Table of findings

Qualitative/Quantitative research:
A grey row means that this article was selected by the literature search.

Study, country	sample size, study population	intervention/control	informed consent	outcomes	Main findings regarding providing information about unsolicited findings	Quality of research
Shirdarreh (2021), Canada Included 10 studies of interest (i.e., about secondary findings)	See table below for more details per study.			- Many patients had unrealistic expectations regarding the potential benefits of secondary findings for themselves and their family members, given opportunities for screening and secondary prevention in some cases. Others expressed significant concerns regarding the emotional impact of such findings on themselves and their children as well as practical issues such as insurability. - Patients with earlier stage disease were more interested in secondary findings than those with advanced disease. - High expectations were related to poor knowledge. - Education materials for patients should not exceed a sixth grade reading level. - In designing and evaluating a tool for providing information, it would be most helpful to have a standardized instrument for assessing patient knowledge. - It is essential to involve patients and healthcare professionals by developing such a materials/tool. - Educational efforts must be directed toward nurses and other oncology healthcare professionals to whom patients frequently turn for clarification of information. - Modular approach to developing patient education material would seem most appropriate.		See table below for more details per study.

Pujol (2019), France	Patients diagnosed with cancer undergoing genetic testing (number of patients not mentioned).	Clear information about the possibility and benefit of knowing a germline mutation of themselves and their relatives. - Additional information on preventive strategies are provide during geneticist consultations.	Yes, see Pujol (2018), for more details.	- Some patients do not want to deal with germline issue after clear information was given.	- Oncologists who received prior training on discussing the role of BRCA mutation (BRCAm) testing and genetic counselling techniques and/or genetic counsellor members of a multidisciplinary team can provide patients with pre-BRCAm test counselling at the first step of somatic analysis. - For patients with positive BRCAm test results or negative BRCA rest results but requiring additional counselling for familial risk, an appointment with a geneticist or a genetic counsellor is recommended. - Model for genetic testing pathways is presented in this article. - Authors of this article made a video as tool for providing information, please see link in this article.	None, data insufficient to assess quality of the study.

Bijlsma (2020), Netherlands	701 completed (845 started), patients diagnosed with cancer undergoing genetic testing.	To ensure that participants had sufficient and the same background knowledge, two digital videos were included in the questionnaire, the first video introduced basic concepts of genetics and the second video provided neutrally worded information on the potential impact of receiving unsolicited findings (UFs) and information on four different categories of UFs.	Yes, after reading background information , patients could accept inclusion in the study.	**Preferences:** 85% of the patients wants to be informed about UFs at start. After viewing videos, 15% changed their answer. Overall, 718 participants (94.2%) wanted to be informed about actionable variants, 537 (72.4%) wanted to receive information on non-actionable variants, 635 (87.0%) were interested to receive information on variants of reproductive significance and 521 (71.8%) participants would also like to receive information on variants of unknown significance. **Sharing information with family members:** 33% of the participants wanted family members to have access to their UFs while the patient is still alive.	- Men would like to receive UFs more often than women. - Academic degree was associated with higher preference of receiving actionable UFs. - Participants with elevated levels of anxiety or depressive feelings were less inclined to receive actionable UFs. - Participants with a higher quality of life were more interested in receiving UFs. - It is important to educate patients with cancer on basic genetics and UFs before a written informed consent is obtained. - One out of seven participants changed their opinion after the second video which introduced more information on the potential impact of receiving UFs and which explained the four categories (see below). - Important to distinguish between the categories (e.g., actionable UFs, non-actional UFs, UFs of reproductive, UFs of unknown). - In summary; 1. careful communicate genetic information towards patients' needs, 2. tiered informed consent procedure, 3. caution with respect to providing information on UFs to family members.	**Valuable research**

				30% of the participant wanted the hospital to actively contact family members without the intervention of the patient.		

Horiuchi (2021), Japan	2480, patients diagnosed with cancer undergoing genetic testing.	The confirmation of the disclosure intention to the participants was conducted at least three times: (i) upon registering for research participation (consent form); (ii) during the postoperative follow-up visit to the attending physician; and (iii) in the first genetic counselling visit before the secondary findings (SF) disclosure. If the patient chose to have the results disclosed, the SF results were presented to the patient by a medical genetics doctor and/or a genetic counsellor after several sessions of genetic counselling.	Yes, three times. Please see under 'intervention'.	- 68.9% of the participants opted for SF disclosure. - SF was found in 36/2480 (1.5%) participants. -28/36 (78%) were disclosed for their SFs. - 16/28 (57%) patients continuing follow-up by clinical experts.	- SFs was found in the WES of 1.5% of the 2480 research participants. - An important step is reconfirmation of the patient's intention before the disclosure of SFs. - It is important to motivate a patient for genetic counselling when the patient has no family history of SF-related diseases. - More effective genetic counselling practices regarding SF disclosure should be developed by collecting further data.	**Valuable research, but results were not precise.**

Hamilton (2017), USA	40, patients with advanced cancer who undergo tumor genomic profiling with an institutional somatic sequencing panel.	Patients were informed about the possibility to discovery incidental germline variants.	Yes, but no information about the content.	**Learning about Secondary germline findings;** - clinical benefit to patient, family members, other cancer patient, - benefits would outweigh possible harms; assistance in interpreting the meaning, - degree of scientific uncertainty, - description of testing procedure, - who will have access to the findings, - negative implications or harms. **Preferences With Regard to Specific Decision Scenarios;** Should actionable secondary germline findings always be returned to patients? *30% yes, 70% no* Should actionable secondary germline findings be made	**Recommendations:** - "Develop educational materials about tumour genomic profiling (TGP) and secondary germline findings (SGFs) that can be easily disseminated to and understood by close others (e.g., siblings, children, spouses/partners) who may play a role in a patient's decision making. - Ensure that individuals who lead 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 SGF decisions. - 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 their families. - Ensure that patients understand that the decision to undergo TGP is separate from the decision about return of SGFs and that varying potential benefits and harms of each choice exist. - 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.	**Valuable research, but low sample size.**

				available to a patient's family or significant other if a patient has died? *90% yes, 5% unsure, 5% no* Should nonactionable secondary germline findings be made available to a patient's family or significant other if a patient has died? *82.5% yes, 2.5% unsure, 15% no.*	- 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 nonactionable SGFs in the event of their death at the time of consenting to TGP and the return of SGFs". - Educational and communication interventions targeted to patients, their families, and oncologists are needed to provide clear information that contextualizes 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 about specific categories of SGFs and management of this information in the event of their death.	

Pinheiro (2017), USA	66, patients who participated in discussions regarding molecular testing.	Conversation with physician about molecular testing. This conversation was observed, and audio recorded. A questionnaire (including 18 topics) was completed after the conversation.	Yes, but no information about the content.	*Informational preferences;* **PATIENT:** - benefits of testing (88%), - how testing determines treatment (88%). Additional topics were; - implication for family (71%), whether the test indicates seriousness of disease (68%), test purpose (64%), incidental findings (56%), explanation of cancer genetics (53%), how the test is done (46%), limitations (44%), explanation of biomarker (42%), risks (42%), and an uninformative result (38%). **PHYSICIANS**; how the test determines treatment (100%), test purpose (93%), and benefits (89%). Physicians also chose limitations (70%), explanation of biomarker (63%),	Not specific about providing information about unsolicited findings, more about molecular testing. - Patient preferences regarding incidental findings were greater compared with physicians (56% vs. 19%). - Patient preferences regarding method of receiving information was (1) discussion with nurse, (2) written information. - Physician preference regarding communication aids were (1) pamphlets (2) website explaining key facts.	**Valuable research, but low sample size.**

				cost (59%), how the test is done (56%), risks (56%), and prognostic information (52%). *Patient preference for method of receiving information;* - discussion with nurse or physician (85%), - written information (67%). *Physician preference for communication aids;* pamphlets (67%), followed by a website explaining key facts (44%), patient video (41%), and scripts for them to use (26%).		

