 335, 2012 [PubMed: 23598841]

10. Yushak ML, Han G, Bouberhan S, et al.: Patient preferences regarding incidental genomic findings discovered during tumor profiling. Cancer 122:1588–97, 2016 [PubMed: 26970385]

11. Yusuf RA, Rogith D, Hovick SR, et al.: Attitudes toward molecular testing for personalized cancer therapy. Cancer 121:243–50, 2015 [PubMed: 25209923]

12. Hamilton JG, Shuk E, Genoff MC, et al.: Interest and attitudes of patients with advanced cancer with regard to secondary germline findings from tumor genomic profiling. J Oncol Pract 13:e590–e601, 2017 [PubMed: 28628391]

13. Won HH, Scott SN, Brannon AR, et al.: Detecting somatic genetic alterations in tumor specimens by exon capture and massively parallel sequencing. Journal of Visualized Experiments:e50710, 2013 [PubMed: 24192750]

14. Cheng DT, Mitchell TN, Zehir A, et al.: Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT): A hybridization capture-based next-generation sequencing clinical assay for solid tumor molecular oncology. J Mol Diagn 17:251–64, 2015 [PubMed: 25801821]

15. Brinkman S, Kvale S: InterViews: Learning the craft of qualitative research interviewing (ed 3rd). Thousand Oaks, CA, Sage Publications, 2015

16. Green J, Thorogood N: Qualitative methods for health research (ed 3rd). London, UK, Sage Publications, 2014

17. Patton MQ: Qualitative evaluation and research methods (ed 3rd). Thousand Oaks, California, Sage Publications, 2002

18. Rubin HJ, Rubin IS: Qualitative interviewing: The art of hearing data (ed 3rd). Thousand Oaks, CA, Sage Publications, 2012

19. Boyatzis RE: Transforming qualitative information: Thematic analysis and code development (ed 5th). Thousand Oaks, CA, Sage Publications, 2009

20. Miles MB, Huberman AM, Saldana J: Qualitative data analysis: A methods sourcebook Thousand Oaks, CA, Sage Publications, 2014

21. Saldana J: The coding manual for qualitative researchers (ed 2nd). London, Sage Publications, 2013

22. Denzin NK: The research act: A theoretical introduction to sociological methods (ed 5th). New Brunswick, NJ, Aldine Transaction, 2009

23. Morse JM, Barrett M, Mayan M, et al.: Verification strategies for establishing reliability and validity in qualitative research. Int J Qual Methods 1:1–19, 2002

