Disclosure of incidental findings in cancer genomic research: investigators’ perceptions on obligations and barriers

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Although there has been significant research surrounding incidental findings (IFs), the guidelines and information provided to investigators remain unspecific, unclear, and often generalize the course of action to everyone in the field. We explored the perceptions and experiences of investigators regarding the return of IFs in genetic research. Researchers and clinician-researchers were invited to participate in semi-structured telephone interviews in Quebec and Ontario. Twenty professionals participated, and thematic analysis was used to analyze the transcriptions. Four contextual elements emerged: (i) degree of significance of results, (ii) respect for persons, (iii) infrastructure implications, and (iv) professional responsibilities. Our findings demonstrate that all investigators raised similar contextual elements surrounding the return of IFs. However, some nuances in participants’ experiences of the understanding of professional responsibilities also emerged. Because of the existing nuances, a one-size-fits-all approach is inappropriate, suggesting that context ought to be considered in decisions about IFs.

Conflict of interest

The authors declare that they have no conflicts of interest.

E. Kleiderman\textsuperscript{a}, D. Avard\textsuperscript{b}, A. Besso\textsuperscript{a}, S. Ali-Khan\textsuperscript{a}, G. Sauvageau\textsuperscript{b,c,d} and J. Hébert\textsuperscript{b,c,d}

\textsuperscript{a}Centre of Genomics and Policy, McGill University, Montreal, Quebec, Canada , \textsuperscript{b}Institute for Research in Immunology and Cancer, Université de Montréal, Montreal, Quebec, Canada , \textsuperscript{c}Leukemia Cell Bank of Quebec and Division of Hematology-Oncology, Hôpital Maisonneuve-Rosemont, Montreal, Quebec, Canada , and \textsuperscript{d}Department of Medicine, Université de Montréal, Montreal, Quebec, Canada

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Corresponding author: Erika Kleiderman, Centre of Genomics and Policy, Faculty of Medicine, Department of Human Genetics, McGill University, 740 Dr. Penfield Avenue, 5th Floor, Suite 5200, Montreal, Quebec, H3A 0G1, Canada. Tel.: +514 398 8415; fax: +514 398 8954; e-mail: erika.kleiderman@mail.mcgill.ca

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The use of biobanks in cancer genomic research has grown considerably in recent years as researchers rely more and more on human tissue samples and associated clinical data as resources for current and future biomedical research. Investigators are increasingly incorporating next-generation sequencing technologies into their research, and as a result are being confronted with the potential to identify genetic information in research participants. Their options in this situation run from following existing but limited ethical norms, selecting certain kinds of results, and excluding others. Efforts to bring the investigator’s perspective into
the debate regarding the return of research results are growing (1–5). Collateral to this has been the growing debate about the duty of investigators to return incidental findings (IFs) during whole-genome sequencing (WGS) based projects, which are becoming more commonplace (3, 5, 6). IFs are defined as discoveries concerning an individual research participant that are found during the course of research but are beyond the scope and purpose of the study (7). They can range ‘from clinically significant information to information relevant to ancestry and genealogy to information that is merely of recreational interest’ (8). However defined, there are numerous opinions from various stakeholders, as to what information should be disclosed to research participants and the feasibility of doing so (9).

IFs have been a longstanding concern in both research and clinics, but the growth of WGS will increase the likelihood of coming across IFs more regularly. ‘WGS is expected to exacerbate the problem of information overload, resulting in increasingly intricate and complex IFs’ (6). As such, it is important to explore the opinions of key stakeholders in the return of results process (5). The increase in availability of exome sequencing, particularly in the clinical setting, has brought with it a handful of challenges surrounding the creation of guidelines detailing the need for proactive attempts to address the how, when and where of communicating IFs (10–12). In both clinical and research settings, there is a general lack of agreement on whether IFs should be disclosed. This debate has come into focus in the research environment where what and how to communicate is not always well established and neither are the ethical guidelines or practices surrounding this issue. Generally, research participants want to be informed about genetic information and to make autonomous decisions about receiving IFs (13, 14). Within a biomedical research setting, cultural competence or professional perspectives may also influence how investigators perceive their role to inform research participants.