Bennette (2013), USA	Focus group methodology (n=12) and cognitive interviews (n=6) with patients who had received conventional genetic testing for familial colorectal cancer or polyposis syndromes.	All included patients received genetic testing. Afterwards the following interventions were performed; - focus group, - interviews, - DCE questionnaire.	Unknown, not mentioned in the article.	Patients reported a wide range of qualitative preferences for incidental findings, although some were emerged as important; treatability and severity, family impact, and lifetime risk of the incidentally identified disease.	Key attributes that summarize patient preferences regarding return of incidental findings; - lifetime risk, - treatability, - severity, - carrier status, - drug response, - total cost. Patients who stated a preference for receiving genomic information often wanted to know the results even in the absence of clinical utility.	**Valuable research, but low sample size and other concerns.**

Stjepanovic (2018), Canada	1960, advanced cancer patients who were candidates for clinical trials with targeted therapies and enrolled in the tumor profiling programs IMPACT or COMPACT.	Patients who consented to return of additional findings or their delegate were contacted by the clinical genetics service, which comprised of a medical geneticist and genetic counsellor if germline medically actionable variants were covered.	Yes, written informed consent for tumour profiling and germline co-analysis was obtained from all participants.	- Of all patients, 92% agreed to return of additional findings, 8% declined. - This did not differ by age, sex, race or prior genetic testing. - A number of 8/1596 (0.5%) patients were found with a germline medically actionable variant.	The interest of patients who undergo tumour testing in germline findings is high. Disclosure of previously unidentified findings present multiple challenges, thus supporting the involvement of a clinical genetics service in all tumour profiling programs. Return of germline medically actionable variants in cancer predispositions genes could be done by a Genomics Tumor Board (e.g., medical oncologist, clinical molecular laboratory geneticists, genetic counsellors, and medical geneticist).	**Valuable research, but heterogeneous population.**

Catenacci (2015), USA	111, patients with adequate tissue had undergone targeted gene sequencing.	Patients were grouped into low, intermediate, high risk based on age at diagnosis and personal/family history (i.e., pre-NSG risk). - Based on NSG results, post-NGS high risk patients were contacted and if they agreed to genetic counselling, they were evaluated.	Yes, consent was obtained from new patients with gastrointestinal cancers.	- 21/111 were classified as high post-NGS risk. - 11/21 were contacted and 10 of them accepted counselling. - 7/10 completed germline testing. - 3/10 confirmed to have germline mutation.	No information about patients' attitudes is provided in the article. Recommendations for screening and genetic counselling based on pre- and post-NGS probability risk are presented in the article. Please see Table 3 for detailed information. In short: - Discuss the implications of NGS testing and the possibility of identifying a somatic mutation that would be suspicious for germline potential. - Ask the patient about their preferences regarding disclosure of this information. - Use post-NGS risk to determine whether referral to genetic counsellor and germline testing is warranted. After a discussion of 20-40 minutes patients are often "information-saturated".	**Valuable research, but only in a selected population.**

Solomon (2020), USA	Eight patients and 5 family members participated in 4 patient focus groups. Nineteen providers participated in 3 focus groups.	HOPE-Genomics tool, for details see article.	Yes, for study participation.	- Patient/family participants were enthusiastic about the tool. - Providers liked the layout of the tool and said the report simplified a lot of information. - Some terms were confusing. - All patients were interested in the tool and 88% had high levels of satisfaction with HOPE-Genomics. - The tool was helpful (100%-88%), and easy to use (100%-75%). - 94% of the providers were interested in the tool for patients.	- Patients with cancer, family members, and providers are enthusiastic about patient-facing genomics reports and view the tool as beneficial. - Patients responded that they would want to use the tool at home. - The tool help patients to better understand their cancer. - The tool has to be optimized before implementation.	**Valuable research, but low sample size.**

Korngiebel (2017), USA	22 oncologists and cancer genetics professionals .	Interviews to elicit participants' narrative accounts of cancer-related genetic testing experiences.	n.a.	Views of medical oncologist and clinical genetics professionals regarding testing for genetic risk.	- Patients are referred to genetic professionals for genetic testing, and there is an opportunity for counselling. - When testing is done, patients may not realize the potential for information about inherited risk. - Post-test genetics referral and counselling would become the norm. - The perceived downside to more widespread genetic test ordering by oncologists is the difficulty posed by the return of unanticipated or otherwise hard-to-interpret results. - Multiple test panels include VUS, which complicates patient management.	**Valuable research, but low sample size.**

Van der schoot (2021), Netherlands	20 semi-structured face-to-face interviews with index patients and/or their family members about the unsolicited findings (UF) that had been disclosed, predisposing to oncological (n = 10) or cardiac disease (n = 10).	semi-structured interviews to ask participants about the impact of the disclosure of an UF on their lives.	Yes, for participation.	*Actionability:* - The majority of the participants valued disclosure as they were offered measures that would enable early detection or prevention. *Understanding:* - Important to understand findings; the relevance of being provided with adequate and timely information through thorough pre- and post-test counselling and follow-up consultations. This contributes to their empowerment.	The perceived impact would not keep patients from undergoing genetic testing again, knowing what they know now. During pretest counselling, counsellors should encourage consideration of all potential outcomes of genetic testing since the desire for a diagnosis potentially lessens the receptiveness for information on UFs. The informed consent has to be obtained during pretest counselling. To understand the findings of the test, post-test counselling should be performed. This contributes to fulfilling its actionability. The importance of the actionability criterion suggests the need for critical consideration of the perceived effectiveness of interventions and the clinical utility of disclosure of variants in the context of UFs.	**Valuable research, but low sample size.**

Tabel 1.2 Review Shirdarreh 2021

Study, country	sample size, study population	intervention/control	informed consent	outcomes	Main findings regarding providing information about unsolicited findings	Level of evidence
Yusuf (2015), USA	100, breast cancer Stage 0–3: 76% Stage 4: 24% Researchers were there to answer any questions. Participants had available a standard list of definitions.	Survey	Not mentioned.	Attitudes toward secondary findings.	- The great majority of the participants wanted to know the risk of developing a new cancer or other preventable or treatable diseases. - Almost half of the participants were concerned about the potential impact of secondary findings on their ability to secure insurance.	**Not valuable research due to risk of bias (response rate of 32%).**

Yushak (2016), USA	413, multiple tumours; - early-stage: 35% - advanced: 41% - unsure: 15% Patients were provided with brief background information on technical terms before survey.	Survey	Not mentioned.	Attitudes toward secondary findings.	- 72% indicated that they would like to know all of the information that is learned during testing, including results for gens that are not relevant to cancer but could affect their health. - 77% wanted to know if they had a variant that increased their risk of a serious but preventable illness, but only 56% wanted to know about variants that always caused a serious and unpreventable illness. - Only 14% of patients would not want to be informed about a genetic mutation that could be passed down to family members. - 75% would share hereditary information with family members who might be affected by a predisposition to a serious but preventable disease; this proportion dropped slightly to 62% for a serious and unpreventable disease. - 41% were concerned about the negative impact of incidental findings on quality of life.	**Valuable research, but some concerns.**
Best (2019), Australia	569, advanced stage, any tumour, no further treatment options, eight patients previously had germline genetic sequencing.	n.a.	n.a.	Knowledge (selfperceived) and attitudes toward secondary finding.	-Participants cognizant of lack of knowledge, but this did not deter them from consenting to testing. - Patients expressed little interest in secondary findings given the very advanced stage of their disease with no further conventional treatment option.	**Valuable research but a clear statement regarding clinical implication is lacking.**

Bijlsma (2018), Netherlands	24, - early stage 29% - advanced stage, * NGS inexperienced[1]: 38% * NGS experienced[1]: 33% [1]= already participating in a tumour and germline NGS study in which patients had been informed about possibility of secondary findings, multiple tumour types 66% highly educated.	Semi-structured interviews, see article for details. In short; - video NGS background information - questions about intentions to receive NGS results and concerns - video 2 clarifying 4 categories of possible results and additional information - questions based on theory of planned behaviour, guidance issues, return of results.	Yes, see article for procedure. In short; eligible patients were informed by an investigator about the aim, procedure, possibility to discover unsolicited findings.	Attitudes toward secondary finding.	- Initially, almost all participants wanted to receive all secondary findings. - After watching the video, including four categories of genetic results, >50% preferred to only receive subsets of information, primarily for own interest but some to prevent a noncancerous disease, for research, or to benefit family members. - The main concern was their own and family members' ability to cope with results. - Request for support and information to help communicate secondary findings to family members. - To be able to make informed decisions, patients expressed several needs and preferences concerning education and counselling during the process of NGS. - Presenting categories of genetic test results was found to be a useful tool in enabling cancer patients to make a well-informed decision about receiving unsolicited findings from NGS. - Provide tailored information related to the return of NGS information. - Healthcare professionals should be supported in the education and counselling of patients when communicating unsolicited results in the context of personalised cancer care and NGS. - Desire of patients to know findings in order to control their lives (preventive measures, screening, foregoing childbearing to avoid a hereditary disease, preparing financially), but some did not want to know about something that would negatively affect their life. - Desire to know information that might help family members but also concerned about the emotional impact of this information on family.	**Valuable research, but relative low sample size.**

					- Concepts and information difficult to understand and remember. - Emotional conflict between desire for knowledge and desire to avoid further stress.	