24. Friese S: Qualitative data analysis with ATLAS.ti (ed 2nd). London, UK, Sage Publications, 2014
25. Burke W, Matheny Antommaria AH, Bennett R, et al.: Recommendations for returning genomic incidental findings? We need to talk! Genet Med 15:854–9, 2013 [PubMed: 23907645]
26. Ross LF, Rothstein MA, Clayton EW: Mandatory extended searches in all genome sequencing: "Incidental findings," patient autonomy, and shared decision making. JAMA 310:367–8, 2013 [PubMed: 23917281]
27. Green RC, Lupski JR, Biesecker LG: Reporting genomic sequencing results to ordering clinicians: Incidental, but not exceptional. JAMA 310:365–6, 2013 [PubMed: 23917280]
28. Klitzman R, Appelbaum PS, Chung W: Return of secondary genomic findings vs patient autonomy: Implications for medical care. JAMA 310:369–70, 2013 [PubMed: 23917282]
29. Rini C, Jandorf L, Goldsmith RE, et al.: Interpersonal influences on patients' surgical decision making: The role of close others. J Behav Med 34:396–407, 2011 [PubMed: 21308408]
30. Coyne JC, Anderson KK: Marital status, marital satisfaction, and support processes among women at high risk for breast cancer. J Fam Psychol 13:629–641, 1999
31. Davison BJ, Oliffe JL, Pickles T, et al.: Factors influencing men undertaking active surveillance for the management of low-risk prostate cancer. Oncol Nurs Forum 36:89–96, 2009 [PubMed: 19136342]
32. Hallowell N, Ardern-Jones A, Eeles R, et al.: Men's decision-making about predictive BRCA½ testing: The role of family. J Genet Couns 14:207–17, 2005 [PubMed: 15959652]
33. Stiggelbout AM, Jansen SJ, Otten W, et al.: How important is the opinion of significant others to cancer patients' adjuvant chemotherapy decision-making? Support Care Cancer 15:319–25, 2007 [PubMed: 17120070]
34. Laidsaar-Powell RC, Butow PN, Bu S, et al.: Physician-patient-companion communication and decision-making: A systematic review of triadic medical consultations. Patient Educ Couns 91:3–13, 2013 [PubMed: 23332193]
35. Kruglanski AW, Gigerenzer G: Intuitive and deliberate judgments are based on common principles. Psychol Rev 118:97–109, 2011 [PubMed: 21244188]
36. de Vries M, Fagerlin A, Witteman HO, et al.: Combining deliberation and intuition in patient decision support. Patient Educ Couns 91:154–60, 2013 [PubMed: 23265430]
37. Scheuner MT, Peredo J, Benkendorf J, et al.: Reporting genomic secondary findings: ACMG members weigh in. Genet Med 17:27–35, 2015 [PubMed: 25394173]
38. Berg JS, Khoury MJ, Evans JP: Deploying whole genome sequencing in clinical practice and public health: Meeting the challenge one bin at a time. Genet Med 13:499–504, 2011 [PubMed: 21558861]
39. Kaphingst KA, Ivanovich J, Biesecker BB, et al.: Preferences for return of incidental findings from genome sequencing among women diagnosed with breast cancer at a young age. Clin Genet 89:378–384, 2016 [PubMed: 25871653]
40. Wolf SM, Branum R, Koenig BA, et al.: Returning a research participant's genomic results to relatives: Analysis and recommendations. J Law Med Ethics 43:440–463, 2015 [PubMed: 26479555]
41. Halpern SD, Ubel PA, Asch DA: Harnessing the power of default options to improve health care. N Engl J Med 357:1340–1344+1280, 2007 [PubMed: 17898105]
42. Ojerholm E, Halpern SD, Bekelman JE: Default options: Opportunities to improve quality and value in oncology. J Clin Oncol 34:1844–1847, 2016 [PubMed: 26884581]
43. Oken MM, Creech RH, Tormey DC, et al.: Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649–656, 1982 [PubMed: 7165009]

Table 1.

Participant characteristics (n = 40)

	***n* (%)**
Age, years (*M±SD)*	58.8±12.8; range: 30–82
Gender (Female) [a]	25 (62.5)
Race	
White/Caucasian	34 (85.0)
Black/African American	1 (2.5)
Asian	4 (10.0)
Refused	1 (2.5)
Ethnicity (Hispanic)	2 (5.0)
Educational attainment	
Less than high school	1 (2.5)
High school graduate	4 (10.0)
Vocational/technical school	1 (2.5)
Some college	11 (27.5)
College graduate	7 (17.5)
Post-graduate	16 (40.0)
Marital status	
Married or partnered	35 (87.5)
Divorced or separated	0 (0)
Widowed	3 (7.5)
Single	2 (5.0)
Parental status (Has children)	28 (70.0)
Cancer type	
Bladder	10 (25.0)
Breast	10 (25.0)
Colorectal	10 (25.0)
Lung	10 (25.0)
Cancer stage (Stage IV)	37 (92.5)
Self-reported health status [b]	
Fully active, able to carry on all pre-disease performance without restriction	13 (32.5)
Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature	23 (57.5)
Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours	4 (10.0)
Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours	0 (0)
Completely disabled; cannot carry on any selfcare; totally confined to bed or chair	0 (0)
Clinical trial status (Actively enrolled in a clinical trial)	18 (45.0)

[a] An equal number of women (n=5) and men (n=5) were interviewed for each cancer type, with the exception of breast cancer, for which all participants were women (n=10).

[b] As assessed with the single-item ECOG Performance Status.[43]

Table 2.