As Canadian ethical policy on IFs is potentially quite vague when it comes to what, exactly, should be disclosed and how, investigators find themselves in a difficult spot, often referring to the consent forms, research ethics boards (REBs), and the research protocol to identify their specific duty. The decision to return IFs to participants may encompass several practical considerations including increased workload, challenges to the variable level of expertise, and potentially creates conflicting duties (4). Moreover, the context in which the IF was found (research or clinic) may influence this decision. In this study, we explored the various considerations and contextual elements of researchers and clinician-researchers in determining IF disclosure.

**Materials and methods**

**Study design**

In this study, ‘investigators’ included basic researchers (hereafter ‘researchers’) representing those not directly involved in clinical care, and clinical oncology researchers (hereafter ‘clinician-researchers’) representing those involved directly or indirectly in patient care in the clinic and in the research project. The interview guide was developed and pilot tested, and ethics approval was obtained from the McGill University Institutional Review Board.

**Sample recruitment**

A list of eligible Canadian investigators in the Quebec and Ontario adult cancer research community was generated using a publicly funded inventory of projects by Génomique Québec, the Fonds de recherche du Québec – Santé (FRQS), the Canadian Institutes of Health Research (CIHR), and the Réseau de Médecine Génétique Appliquée (RMGA). Purposeful sampling was used to collect perspectives from clinical trials, biobanking, epidemiology and social science project. Between August 2012 and April 2013, investigators were contacted by electronic mail to participate in a 30–40 minute telephone interview. Characteristics of the 20 researchers who participated are presented in Table 1. Participant recruitment continued until we were satisfied that no new issues were arising and we were no longer hearing new information (15).

**Data collection**

The telephone interviews were conducted at the respondents’ convenience by two experienced researchers (DA and SAK). We used the same interview guide for all interviews, and this was distributed to the participants prior to the interview. The guide consisted of demographic questions and semi-structured interview questions, using vignettes highlighting the ethical, legal and social implications (ELSI) that may arise during genetic research (Appendix S1).

Respondents were asked about three specific contextual situations: perceptions and experiences, institutional

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|----------------------------------|
| **Table 1. Demographics of investigators interviewed** |
| **Demographic** | **N = 20** | **%** |
| Gender of participants | | |
| Male | 14 | 70 |
| Female | 6 | 30 |
| Age of participants | | |
| 21–40 | 4 | 20 |
| 41–55 | 12 | 60 |
| Older than 55 | 4 | 20 |
| Years in practice | | |
| Less than 1 | 0 | - |
| 1–5 years | 2 | 10 |
| 6–10 years | 1 | 5 |
| 11–20 years | 10 | 50 |
| More than 20 years | 7 | 35 |
| Specialty | | |
| Researcher | 12 | 60 |
| Clinician-researcher | 8 | 40 |
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practices, and potential solutions, while probing the reason behind their responses.

Data analysis

Based on conventions of qualitative research, interviews were audio-recorded and transcribed verbatim, and analysis was iterative and thematic, and carried out by three reviewers (AB, EK and DA). We used a mixed coding strategy, whereby pre-thematic codes stemming from a review of the literature were used as a framework to explore contextual elements, while allowing codes to emerge empirically from the ‘grounded’ data (thematic analysis). AB, EK and DA coded the data independently and met to agree on the way the data would be labeled. The benefit of multiple coders is its capacity to generate other interpretations. Consensus was reached about the themes through informal discussions. NVivo 10 software was used to assist in the analysis.

Results

Delivering IFs and obligations

Respondents raised four main contextual elements: (i) degree of significance of results, (ii) respect for persons, (iii) infrastructure implications, and (iv) professional responsibilities. Some nuances in participants’ experiences of the understanding of professional responsibilities emerged. Where relevant, we present the viewpoints of researchers and clinician-researchers who were involved in clinical care.