Blanchette (2014), Canada	98, advanced stage multiple tumour types referred for phase I trial or genomic testing.	Questionnaire	Discussed in article.	Knowledge (objectively tested and self perceived) and attitudes toward secondary findings.	- Median knowledge score 8/12 (67%) true/false items correct; scores significantly associated with education level and income. - 48% reported having sufficient knowledge, and 34% indicated a need for formal genetic counselling to decide regarding testing. - 76% of patients were interested in learning more about testing. - 80% of patients would wish to receive incidental results that would have an impact on their own risk of developing diseases other than cancer. - Patients should receive appropriate counselling and have the option whether or not they wish to receive incidental test results. Consent should occur before testing and should clearly document which specific incidental results will be disclosed and whether or not other family members have the patient's consent to access their genomic test results. - Educational programs are needed to support patients interested in pursuing genomic testing in cancer.	**Valuable research**

Gray (2016), USA	167 advanced stage of lung (53%) or colorectal (47%) cancer, and 27 medical oncologists with Extensive experience ordering tumor NGS.	Surveys and interviews.	Discussed in article.	Knowledge (objectively tested).	Patients: - Participants had moderately low genetic knowledge (mean score 4/7 correct). - Interest in somatic testing correlated with interest in germline testing. - Almost all would wish to earn most cancer-related results including negative prognostic results Overall positive attitudes. Oncologist: - 97% moderately to very confident in their ability to interpret somatic results in their disease area, to explain concepts to patients, and to make treatment recommendations based on somatic information. - 78% wanted to disclose results if they have clinical utility, 67% if no clinical utility. - Some expressed concern about management of patients' expectations and how much of the information should be shared with patients.	**Valuable research, but a statement about de clinical implication is lacking.**

Gray (2012), USA	69, stage not specified, multiple tumour types tested, after survey patients were provided with baseline knowledge about test types (somatic and germline).	Interview and surveys.	Unknown, not mentioned in article.	Knowledge (objective) and attitudes toward secondary findings.	- 74% had never heard of cancer genetic testing of whom 60% thought it was only to determine risk. - 96% expressed willingness to undergo selective somatic testing if predictive and 93% if prognostic. - 71% had concerns, particularly disclosure of unwanted information about poor prognosis and other psychological harms. - Only 62% would consent to whole genome sequencing; those willing hoped to help children avoid illness; those against feared information overload, concern about noncancerous disease.	Valuable research, but a statement about de clinical implication is lacking.

Roberts (2019), USA	297, advanced stage multiple tumour types.	Surveys	Yes, for details see article. In short: - Participants were informed that they would always be told about sequencing results that "have a direct impact on care of your current cancer," but that "the results are not guaranteed to help your doctor take care of you." As part of the consent process, participants chose whether or not they would want to receive secondary sequencing findings unrelated to the treatment of their current cancer.	Knowledge (objective and self-perceived) and attitudes toward secondary findings.	- Average knowledge score of 88%. - 55%–60% indicated that they understood the study purpose, procedures, and risks and benefits. - 40% expected to receive direct benefits from testing including participation in clinical trials. - 84% expected notifications for relevant clinical trials. - 74% expected to learn more about the causes of their cancer. Low levels of concern - Despite explanations from study personnel to the contrary, most participants (67%–76%) presumed that incidental germline sequencing findings relevant to noncancerous health conditions would automatically be disclosed to them.	**Valuable research, but results based on a subpopulation.**

Hamilton (2017), USA	40, advanced stage multiple tumour types, tumour profiling results but not secondary findings disclosed.	Participants were informed about the possibility to discovery incidental germline variants. - interview	Yes, all participants provided this before the interviews.	Attitudes toward secondary findings.	- 57% of the participants expressed interest in learning about secondary germline findings. - Anticipated diverse benefits for themselves or their families (disease prevention or management), other patients, and society. - 53% of the participants did not anticipate any harms. - Concerns were primarily related to emotional distress to family if increased risk of disease disclosed and to other patients with cancer. - A small number were concerned with privacy and insurance issues.	**Valuable research, but low sample size.**

Miller (2014), Canada	29, advanced stage multiple tumour types, and 14 oncologists.	Participants received information about an oncogenic mutation that might be clinically actionable. - semi structured interviews	Yes, for study participation.	Motivations for study participation and attitudes toward secondary findings.	- Patients enrolled themselves in research because they were out of options and valued the hope that experimental approaches might offer. - Patients who received information about tumour mutations were especially hopeful of the experimental therapeutics these test results made relevant, and disappointed when suitable clinical trials were not available. - 93% of the participants felt obligation to receive all the genetic information for benefit of family. - Physicians were optimistic about long-term potential but cautious about immediate benefits and mindful of elevated patient expectations. - Consent and counselling expected to mitigate challenges from incidental findings. - The findings suggest the need for information and decision tools to support physicians in communicating realistic prospects of benefit, and for cautious approaches for the generation of incidental genetic information.	**Valuable research, but low sample size**

Tabel 1.3 Guidelines and statements:

Study, country	**sample size, study population**	**outcomes**	**Main findings regarding providing information about unsolicited findings**
de Wert (2021), *Europe*	n.a., patients diagnosed with cancer undergoing genetic testing.	Recommendations of the European Society of Human Genetics	**Recommendations:** - In view of the many uncertainties, directly impacting the required proportionality of any opportunistic genomic screening (OGS), the ESHG continues to recommend a generally cautious approach. Priority should be given to well known, highly penetrant variants, predisposing for genetic disorders which can be adequately and effectively prevented and/or treated. - Clear procedures and criteria are needed for decision making about the composition and extension of the list of genetic variants included in any OGS, and its implementation. - Informed consent should be a central ethical norm in the framework regarding genetic screening generally and OGS particularly. Patients' preference should be respected as far as possible. Allow professionals to still inform patients about specific findings of great importance. - During counselling for OGS, the provisional nature of current knowledge on penetrance should be addressed as well as potential crossovers with research and options for recontacting in case new scientific evidence of clinical relevance arises.

Vears (2018), *International working group*	n.a., patients diagnosed with cancer undergoing genetic testing.	A working group of 12 experts (Europe, Canada, Australia) was formed in order to develop a set of points to consider for laboratories reporting results from diagnostic NGS.	**Approaches for reporting unsolicited findings:** - Laboratories should not report unsolicited finding where there are no health implications for the patient, or their family. - Unsolicited findings that are relevant to the health of patients should be reported to clinicians, provided that informed consent has been obtained for such reporting from patients prior to sequencing. A patient's choice not to know unsolicited findings should generally be respected. Keep in mind that definitions of terms as 'actionability', 'medical relevance', or 'clinical significance' varies according to the context and individual meaning. - If carrier status is identified in adults, regardless of whether it relates to the clinical question, it should be reported if informed consent is obtained prior to testing. This is because knowing one's carrier status can increase reproductive options. - Reporting unsolicited findings where there is insufficient evidence of pathogenicity (i.e., VUS) should be avoided. **Approaches for reporting secondary findings:** - Laboratories should not actively search for secondary findings. However, if a laboratory chooses to actively search for secondary findings, this should be performed separately from the original analysis and only if prior informed consent for the separate analysis has been obtained from the patient. * information should be provided by adequate genetic counselling. * results of this analysis should be reported separately. **Reanalysis of the data & recontact:** **-** There is no obligation for laboratories to routinely reanalyse data. However, if the laboratory learns that the status of a specific variant has been reclassified from a pathogenic or likely pathogenic to a benign or likely benign variant, or vice versa, it is good clinical practice for laboratories to identify patients with this variant from their database and issue a new report to the referring clinician. Any other requests for reanalysis of sequence data should be initiated by the patient, either via the referring clinician, or another clinician who has taken over their care.