Decision-making process and preferences regarding secondary germline findings[a] and illustrative participant quotes

Theme 1: Degree of decisional autonomy	
Patient as an autonomous decision maker	*"Well, I think that would be up to me to decide so I wouldn't be asking my family what they think about doing that. I would just say—I would make my own decision about that to begin with. That's where it starts."* (F/CC)
Close others play a consultative role in decision-making	*"Well, I'd like their input, but ultimately I make the decisions for what, you know, what kind of treatment, or, that would, I'd be—you know, I would make the final decision. It's my body. I don't really—you know, I'll take their input, but other than that, you know, I'm going to make the decision whether or not to proceed with whatever."* (F/BrC)
Close others serve as active partners in decision-making	*"I would expect my wife to be involved…I trust her knowledge and judgment in these matters. So she'll be in a better position to help me make a decision on—about the decision to find out the outcome of the research and also to help manage it differently if I have an option to. [She would] be a partner in that decision making."* (M/BlC)
Process of selecting close others for communication	*"I don't think they should be involved in the decision. And it is very peculiar to my situation. I don't think my husband could deal with it so I don't want him burdened with it and I don't think my step-kids have enough of a—enough skin in the game, so to speak, that they should actually be involved in making the decision… and I guess I feel similarly about sisters and brother that that's too distant. They don't really—wouldn't make sense for them to be a part of the decision-making process."* (F/CC)
Theme 2: Vital role of doctors	
Nature and quality of the doctor-patient relationship	*"Believe me, it's been a rough road, and so like I said, my oncologist and I, we have a good understanding. And so far, he's steered me in the right—he was the one that put me in the tumor profiling and also on this new research, and anything he decides with me, I'm okay with it, because we have that doctor-patient trust. You know, so if he agrees with it, I'm with him. He hasn't steered me wrong yet."* (M/BlC)
Primary source of relevant and valuable information	*"No, I think my doctor would be enough. He's the only one who really knows my condition, you know?...If he felt it was important—I do whatever they tell me at Sloan. I mean, you know, if they tell me to go get this test, I go get that test, you know, go get that test, I do it because I think it's in the interest of my health… You know, you would have to make a strong argument for that case, but if he was insistent I would do it."* (M/BlC)
Theme 3: Information needs	
Clinical benefits	*"I think from a personal standpoint I would ask, you know, how realistic do you think – or how probable do you think something that came up as high risk is likely to happen or is there anything I can do to prevent it? I mean, it's more so in the latter that I would care about more if there's anything I can do to prevent it, to minimize the risk."* (M/CC)
Assistance in interpreting meaning	*"Well, I guess I would want the doctor to explain to me what mutations might mean. Is it certain mutations, is it only certain diseases that we're talking about or, you know, is it kind of open ended? You know, I guess I would want to learn more and hear more about the science of what the mutations might mean."* (M/CC)
Degree of scientific uncertainty	*"What I'm trying to have connection with is that if this testing were predictive of something they would be more interested than if this testing, nobody understood or knew how to interpret the results. So I guess it would be depending about how far along the continuum we are in being able to use this information would make a difference."* (M/LC)
Testing procedure	*"Yes, and if it's nothing invasive and they won't do—they won't poke me anymore and they won't do anything to me, it's fine with me. You know, I would like to know. But if there is any surgical thing involved or any invasive anything involved, I don't want to do it because I have been through a lot."* (F/BlC)
Who will have access	*"Who would have that information, would healthcare providers, you know, have to have access to that, or insurance providers have to have access to that information?"* (F/BrC)
Negative implications or harms	*"Yes, what are the possible ramifications, like everything? Like the question that I have now, like what haven't I thought of that could be a possible ramification of knowing? Yeah. So a doctor, speaking to a doctor about it would be great. Speaking to my doctor about what I could possibly learn that I might not want to know, that would be great."* (F/BrC)
Theme 4: Process of deliberation	