Element (i): degree of significance of results

Factors such as clinical significance, a high level of risk, the availability of treatment (actionability), and the impact on future generations were considered by respondents.

Unsurprisingly, they stated that research infrastructure and study design are not in place in many settings to confirm IFs, or to return IFs to participants. Some indicated that the quality of the test, the risk for false positive results, and the predictability and validity of the findings were a concern.

Actionability

Actionability was an important prerequisite to justify the return of results. Thus, the respondents expressed a need for clinical validation, treatment or prevention options and international consensus.

Prevention

Prevention was voiced repeatedly by respondents due to its beneficial effect on the health of the patient. For example, some respondents felt that finding problems early could be beneficial in improving an individual’s well-being. Others stressed that prevention, from a socioeconomic point of view, is just as valuable considering it provides a cost efficient option that is beneficial to everyone.

Element (ii): respect for persons

Informed consent

Investigators agreed that the return of research findings should be limited to the research question, as presented in the consent form. The lack of any mention of IFs is a limiting factor for them, as they felt that if it is not explained in the consent form, it should not be returned.

Nonetheless, they were open to, and positive about broadening consent forms so as to include any future findings. All favored the idea of anticipating IFs and giving participants a choice.

Researchers stated that a duty toward the patient exists. They placed a strong focus on the need to respect the patient’s wishes as expressed in the consent form. Clinician-researchers stated that a moral obligation lay in identifying IFs and then communicating them, regardless of what was in the consent form. Furthermore, they brought forth a potential moral obligation to override patient consent and confidentiality should there be a possible impact for society at large.

Respondents also felt that consent forms are usually rather paternalistic. They perceived this as problematic because it furthers the perception that professionals know what is best, which is not necessarily the case.

Participant empowerment

Respondents believed that providing a choice to participants and obtaining their consent guides decision making and is the foundation of their relationship with them.

They acknowledged that participants expect the return of results for their involvement in the research – the principle of reciprocity. Yet, it was expressed that participation might not be entirely altruistic, as participants do expect benefits to come of their involvement.

Furthermore, the issue of data ownership was mentioned. For example, the information belongs to the participant; therefore, they should be able to have access to it. As well, respondents reinforced the aforementioned concept of respecting patient autonomy, as they perceived patient participation in decision making to be beneficial wherever possible.

Psychosocial aspects

According to respondents, the return of IFs can trigger psychosocial and emotional implications. Some respondents thought the issue of insurance and disclosing of IFs will generate more worries, and render insurability more difficult as a result of the diagnosis.

They expressed the belief that it is unacceptable to provide participants with information that they cannot handle, noting that the whole process of returning genetic findings is fraught with emotions ranging from anxiety and stress to relief.

It was further suggested that sometimes participants may even feel anger about developing a disease and not having been told about it sooner, which respondents felt supported the general desire of participants to want to know the information, despite the potential negative emotions that may be attached.
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Furthermore, legal issues surrounding the return of IFs were also brought to light, such as concerns over the possibility for lawsuits and liability issues associated with accommodating what was specified in the consent form. Thus, there is a need to assure adequate communication of such results.

Finally, respondents said they look to REBs as the most appropriate body to provide guidance on how to manage IFs discovered in the research context; however, some feel that REBs are falling short in this area. They agreed that a clear outline of the procedure on what and how to report IFs to participants is needed, as it can be daunting to approach this situation alone without guidance.

Discussion

Our results are in line with the literature in which investigators tend to put forward various considerations when discussing the return of IFs. Generally, investigators are facing the dilemma of whether or not to return IFs to patients, and at the moment, there is little consensus or established practice on how to do this (4–6, 16, 17). For their part, patients express a strong desire to know and to have control over the choice to know, as highlighted in the literature (1, 13, 14, 18, 19). Being aware of the contextual elements highlights the need to understand the degree of significance of results, respect for persons, infrastructure implications, and professional responsibilities as they raise important questions about the impact of context. Future research will thus be needed to help address the gap between current practices and the idealistic opinions of stakeholders.