Li (2020), USA	n.a., patients diagnosed with cancer undergoing genetic testing.	A statement of the American College of Medical Genetics and Genomics (ACMG).	- In tumour-normal paired testing, informed consent should be obtained if germline results will be disclosed. - The ordering clinical should understand what genes are included in the genetic test. - The consenting process should include an option to opt out of germline reporting although germline inference may still unexpectedly occur. - The informed consent should outline the potential benefits, harms, and limitations of learning about a germline result. - The informed consent process may be done using traditional models (e.g., in person, or by phone with the ordering provider) or by using innovative methods (e.g., online videos, validated artificial intelligence–based methods such as chatbots). - When automated methods are used for education and counselling, clinicians with experience in cancer genetics should be available to answer specific questions. - Positive germline test results should be returned by qualified and experienced clinicians (e.g., oncologists with genetics expertise, geneticists, and genetic counsellors). - Ideally, the pretesting discussion should also review insurance coverage issues. - Patient choice and autonomy should be respected.
Kalia (2017), USA	n.a., patients undergoing genetic testing.	Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics.	Gene list including genes and associated phenotypes recommended for return of secondary findings in clinical sequencing. See paper for specific list

Mandelker (2019), *International*	n.a., patients undergoing genetic testing.	Germline-focussed analysis of tumour-only sequencing: recommendations from the ESMO Precision Medicine Working Group.	**Recommendations:** - Germline-focussed tumour analysis can be restricted to gene-scenarios for which the germline conversion rate is >10%. For selected genes, it may therefore be appropriate to restrict germline-focussed tumour analysis to just those tumours arising age <30 years. - Formal variant review and classification should be undertaken by an experienced clinical scientist before initiation of patient re-contact and/or germline testing. - Before analysis of their germline sample for the pathogenic variant, adequate information should be provided to the patient regarding the implications of germline testing, along with documentation of their consent. - A patient in whom a germline pathogenic variant is detected should be referred to a specialist genetics service for long term follow-up and management of the family. -

Robson (2015), USA	n.a., patients undergoing genetic testing.	American Society of Clinical Oncology Policy Statement Update: Genetic and Genomic Testing for Cancer Susceptibility	**GERMLINE IMPLICATIONS OF SOMATIC MUTATION PROFILING:** - ASCO supports the communication to patients of medically relevant incidental germline findings from somatic mutation profiling conducted in the clinical setting. - Oncology providers should (1) communicate the potential for incidental and secondary findings, (2) review benefits, harms and risks before testing, (3) ascertain patient preferences regarding information, (4) and allow patients to decline information. Additional counselling could help the patient to clarify the preferences. - Deliver pretest education, support patient preferences, and understand outcomes of providing incidental and secondary germline information with somatic testing. **MULTIGENE PANEL TESTING FOR CANCER SUSCEPTIBILITY:** - ASCO recognizes that concurrent multigene testing (i.e., panel testing) may be efficient in circumstances that require evaluation of multiple high-penetrance genes of established clinical utility as possible explanations for a patient's personal or family history of cancer. **EDUCATION OF ONCOLOGY PROFESSIONALS:** - ASCO recommends continued education of oncologists and other health care professionals in the area of cancer risk assessment and management of individuals with an inherited predisposition to cancer. - Oncology training programs should develop a set of core skills for new trainees and ensure adequate time in training for achieving these skills. - Suggested learning objectives: 1. Understand hereditary predisposition to cancer. 2. Hereditary cancer risk assessment; describe elements of pretest consent, collect/interpretate cancer family history. 3.Genetic testing; understand test incl. interpretation of variants, incidental and secondary findings. 4. Recognition of major hereditary cancer syndromes; discuss benefits and limitations of available management strategies. 5. Management of individuals at increased hereditary cancer risk; review how to use available models for estimating and communicating risk in cancer genetics.

Tabel 1.4 Expert opinion:

Study, country	**sample size, study population**	**Main findings regarding providing information**
Bunnik (2021), Netherlands	n.a., patients diagnosed with cancer undergoing genetic testing.	- Oncologists should be able to explain key information elements in general terms to cancer patients. Upon referral patients can be informed in more detail. - Ideally, patients should be prepared beforehand for the clinical and psychosocial consequences of such unsolicited findings, for themselves and for their family members, and be given the opportunity to autonomously decide whether or not to receive such unsolicited genomic information. - When the chances are so slim, routinely inviting all patients to consider various categories of possible unsolicited findings may be disproportionally stressful and burdensome. - It may be useful to offer patients written information materials or help them find educational websites or decision tools. - Clinicians may need to give patients time to consider and process additional information about genomic sequencing. - Physicians should focus on getting across the first layer of information, i.e., on helping patients prepare for possible outcomes and implications. - Mainstream informed consent practices should focus on preparing patients for three types of unsolicited outcomes, briefly and effectively. - The chance of unsolicited findings is very low, opt-out options need not be actively offered. - (Inter) national guidelines for mainstreaming informed consent for genomic sequencing must be developed.
Dungey (2021), UK *comment on Bunnik (2021)	n.a., patients diagnosed with cancer undergoing genetic testing.	- It is vitally important that mainstream clinicians are given appropriate training on consenting for genetic tests (and documentation of discussions), with an emphasis on how to do this in a time efficient way. - Standardized consent forms are often time-consuming. - Extra time allocated to the clinical appointment, advanced nurse practitioner support or an embedded genetic counsellor are options to optimize the process.

Vos (2018), Netherlands	n.a., patients diagnosed with cancer undergoing genetic testing.	- Patients should be able to give explicit consent about whether they would like to be informed about clinically significant unsolicited findings. - Information should be provided based on the number of genes involved. - Unsolicited findings could only be reported if the patient has given consent. - It is important to classify unsolicited findings based on their clinically relevance. - The decision on what to report to the patient has been traditionally given to the clinician. However, it becomes difficult for clinicals which information is important and appropriate to report to patients. Therefore, a more active role for pathology in providing patients the required information has been proposed. - Pathologists should actively engage and promote discussions with other medical specialists and with patients on the handling of unsolicited findings and uncertain findings in genes of interest. - Patients should be aware of DNA analysis, with its associated benefits and risk, and that clinically significant findings are returned.
Hicks (2021),	n.a., patients diagnosed with cancer undergoing genetic testing.	**Education of providers and patients:** - Clinicians have identified a lack of knowledge on how to interpret genetic test results and modify treatment plans as impeding clinical applications. They should be train in special training programs. - Patients could be educated with printable materials, videos and other interactive media, patient preferences for content and delivery should be taken into account. - Education contents differ across age ranges. Cultural difference should also be taken into account. - Collaboration with patients and patient advocacy groups can help identify education needs and effective delivery methods.
Borad (2017), USA	n.a., patients diagnosed with cancer undergoing genetic testing.	- To ensure success, greater attention to ethical, legal, and social implications of genetic tumour testing have to be considered. - It should be clear how to deal with disclosure of incidental findings that may affect individuals other than the patients. - It is important to closely integrate disclosure of incidental findings with data and privacy sharing concerns. This have to be discussed with the patient.

Ayuso (2013), Spain *IC	n.a., patients undergoing genetic testing.	- Pre-test counselling is strongly recommended before WGS. - General information common to all genetic tests should be included in the informed consent form for WGS for diagnostic purposes. - Additional information addressing specific issues on WGS are proposed, such as a plan for the ethical, clinically oriented return of incidental findings. - Storage of additional information for future use should also be agreed upon with the patient in advance.
Henderson (2014), USA *IC	n.a., patients undergoing genetic testing.	Final list of concepts for informed consent for genetic testing: - Genetic testing is always voluntary (optional) - Why are we doing this test and what does it test for? (generally) - What results will be returned (generally)? - What other types of results will potentially be returned, and options for choice (such as secondary findings)? - How, if at all, will your prognosis and management (including health screening) be impacted by the results? - The results may also impact your family in different ways (their health, emotions, or relationships), and you may want to share the results. - What are the limitations of the test, and if there is no answer what happens next? - To whom the results will be reported? - There is a potential risk for genetic discrimination and/or stigma/GINA and relevant state laws provide some protection.