Deliberative decision-making process	*"The only potential benefit I see is if it discovers something that could be dealt with and prevent serious illness or genetic problems in the future. So then, that would have to be weighed against the emotional and psychological effects. I guess it depends on the particulars."* (M/CC)
Take time to decide	*"I think I would want to think about it and talk about it a little more before I made that quick decision, yeah."* (F/BrC)
Desire to consult others	*"Well I would probably discuss it with my wife. I think we're pretty much on the same page as far as the more information the better. It all depends on the information I guess. But I don't think it's something that we would shy away from."* (M/LC)
Conduct independent research	*"Well, I think I would research mutations first and find out a little about it before I answered him, but my nature is to go ahead and find out as much information as I can. So I would probably want him to do it. But, like I said, research it first."* (F/BlC)
No need for extensive deliberation	*"I would say, 'Great, where do I sign?' When I first got diagnosed I offered to have my DNA sequenced. And the doctor said, 'Why would you bother? There's only 30 markers and we've already looked at them.' So yeah, to me it was like a no-brainer and required no thought."* (M/CC)
High value and utility of information	*"Just my general feeling that more information is better. Information is power. I'd rather know than not know in most cases, in most cases...I value more information than less."* (F/BrC)
Preference for quick decisions	*"Minutes. I mean, it's—for me, I'm generally a very fast decision maker. So for me, it's really once I understand what exactly I'll be getting out of the study or what benefit it can provide, that's enough of what I need to make a decision on. I wouldn't need to go back home and think about it."* (M/CC)
Sense of urgency	*"Oh, no, I'd definitely make a quick decision… because I'd want to seek treatment right away. I wouldn't want to procrastinate or even—you know, it would be my decision. You know, I'd discuss with family members, but other than that—you know, my husband and my sister, but, you know, it would be my decision ultimately, and I'd really want to make it quickly."* (F/BrC)

Note: Participant characteristics are denoted after each quote as "Gender/Cancer type." F = female; M = male; BlC = bladder cancer; BrC = breast cancer; CC = colorectal cancer; LC = lung cancer.

[a] In the interview, "secondary germline findings" were described as: "I mentioned that with tumor genomic profiling, sometimes the lab will also look for mutations in the genes in your normal cells. Although the lab at MSK is *not* looking for mutations in the genes in *your* normal cells, let's imagine what would happen if a lab did. The lab could find mutations in the genes in your normal cells that mean different things. The meaning of some of these mutations is currently unknown, but other mutations could be associated with many different disease risks for you. These mutations would likely be something that you were born with. Because mutations in genes in your normal cells could be inherited or passed on, they could also affect the health of your family."

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Table 3.

Preferences regarding specific decision scenarios involving secondary germline findings and illustrative participant quotes

Should actionable secondary germline findings[a] always be returned to patients?	
Yes (30%)	*"Yes, I agree with that because they may not want to know, but they're still going to be affected by it. So I would—I agree with that. Because at least they'd have the opportunity to know that this is going—what's going on with them. They may not want to know, and it may be painful, but I think that they should be told."* (F/CC)
No (70%)	*"Oh my goodness, that's hard. I don't know if I can answer that. I guess, I guess, yeah, there should be a choice, because someone that might not be able to handle the information can choose to say, 'I don't want to know.'…I think the burden of having a terminal illness and then finding out that there's more—I think of a very close friend that was diagnosed with cancer and he was in his twenties and he survived, but when I learned that I had cancer I reached out to him and he said that at his lowest point he begged, 'I don't want to know any more information. I can't handle it, just have my mom and dad.' And that was part of the healing for him, so I always think about that because that was a poignant point that he made and I think it's so personal. So I think the person, the individual should definitely have the choice.* (F/BrC)
Should actionable secondary germline findings be made available to a patient's family or significant other if a patient has died?	
Yes (90%)	*"Yes. Well if it in any way could, could impact the timing of treatment or care for someone else in the family, they should, you know, I would want them to know about it… Yeah, I mean I guess at the end of the day that you should get consent from the patient—from the patient as to what you're going to do with anything—any—with anything you take from them."* (M/LC)
Unsure (5%)	*"You got a coin, you wanna flip a coin? Because the problem that comes to me is that my family is very tight, and it wouldn't be a problem with my family, but you always have a family that has—they're on the outs so to speak and if you tell one, you got to tell all. So I guess it's all or nothing. It's not like you can pick and choose. I think the family has a—I don't want to use the word right, because I think they may need to know, to understand. But have the right? It's a tossup. I guess it's situational."* (M/LC)
No (5%)	*"That's a good question because I'm thinking that if the spouse, for example, were told after the person passed away that we had discovered this, I guess the first reaction would be how come we didn't discover it earlier while the person was still alive and there may have been time for some kind of treatment. So it might cause some kind of anger. It might cause some kind of feeling that there was negligence on the part of doctors not to have discovered this or reveal it or whatever. So I don't know if that would necessarily be a good thing after a person passes away, to do that—unless there was a very strong reason to do that. But I would be cautious about that."* (M/CC)
Should non-actionable secondary germline findings[b] be made available to a patient's family or significant other if a patient has died?	
Yes (82.5%)	*"Yeah, I think it should be available. Well, just, you know, helpful in identifying for them if they feel they should [have] mutation testing done to see if they also are carriers. I think they should be able to make that choice if it's been identified in one family member."* (F/BlC)
Unsure (2.5%)	*"So it's a very—I mean I can project how I might think in the future, but it's hard for me to say at this time in a practical way how I would feel about, you know, releasing."* (F/LC)
No (15%)	*"My gut reaction is no. And that's based on my personal experience. If they want the information they should go and get it, right, and I think that if they get it just because it was available for me, like as part of my estate, here's her genetic testing—and again, I'll use my brother because he has the kids. If he says—if he sees in black and white that there's an indicator that we have a gene—I have a gene so that becomes a family gene, so he's now gotten a worry he didn't ask for in his life. You know, it's that gene. If I have a gene that could be terminal, not actionable, right, in today's world, like pancreatic cancer, right, which is my—like that's the worst cancer I know of in terms of how quickly it kills people that I know. I don't want him to know that."* (F/CC)