In the current IFs debate, we observed more of a continuum than a clear division, with the need to consider context in decisions surrounding the return of IFs. In general, all investigators raised similar contextual elements, irrespective of their educational background (i.e. researcher vs. clinician-researcher). However, it was also noted that with some issues, professional context might come into play. In this context, a one-size-fits-all approach would be inappropriate, as nuances exist between what respondents perceived as important in certain cases, namely surrounding professional responsibilities.

It seems unfeasible, in terms of time, and human and financial resources, for researchers to interpret, understand and communicate all the newly discovered findings (4, 20, 21). This is supported by respondents’ concern over who will be responsible for covering the added costs to the health care system of returning IFs, particularly in a context where funding is already short.

In genomic research, there is a growing consensus that under certain circumstances and in certain contexts, investigators have an ethical obligation to disclose individual research results and IFs to research participants. While critiques of IFs disclosure remain, the ethical obligation to disclose such findings is supported in Canada by the second edition of the Canadian Tri-Council Policy Statement (TCPS 2) (22). This obligation was disputed by respondents, as they agreed that the TCPS 2 was unrealistic due to a disconnect between theory and

Comprehension

Respondents thought that patients and the general public were not educated enough to fully comprehend and be aware of the implications surrounding genetic test results. They would have difficulty interpreting the results and dispelling the misinformation that is available.

Two interrelated participant education issues would be helpful: the need to use layman’s terms and a better explanation of genetic concepts.

Element (iii): infrastructure implications

For investigators, costs, time barriers, and lack of guidelines and resources affected their decisions to return IFs.

Returning IFs could result in increased time spent locating families and annotating findings, resulting in additional research costs. They agreed this was an impractical use of time taken away from research, especially in a context where funding is already lacking.

It was pointed out that they are not equipped to deal with all of the data analysis and delivery of IFs. Canada, for its part, also lacks a system to process such information.

Moreover, they voiced concern regarding who is going to be responsible for paying for the added costs to the health care system, without necessarily any increased benefits. They pointed out that it is not feasible to return IFs because it would simply require too many unavailable resources.

Element (iv): professional responsibilities

Respondents generally felt that professional responsibilities vis-à-vis their research participants played a significant role. However, clinician-researchers compared with researchers, sometimes were more likely to provide different reasons with respect to offering or not offering IFs.

For example, clinician-researchers perceived a clinical obligation toward the patient and had the patient’s best interests at heart. They pointed out that the researcher should contact the treating physician who has direct and ongoing contact with the patients to inform them of the findings.

Researchers, as a whole, were more likely to invoke a scientific rationale claiming that their professional obligation to communicate the findings should be limited to the scientific scope of the study. Moreover, they acknowledged that their relationship with participants is of a different nature, as there is both a lack of clinical relationship, as well as a lack of training in the delivery of genetic information.

Reference to the distinction between ethical principles in research and in the clinic was made. Clinician-researchers are expected to abide by the ‘do no harm’ principle, whereas that same principle is broadened in a research context. Researchers’ perspectives revolved solely around respecting what was laid out in the consent form.

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reality making it difficult to fully implement, as well as adding a burden for researchers in terms of compliance to the Statement, because conditions that were not applicable when the project first started cannot retroactively be imposed. In response to such criticism, the Tri-Council has proposed clarifications to the requirements for IFs, but these have not yet been adopted.

Furthermore, the American College of Medical Genetics and Genomics, in their recent policy statement, provide their input on the ongoing IFs debate and adopt a more permissive approach to the subject by recommending a ‘minimum list’ of conditions and gene variants that must be returned (23). A strict non-disclosure approach is frowned upon, as it could prevent individuals from obtaining information relevant to their well-being (12, 23).