Christensen (2019), *International* *http://www.uptofate.icu/contents/table-of-contents/primary-care-adult/genetics-and-basic-science/secondary-findings-from-genetic-testing.html#H70236	n.a., patients undergoing genetic testing.	- Actionable findings have been found approximately 1 to 5 percent of de individuals undergoing genomic testing. - Patients undergoing genomic testing should be informed about secondary findings (i.e., genetic variants would be disclosed, how it would be communicated, procedure before testing, discuss 'opt out', discuss what to do with secondary findings after patient's death). - Clinical should review patient preferences (communicated at time of consent for genomic testing), weigh potential harms and benefits of reporting secondary findings, understand clinical implications of findings for the patient, and re-evaluate the patients' personal medical history. - The decision about whether and when to disclose secondary findings will depend on the clinical context and the judgment of clinicians involved in the patient's care. - Disclosure of secondary findings from genomic testing involves informing the patient that the findings are present, counselling regarding the clinical implications of the result, and discussing whether any additional intervention is needed.

Bijlsma, 2016	N= 376, patients undergoing genetic testing	- Inform patient before procedure about the procedure itself, and the possibility of discovering unsolicited findings. - Patient should have (reasonable) time to sign the informed consent. - Unsolicited findings were present in 3/376 (0.8%) - How should the informed consent be obtained? **the option to refuse genetic results should be made at time the informed consent is signed, or **patient should be able to reconsider their choice (dynamic consent). - How should information be provided? 1. give patients a set of choices 2. inform about actionable findings that is relevant for the patient 3. optional information (e.g., personalized) should be given according to patient preferences. - How to return information? Health-care professionals should inform patients about the potential risk for their family members. - When should patients be informed about unsolicited findings? Depending on preferences mentioned during pre-test if this was performed; providing information could also be a burden for the patients, most cases will have no unsolicited findings. - When should patients have the option to opt out? Patients have the right to refuse the return of results. - How should family members be involved? Patients should be counselled on the familial importance and postmortem disclosure to relatives.

Rigter, 2013	n.a., patients diagnosed with cancer undergoing genetic testing.	**Points to consider for next-generation sequencing and informed consent in diagnostics** **"***(1) Who is giving consent: the patient or his/her legal representative? (i.e., how strong is the "right not to know")* *(2) What is the initial clinical enquiry?* *(3) Which unsolicited findings can be expected?* *(4) How can the different possible unsolicited findings be categorized? (Supp. Table S1)* *(5) What should be communicated to the patient?* *(a) Which pretest information? (Fig. 1: cycle of communication1)* *(b) Which results? (Fig. 1: cycle of communication 2)* *(6) What does this mean for the consent procedure?* *(a) General/detailed?* *(b) Oral/written consent?* *(c) Advisory Board involved?* *(d) Opt in or opt out of unsolicited findings?''* - Patients' right to informed consent requires a balance between information overload and uniformed consent. - Patients have the right not to be informed about unsolicited findings. - Each context leads to a different focus for discussion during the procedure for informed consent. - If testing is performed within research, it should be clear what information will be provided to the patient. - Counselling of the clinical geneticist should include information from the laboratory about the amount and type of expected unsolicited findings. This has implications for the specialists regarding communication, training, and education. - Different types of variants have to be categorized according to the nature of condition, differentiating between early and late-onset, the level of risk/predictivity, burden of the disease/severity, and options for treatment or prevention. ** see figure 1 for ideal procedure*

Lolkema, 2013	n.a., patients diagnosed with cancer undergoing genetic testing.	**Emerging ethical duty to return genetic results:** 1. Respect for the autonomy of the study participant and patients a like warrant disclosure of genetic results. Important to inform patients' family about whether they are exposed to a hereditary risk of cancer. 2. Provide the results that are clinically and analytically valid, useful, and actionable. Important that meaningful options are available, such as prevention, avoidance of deterioration, treatment, and potential to adjust life plans or strategies for coping. 3. Offer the possibility of feedback of genetic results that may engage and education research participants. Important that feedback provides an acknowledgement that translational genomics research can only progress with active contributions form research participants and the patient community. **What should be returned?** - Difficult to foresee all consequences of the study participants in the informed consent, because informing the patient about all potential outcomes is impossible. - Work with a predefined menu of options (clear; default is to return, however opt-out is offered, possible; opt-in, unlikely; opt-in, unknown; -). - Respect the autonomy of the patients/participant and acknowledge that it is needed to limit the number of choices that they need to make. - Post-mortem disclosure should at least be foreseen and agreed during inclusion to a research participant's relatives. **Privacy and data sharing:** - Transferring data may potentially harm the privacy of the patient. - Data can often be traced back to the patient. - Protection of privacy is key to keeping the public trust and it needs to be considered when designing strategies for returning genetic results. **Returning results:** - The physician is obligated to warn the patient if a certain condition is heritable and may affect relatives. - *Figure 1* illustrates a patient-oriented flow chart on tiered consent for return of genetic results in oncology. - It is important to involve all relevant stakeholders (i.e., patients, patient advocates, medical oncologists, ethicists, clinical and molecular geneticists, policy makers, and insurance companies) in forming the framework for 'return results' to patients.

Tabel 1.5 Nederlandse leidraden/richtlijnen:

Rapport	Samenvatting

Consensus-based leidraad (Stemkens, 2020)	**Classificatie genetische varianten** *Klasse 1: Variant die ZEKER GEEN verhoogd risico op ziekte geeft.* *Klasse 2: Variant die WAARSCHIJNLIJK GEEN verhoogd risico op ziekte geeft.* *Klasse 3: Variant waarvan NIET BEKEND is of deze een zeikte veroorzaakt.* *Klasse 4: Variant die WAARSCHIJNLIJK een verhoogd risico op ziekte geeft.* *Klasse 5: Variant die ZEKER een verhoogd risico op ziekte geeft.* **Nevenbevindingen** *Additionele bevindingen die los staan van de hulpvraag of klachten waarmee de patiënt bij de dokter kwam en op grond waarvan de dokter tot diagnostisch onderzoek besloot***.** **Risicopatiënt;** - gezondheidsrisico kunnen zijn voor de patiënt en/of zijn bloedverwanten, - gezondheidsrisico kunnen zijn voor het nageslacht van de patiënt of zijn bloedverwanten. **Type aandoening;** - beïnvloedbaar door medisch ingrijpen, - niet beïnvloedbaar door medische ingrijpen. **Verantwoordelijkheden:** De aanvragen van de test is verantwoordelijk voor het counselingsgesprek met de patiënt, vraagt de test aan en rapporteert eventuele nevenbevinden aan de patiënt. **Beleidsregels:** 1. Nevenbevindingen worden in principe in hetzelfde tijdsbestek als de uitslag van de exoom- of genoom sequecing aan de patiënt teruggekoppeld. 2. Nevenbevindingen betreffende een ziektebeeld dat door medisch ingrijpen beïnvloedbaar is, worden ALTIJD teruggekoppeld, tezijn er sprake is van opt-out. 3. Nevenbevindingen betreffende een aandoening welke NIET door medisch ingrijpen beïnvloedbaar is, worden NIET teruggekoppeld, tenzij er sprake is van opt-in. 4. Nevenbevindingen betreffende dragerschap van een genetische aandoening worden NIET gerapporteerd, tenzij uit de verrichte test blijkt dat de patiënt of bloedverwanten een kans van tenminste 25% heeft/hebben op het krijgen van een kind met de genetische aandoening.***

Handreiking counseling	**Aandachtspunten:** - Gesprek afstemmen op individuele patiënt. - Zorg dat de informatie wordt uitgewisseld door 'in gesprek te gaan'. Stel open vragen en toets of de patiënt de informatie begrijpt. - Geef schriftelijke informatie aan de patiënt. - Vraag informed consent en noteer de uitkomst in o.a. het EPD. Vermeld eventueel welke informatie is verstrekt, welke afspraken er gemaakt zijn omtrent nevenbevindingen, welke afspraken gemaakt zijn omtrent her-contact. - Geef voldoende bedenktijd aan de patiënt. **Welke informatie bespreken:** - Informatie over testmethoden/genpakketten. - Beschrijving van de procedure. - Doel van de test inclusief voordelen en nadelen. - Mogelijke resultaten (m.n. klasse 4 of 5). - Mogelijke nevenbevindingen, inclusief terugkoppeling. - Mogelijke financiële consequenties. - Opslag resterend materiaal. - Deelname aan wetenschappelijk onderzoek. - Her-contact. - Informeren familieleden. * een gedetailleerde checklist is weergegeven in het document. **Categorieën nevenbevindingen:** 1. Nevenbevindingen betreffende een aandoening welke door medisch ingrijpen beïnvloedbaar is, worden ALTIJD teruggekoppeld tenzij opt-out. 2. Nevenbevindingen betreffende een aandoening welke op dit moment/met de huidige kennis, behandelingen, of technologie NIET door medisch ingrijpen beïnvloedbaar is, worden NIET teruggekoppeld tenzij opt-in. 3. Nevenbevindingen betreffende dragerschap van een AR of X-linked aandoening worden NIET gerapporteerd, tenzij uit de verrichte test blijkt dat de patiënt en/of bloedverwanten een kans van tenminste 25% hebben op het krijgen van een kind met de genetische aandoening.