Note: Participant characteristics are denoted after each quote as "Gender/Cancer type." F = female; M = male; BlC = bladder cancer; BrC = breast cancer; CC = colorectal cancer; LC = lung cancer.

[a] In the interview, "actionable secondary germline findings" were described as: "There are different ways to think about the many kinds of mutations or disease risks that you could theoretically learn about. On the one hand, you could learn about conditions that have effective medical interventions. These could be conditions like some forms of cancer, or conditions that put you at risk of heart disease or of having a heart attack. When doctors know that someone has one of these mutations, they can recommend ways to help prevent a disease from developing or help find it earlier when it is more likely to be treatable. The doctors may also change the kinds of medications that they prescribe."

[b] In the interview, "non-actionable secondary germline findings" were described as: "It is also possible that the lab will find mutations for conditions that do not have recommended or effective medical interventions. These could be common conditions like diabetes, or incurable conditions like Alzheimer's disease. It is possible that learning about these mutations could motivate some people to change their lifestyle or make personal decisions about how they live their lives. The lab could also learn that you have a mutation that makes you a healthy carrier for a recessive disease such as sickle cell anemia or cystic fibrosis. Being a carrier has little or no effect on your health. But, when two carriers of the same recessive mutation have a child, then the child could have the disease."

Table 4.

Recommendations for developing precision oncology programs regarding how to manage and support patient decision-making about secondary germline findings (SGFs) from tumor genomic profiling (TGP)

● Develop educational materials about TGP and SGFs that can be easily disseminated to and understood by the close others (e.g., siblings, children, spouses/partners) who may play a role in a patient's decision-making.
● Ensure that individuals leading education and consent discussions about the return of SGFs are prepared to help patients with varying preferences for decisional autonomy from their close others.
● Patients attribute high trust and expertise to their oncologists; therefore, prepare oncologists to serve as a primary resource who can provide balanced advice to patients about the SGFs decision.
● Create patient educational materials that provide clear information about the potential benefits and harms of SGFs. Distinguish between potential outcomes of SGFs for patients (with a consideration of their cancer stage and prognosis) and for their families.
● Ensure that patients understand that the decision to undergo TGP is separate from the decision about return of SGFs (and that there are varying potential benefits and harms of each choice).
● Structure education and consent discussions about TGP and the return of SGFs to be temporally flexible, and therefore capable of accommodating patients' preferences to take time to deliberate, seek additional input from close others, and conduct independent research.
● Give patients a choice about the return of actionable SGFs. Either opt-in or opt-out models of germline variant management could allow such patient choice, but each has unique implications for resources to support informed patient decision-making and subsequent uptake of SGFs.
● Require patients to make decisions about the management of actionable and non-actionable SGFs in the event of their death at the time of consenting to TGP and the return of SGFs.