Informatieblad voor patiënten	**Informatie:** 1. Welk onderzoek. 2. Wat kan de uitslag zijn. 3. Nevenbevindingen. 4. Welke soorten nevenbevindingen zijn er en worden besproken met u. 5. Gevolgen familie. 6. Terugkoppeling uitslag. 7. Financiële gevolgen. 8. Her-contact.
Doneer je ervaring (NFK)	Doel; meer inzicht krijgen in de informatiebehoefte en -voorziening van mensen met een *verhoogde risico op kanker* en of zij zich gesteund voelden door het ziekenhuis en de huisarts. - 2 op 3 patiënten heeft behoefte aan informatie (o.a., algemeen, medische controles, gevolgen familie) gedurende het erfelijkheidsonderzoek. - 3 op 4 patiënten geeft aan deze informatie te hebben gekregen gedurende het erfelijkheidsonderzoek. - 1 op 3 patiënten geeft aan graag één vast aanspreekpunt te hebben over gen mutatie op alle gebieden.
Adviezen projectgroep tumor- en erfelijkheidsdiagnostiek (Ligtenberg, 2021)	Klinisch genetische zorg valt onder de Wet Bijzondere Medische Verrichtingen (WBMV). **Organisatie van zorg** - Kwaliteit van tumoranalyses kan het best worden geborgd in centra met klinische genetische laboratoria waarin wordt samengewerkt met o.a. LSKG en KMBP. - Genetische counseling en informed consent op basis van kans op onderliggende erfelijke problematiek - Indeling op basis van 4 categorieën, zie Tabel 1 van adviesrapport.
Counseling bij chromosoomveranderingen CNV (VKGN, richtlijnendatabase)	

Tabel 1.6 Quality of research

Major Components – Pujol, 2019	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	Not a specific aim; Propose a process for patients undergoing somatic tumor analysis that included delivery of appropriate information, collection of informed consent, and a scheme for interactions among oncologist, molecular biologist/pathologist, and geneticist in a multidisciplinary approach.
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	The authors refer to another article.
Is it worth continuing?				No
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	
9. Is there a clear statement of findings?	Yes	No	Can't Tell	
Section C: Will the results help locally?				

10. How valuable is the research?	Yes	No	Can't Tell	The aim is not clear, and specific information, or even a brief description, of the method part is missing.

Major Components – Bijlsma, 2020	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	Describe preferences of a large cohort of patients with cancer on how they want to receive genetic information by WGS/WES and their wish for haring this information with their family.
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	See figure 2
Is it worth continuing?				Yes
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	Survey
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	See data analysis
9. Is there a clear statement of findings?	Yes	No	Can't Tell	Provided in tables.
Section C: Will the results help locally?				

10. How valuable is the research?	Yes	No	Can't Tell	Valuable research

Major Components - Horiuchi, 2021	Response options			
Section A: Are the results of the study valid?				
1. Did the study address a clearly focused issue?	Yes	No	Can't Tell	The aim of this study was to examine the incidence of SFs in Japanese cancer patients using whole exome sequencing (WES) and to understand patient preferences regarding SF disclosure
2. Was the cohort recruited in an acceptable way?	Yes	No	Can't Tell	Patients registered in Project HOPE
Is it worth continuing?				Yes
3. Was the exposure accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned
4. Was the outcome accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned
5. (a) Have the authors identified all important confounding factors?	Yes	No	Can't Tell	Not mentioned
5. (b) Have they taken account of the confounding factors in the design and/or analysis?	Yes	No	Can't Tell	Not mentioned
6. (a) Was the follow up of subjects complete enough?	Yes	No	Can't Tell	
6. (b) Was the follow up of subjects long enough?	Yes	No	Can't Tell	
Section B: What are the results?				
7. What are the results of this study?	Majority of the participants (68.9%; 1709/2480) opted for disclosure of their SFs.			
8. How precise are the results?	Bias is present			
9. Do you believe the results?	Yes	No	Can't Tell	
Section C: Will the results help locally?				

10. Can the results be applied to the local population?	Yes	No	Can't Tell	Relatively large study.
11. Do the results of this study fit with other available evidence?	Yes	No	Can't Tell	
12. What are the implications of this study for practice?	Yes	No	Can't Tell	more effective genetic counseling practices regarding SF disclosure should be developed by collecting further data

Major Components – Hamilton, 2017	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	examined patients' perspectives with regard to factors influential to their hypothetical decision about learning SGFs and preferences about their role in this decision-making process.
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	Yes clearly described in the method part
Is it worth continuing?				Yes
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	Interviews.
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	Not mentioned.
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved.
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	ATLAS.ti
9. Is there a clear statement of findings?	Yes	No	Can't Tell	recommendations

Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research

Major Components - Pinheiro, 2017	Response options			
Section A: Are the results of the study valid?				
1. Did the study address a clearly focused issue?	Yes	No	Can't Tell	identify physician and patient preferences regarding information and who should communicate this information and how to inform guidelines for these conversations
2. Was the cohort recruited in an acceptable way?	Yes	No	Can't Tell	Only physicians but not patients.
Is it worth continuing?				Yes
3. Was the exposure accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned
4. Was the outcome accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned
5. (a) Have the authors identified all important confounding factors?	Yes	No	Can't Tell	Not mentioned
5. (b) Have they taken account of the confounding factors in the design and/or analysis?	Yes	No	Can't Tell	Not mentioned
6. (a) Was the follow up of subjects complete enough?	Yes	No	Can't Tell	
6. (b) Was the follow up of subjects long enough?	Yes	No	Can't Tell	
Section B: What are the results?				
7. What are the results of this study?	The 2 most frequently chosen topics of information for both patients and physicians were the benefits of the test and how the test determines treatment.			

8. How precise are the results?	Bias is present			
9. Do you believe the results?	Yes	No	Can't Tell	
Section C: Will the results help locally?				
10. Can the results be applied to the local population?	Yes	No	Can't Tell	Small sample size.
11. Do the results of this study fit with other available evidence?	Yes	No	Can't Tell	Valuable research
12. What are the implications of this study for practice?	Yes	No	Can't Tell	The topics identified as important to discuss can inform future guidelines and can contribute to effective communication regarding molecular testing.

Major Components - Stjepanovic, 2018	Response options			
Section A: Are the results of the study valid?				
1. Did the study address a clearly focused issue?	Yes	No	Can't Tell	patient preferences in the return of additional gMAVs in cancer predisposition genes detected through tumor profiling, the types of variants detected and considerations in the interpretation and disclosure of the findings.
2. Was the cohort recruited in an acceptable way?	Yes	No	Can't Tell	advanced cancer patients who were candidates for clinical trials with targeted therapies and enrolled in the tumor profiling programs IMPACT or COMPACT
Is it worth continuing?				Yes
3. Was the exposure accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned
4. Was the outcome accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned
5. (a) Have the authors identified all important confounding factors?	Yes	No	Can't Tell	Not mentioned

5. (b) Have they taken account of the confounding factors in the design and/or analysis?	Yes	No	Can't Tell	Not mentioned
6. (a) Was the follow up of subjects complete enough?	Yes	No	Can't Tell	
6. (b) Was the follow up of subjects long enough?	Yes	No	Can't Tell	
Section B: What are the results?				
7. What are the results of this study?	Of the whole cohort 94% of patients consented to be informed of additional germline results and 5% declined, with no statistically significant differences based on age, sex, race or prior genetic testing. Eight patients were found to have gMAVs in a cancer predisposition gene.			
8. How precise are the results?	Bias is present			
9. Do you believe the results?	Yes	No	Can't Tell	
Section C: Will the results help locally?				
10. Can the results be applied to the local population?	Yes	No	Can't Tell	Heterogeneous population
11. Do the results of this study fit with other available evidence?	Yes	No	Can't Tell	
12. What are the implications of this study for practice?	Yes	No	Can't Tell	Disclosure of previously unidentified gMAVs present multiple challenges, thus supporting the involvement of a clinical genetics service in all tumor profiling programs.

Major Components - Catenacci, 2015	Response options	
Section A: Are the results of the study valid?		

1. Did the study address a clearly focused issue?	Yes	No	Can't Tell	to identify those patients who might need follow-up for unsuspected underlying germline events, and to determine whether we could confirm the "high risk" cases post-NGS as germline carriers
2. Was the cohort recruited in an acceptable way?	Yes	No	Can't Tell	Consent was obtained from new patients with gastrointestinal cancers seen in the University of Chicago Gastrointestinal Oncology Clinic between September 2012 and September 2013.
Is it worth continuing?				Yes
3. Was the exposure accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned.
4. Was the outcome accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned.
5. (a) Have the authors identified all important confounding factors?	Yes	No	Can't Tell	Not mentioned.
5. (b) Have they taken account of the confounding factors in the design and/or analysis?	Yes	No	Can't Tell	Not mentioned.
6. (a) Was the follow up of subjects complete enough?	Yes	No	Can't Tell	*data retrospectively collected.
6. (b) Was the follow up of subjects long enough?	Yes	No	Can't Tell	*data retrospectively collected.
Section B: What are the results?				
7. What are the results of this study?	High-risk patients (determined from NGS results) were contacted and counseled in person by a genetic counselor (N521). When possible and indicated, germline genetic testing was offered. Of 8 evaluable high-risk patients, 7 underwent germline testing. Three (37.5%) had confirmed actionable germline mutations (all in the BRCA2 gene).			
8. How precise are the results?	Bias is present			
9. Do you believe the results?	Yes	No	Can't Tell	
Section C: Will the results help locally?				

10. Can the results be applied to the local population?	Yes	No	Can't Tell	Only patients with metastatic gastroesophageal, hepatobiliary or colorectal cancer
11. Do the results of this study fit with other available evidence?	Yes	No	Can't Tell	
12. What are the implications of this study for practice?	Yes	No	Can't Tell	the need for oncologists to develop a framework for pre- and post-test communication of risks to patients undergoing routine tumor-only sequencing

Major Components – Bennette, 2013	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	identify the attributes and levels of incidental genomic findings in the context of genetic testing for colon cancer susceptibility that are most important to, and cognitively understood by, patients, and to develop a DCE instrument that will enable the quantification of patients' personal utility for incidental findings from next-generation genomic sequencing technologies.
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	
Is it worth continuing?				Yes
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	Focus groups and interviews

4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	Patients who underwent a clinical workup for familial colorectal cancer/polyposis syndromes at the University of Washington Genetic Medicine Clinic within the past 24 months.
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	Not mentioned.
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved.
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	Not mentioned, no analysis performed?
9. Is there a clear statement of findings?	Yes	No	Can't Tell	Results are described and a conclusion is stated but no clear statements.
Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research, but analysis is lacking even as a clear statement.

Major Components – Solomon, 2020	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	To determine whether patients who use HOPE-Genomics have better knowledge of their disease, more effectively communicate with providers, and more compliant with genomically guided therapy.

2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	
Is it worth continuing?				Yes
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	Focus groups, but only 3.
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	Adult patients with solid tumors at City of Hope (COH) were eligible to participate
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	See figure 1
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	
9. Is there a clear statement of findings?	Yes	No	Can't Tell	
Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research

Major Components – Korngiebel, 2019	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	Not a specific aim, more what is performed
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	
Is it worth continuing?				Yes
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	Interviews

4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	Participants from different institutions
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	Not mentioned
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	ATLAS.ti
9. Is there a clear statement of findings?	Yes	No	Can't Tell	Results are described and a conclusion is stated but no clear statements.
Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research, only a clear overview with statements is lacking.

Major Components – van der Schoot, 2021	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	Characterize the perceptions of the impact of UFs in clinical exome sequencing.
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	
Is it worth continuing?				
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	interviews
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	participants to whom an UF had been disclosed, predisposing to either oncological or cardiac disease.

5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	Not mentioned in article.
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved.
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	ATLAS.ti
9. Is there a clear statement of findings?	Yes	No	Can't Tell	Described in text and summarized in the conclusion.
Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research, although only n=10 is applicable for the current research aim.

Tabel 1.7 Review Shirdarreh 2021

Major Components - Yusuf, 2015	Response options			
Section A: Are the results of the study valid?				
1. Did the study address a clearly focused issue?	Yes	No	Can't Tell	assess breast cancer patients' attitudes toward molecular testing for personalized therapy and research as well as the return of incidental research results
2. Was the cohort recruited in an acceptable way?	Yes	No	Can't Tell	Patients registering at the breast center between October and December 2012 were invited to participate in a questionnaire study.
Is it worth continuing?				Yes
3. Was the exposure accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned.
4. Was the outcome accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned.
5. (a) Have the authors identified all important confounding factors?	Yes	No	Can't Tell	Not mentioned.
5. (b) Have they taken account of the confounding factors in the design and/or analysis?	Yes	No	Can't Tell	Not mentioned.
6. (a) Was the follow up of subjects complete enough?	Yes	No	Can't Tell	
6. (b) Was the follow up of subjects long enough?	Yes	No	Can't Tell	
Section B: What are the results?				
7. What are the results of this study?	Most participants were willing to undergo molecular testing to assist in the selection of approved drugs (81%) and experimental therapy (59%) if testing was covered by insurance. Most participants wanted to be informed when research results had implications for treatment (91%), new cancer risk (90%), and other preventable/treatable diseases (87%).			
8. How precise are the results?	Bias is present			

9. Do you believe the results?	Yes	No	Can't Tell	Response rate of 32% is somewhat low.
Section C: Will the results help locally?				
10. Can the results be applied to the local population?	Yes	No	Can't Tell	Response rate o 32%, bias not taken into account.
11. Do the results of this study fit with other available evidence?	Yes	No	Can't Tell	
12. What are the implications of this study for practice?	Yes	No	Can't Tell	Novel approaches are needed to prevent disparities in the delivery of genomically informed care and to increase minority participation in biomarker-driven trials.

Major Components - Yushak, 2016	Response options			
Section A: Are the results of the study valid?				
1. Did the study address a clearly focused issue?	Yes	No	Can't Tell	assess disclosure preferences among cancer patients about incidental genomic variants that may be discovered during tumor profiling.
2. Was the cohort recruited in an acceptable way?	Yes	No	Can't Tell	Administered a 45-item questionnaire to 413 patients in ambulatory oncology clinics
Is it worth continuing?				Yes
3. Was the exposure accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned.
4. Was the outcome accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned.
5. (a) Have the authors identified all important confounding factors?	Yes	No	Can't Tell	Not mentioned.
5. (b) Have they taken account of the confounding factors in the design and/or analysis?	Yes	No	Can't Tell	Not mentioned.
6. (a) Was the follow up of subjects complete enough?	Yes	No	Can't Tell	

6. (b) Was the follow up of subjects long enough?	Yes	No	Can't Tell	
Section B: What are the results?				
7. What are the results of this study?	77% wanted to be informed about variants that could increase risk of a serious but preventable illness, 56% wanted to know about variants that cause a serious but unpreventable illness, and 49% wanted to know about variants of uncertain significance. Most patients (75%) would share hereditary information about predisposition to preventable diseases with family and 62% about unpreventable diseases. The most frequent concerns about incidental findings were ability to obtain health (48%) or life (41%) insurance. Only 21% of patients were concerned about privacy of information.			
8. How precise are the results?	Bias is present			
9. Do you believe the results?	Yes	No	Can't Tell	
Section C: Will the results help locally?				
10. Can the results be applied to the local population?	Yes	No	Can't Tell	Bias not taken into account.
11. Do the results of this study fit with other available evidence?	Yes	No	Can't Tell	
12. What are the implications of this study for practice?	Yes	No	Can't Tell	Personal preferences for disclosure of different types of incidental findings be clarified before ordering a tumor profiling test.

Major Components – Best, 2019	Response options	Comment
Section A: Are the results valid?		

1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	elicit the attitudes and expectations of participants with advanced cancer towards MTP and return of results prior to undergoing testing, to determine what support and information may need to be provided for patients in the clinical setting, specifically at the time of consent.
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	
Is it worth continuing?				Yes
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	Interviews
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	Not mentioned in the text.
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	
9. Is there a clear statement of findings?	Yes	No	Can't Tell	Results are described and a conclusion is stated but no clear statements.
Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research but a clear statement is lacking.

Major Components – Bijlsma, 2018	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	explore their decisions about whether or not to receive unsolicited findings from NGS and their corresponding concerns.
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	
Is it worth continuing?				Yes
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	Interviews.
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	Not mentioned
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	
9. Is there a clear statement of findings?	Yes	No	Can't Tell	Short statement per theme.
Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research

Major Components – Bijlsma, 2018b	Response options	Comment
Section A: Are the results valid?		

1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	examine the preferences of cancer populations
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	
Is it worth continuing?				Yes
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	Interviews
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	24 Dutch patients with different types of cancer, both NGS-experienced and NGS-inexperienced
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	Figure 1
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	Not mentioned.
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	
9. Is there a clear statement of findings?	Yes	No	Can't Tell	Yes, clinical implications.
Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research

Major Components - Blanchette, 2015	Response options			
Section A: Are the results of the study valid?				
1. Did the study address a clearly focused issue?	Yes	No	Can't Tell	to describe patients' knowledge, attitudes, and expectations toward GTC.

2. Was the cohort recruited in an acceptable way?	Yes	No	Can't Tell	Patients with advanced solid tumors who were referred either for GTC testing or for phase 1 clinical trial participation at the Princess Margaret Cancer Center (Toronto, Ontario) were eligible.
Is it worth continuing?				Yes.
3. Was the exposure accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned.
4. Was the outcome accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned.
5. (a) Have the authors identified all important confounding factors?	Yes	No	Can't Tell	Not mentioned.
5. (b) Have they taken account of the confounding factors in the design and/or analysis?	Yes	No	Can't Tell	Not mentioned.
6. (a) Was the follow up of subjects complete enough?	Yes	No	Can't Tell	
6. (b) Was the follow up of subjects long enough?	Yes	No	Can't Tell	
Section B: What are the results?				

7. What are the results of this study?	Results were reported from 98 patients with advanced cancer, representing 66% of the patients surveyed. Seventy-six percent of patients were interested in learning more about GTC, and 64% reported that GTC would significantly improve their cancer care. The median score on a 12-item questionnaire to assess knowledge of cancer genomics was 8 of 12 items correct (67%; interquartile range, 7-9 of 12 items correct [58%-75%]). Scores were associated significantly with patients' education level (P<.0001). Sixty-six percent of patients would consent to a needle biopsy, and 39% would consent to an invasive surgical biopsy if required for GTC. Only 48% of patients reported having sufficient knowledge to make an informed decision to pursue GTC whereas 34% of patients indicated a need for formal genetic counseling.			
8. How precise are the results?	Bias is present			
9. Do you believe the results?	Yes	No	Can't Tell	
Section C: Will the results help locally?				
10. Can the results be applied to the local population?	Yes	No	Can't Tell	Relatively high response rate of questionnaires.
11. Do the results of this study fit with other available evidence?	Yes	No	Can't Tell	
12. What are the implications of this study for practice?	Yes	No	Can't Tell	The need for better education and counseling services to support patients who undergo GTC is apparent from our results. A wide variety of educational resources should be explored, including web-based technologies, videos, and written educational materials. Formal genetic counseling may also be required in some patients.

Major Components – Gray, 2016	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	explore how introducing WES into care might affect cancer patients and oncologists

2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	
Is it worth continuing?				Yes
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	Interviews + questionnaire
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	population for the CanSeq
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	clinical research assistants approached patients.
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	In tables and figures
9. Is there a clear statement of findings?	Yes	No	Can't Tell	Only a summary of findings, no clinical implications and/or statement
Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research but clinical implications are lacking.

Major Components – Gray (2012)	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	to understand patient attitudes about a spectrum of genomic technologies
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	
Is it worth continuing?				

3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	Interviews
4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	patients with colorectal, breast, and lung cancers, stratified
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	NVivo 8
9. Is there a clear statement of findings?	Yes	No	Can't Tell	Only summary of findings.
Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research but clinical implications/statements are lacking.

Major Components - Roberts, 2019	Response options			
Section A: Are the results of the study valid?				
1. Did the study address a clearly focused issue?	Yes	No	Can't Tell	assessed cancer patients' understanding, expectations, and outcomes regarding participation in research examining the impact of matched tumor and germline sequencing on their clinical care.
2. Was the cohort recruited in an acceptable way?	Yes	No	Can't Tell	A total of 297 patients (mean age: 59 years; 50% female; 96% white) with refractory, metastatic cancer were surveyed.
Is it worth continuing?				Yes.

3. Was the exposure accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned.
4. Was the outcome accurately measured to minimise bias?	Yes	No	Can't Tell	Not mentioned.
5. (a) Have the authors identified all important confounding factors?	Yes	No	Can't Tell	Not mentioned.
5. (b) Have they taken account of the confounding factors in the design and/or analysis?	Yes	No	Can't Tell	Not mentioned.
6. (a) Was the follow up of subjects complete enough?	Yes	No	Can't Tell	
6. (b) Was the follow up of subjects long enough?	Yes	No	Can't Tell	
Section B: What are the results?				
7. What are the results of this study?	At baseline, the vast majority of patients expected to receive several potential direct benefits from study participation, including written reports of sequencing findings (88%), greater understanding of the causes of their cancer (74%), and participation in clinical trials for which sequencing results would make them eligible (84%). In most cases, these benefits were not realized by study completion. Despite explanations from study personnel to the contrary, most participants (67%-76%) presumed that incidental germline sequencing findings relevant to noncancerous health conditions (eg, diabetes) would automatically be disclosed to them. Patients reported low levels of concern about study risks at baseline and low levels of regret aboutstudy participation at follow-up.			
8. How precise are the results?	Bias is present			
9. Do you believe the results?	Yes	No	Can't Tell	

Section C: Will the results help locally?				
10. Can the results be applied to the local population?	Yes	No	Can't Tell	No results are based on a subpopulation of a larger cohort.
11. Do the results of this study fit with other available evidence?	Yes	No	Can't Tell	
12. What are the implications of this study for practice?	Yes	No	Can't Tell	the need for careful communication with cancer patients considering the use of genome sequencing to inform their treatment plans. Clarifying the likelihood of clinical benefit from sequencing and the "what, when and how" of reporting sequencing results are essential to managing patient expectations and ensuring truly informed consent. As genome sequencing is increasingly incorporated in precision oncology, we must pay sufficient attention to the critical role that health communications can have in the patient experience.

Major Components – Hamilton 2017b	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	perceptions of the benefits and harms of learning SGFs aswell as of how these attitudes shaped their personal interest in receiving this risk information
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	
Is it worth continuing?				
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	interviews

4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	patients with late-stage solid tumors could undergo TGP with the MSK-IMPACT
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	Not mentioned.
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved.
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	ATLAS.ti
9. Is there a clear statement of findings?	Yes	No	Can't Tell	On first page
Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research.

Major Components – Miller, 2014	Response options			Comment
Section A: Are the results valid?				
1. Was there a clearstatement of the aims of the research?	Yes	No	Can't Tell	To explore the experiential context in which much of personalized cancer care will be developed and evaluated
2. Is a qualitative methodology appropriate?	Yes	No	Can't Tell	
Is it worth continuing?				
3. Was the research design appropriate to address the aims of the research?	Yes	No	Can't Tell	interviews

4. Was the recruitment strategy appropriate to the aims of the research?	Yes	No	Can't Tell	adult patients with advanced solid malignancies enrolled in the tumor biopsy study
5. Was the data collected in a way that addressed the research issue?	Yes	No	Can't Tell	
6. Has the relationship between researcher and participants been adequately considered?	Yes	No	Can't Tell	
Section B: What are the results?				
7. Have ethical issues been taken into consideration?	Yes	No	Can't Tell	Study approved
8. Was the data analysis sufficiently rigorous?	Yes	No	Can't Tell	
9. Is there a clear statement of findings?	Yes	No	Can't Tell	
Section C: Will the results help locally?				
10. How valuable is the research?	Yes	No	Can't Tell	Valuable research