The literature shows that research participants believe that sharing IFs would motivate them to take action toward their health and that withholding such information is a paternalistic way of conducting research, which takes autonomy and choice away from them (3, 7, 24, 25). Respondents supported these claims and favored patient participation in decision making (12), as a means of dissipating paternalism (6, 13) and encouraging respect for persons (26).

The psychological risks to participants, such as anxiety and depression, were another concern for professionals; however, this would not be a valid argument for withholding genetic information. Patient autonomy and their ability to assess the impact of such information for themselves should be prioritized instead (13).

Mention was also made of the need for legal protection for genetic information in order to prevent discrimination by health insurers within Canada. An example would be to have an act similar to the US Genetic Information Nondiscrimination Act of 2008 that prevents discrimination in the areas of employment and health insurance by prohibiting the use of genetic information in such domains. Similarly, the province of Ontario has recently proposed a modification to the Ontario Human Rights Code with the goal of protecting an individual’s genetic information by preventing insurance companies and employers from accessing it.

The contextual elements also raise an important question regarding whether investigators might feel there is a blurring of lines between scientific research and clinical care, causing difficulties for investigators to draw the line on when, how and what to deliver when it comes to IFs in genomic research (27, 28).

Another factor leading to distinctions between researchers and clinician-researchers was the relationship with the participant. The nature and depth of the relationship varies depending on the role of the investigator ranging from a one-time meeting to collect a sample, to an ongoing researcher-patient relationship (18). Our findings supported this, as clinician-researchers held the participant’s best interests to a higher esteem than did researchers who lack the rapport and training in delivering genetic information, leading to a more limited professional obligation (18).

This, however, would not appear to be unethical as clinical care aims to favor ‘the advancement of the patient’s health-related welfare’, which makes decisions about disclosure rather easy, as priority must be given to the patient’s health (6, 26). For clinicians, due to the clinical relevance of the information, they feel responsible to share these results with patients (26), based on their duty toward the patients (2, 5, 7, 29, 30). Furthermore, as fiduciaries to their patients, clinicians are both ethically and legally actionable to act for the benefit of the patient (26). Researchers, on the other hand, do not possess these duties, adopt a more disease-oriented research approach, and aim to ‘produce generalizable knowledge for society at large’ (4, 5, 16, 26, 29).

Several recommendations emerged from our findings (Table 2). They have been regrouped under participant empowerment, and infrastructure and guidelines.

Limitations

Our research focused on the perspectives of investigators in the field of cancer research. As a result, the views expressed may not be representative of those in a non-cancer genomic research context. These findings simply provide a glimpse into the reasoning behind common opinions surrounding the disclosure of IFs. Furthermore, the use of volunteer respondents in this study reveals the opinions of those most interested in the issue of returning IFs. Moreover, given this is a fast moving field of research, further investigation regarding context issues is important. Finally, the use of vignettes to gather data leads to the question of whether they provide a straightforward parallel between the vignette (the ‘ought’ to do) and social reality (the ‘actually’ do) (31). However, vignettes can provide ‘a useful tool to illuminate and tap into these complex processes by isolating certain aspects of a given social issue or problem’ (31).

In conclusion, many contextual elements including degree of significance of the results, respect for persons, health care system, and scope of professional responsibilities can impact the decision to disclose or not to disclose IFs. All investigators feel a general ethical responsibility to disclose IFs if they have clinical use; however, participants are aware that the practical challenges of individually communicating these results are too large to actually act upon this responsibility. The literature reveals that research participants and patients feel that genetic information belongs to them; thus they should be able to choose what and how they wish to learn about it (13). The barriers for disclosure should be addressed, and patients should be enabled in their consent procedure to indicate their choice of what they want.

This study suggests that the research community’s perceptions about returning IFs in the research-clinical context contain nuances. Future research is needed to explore the obligations of disclosing IFs by researchers and also by tissue bank directors, as tissue banks usually involve teams of researchers seeking to handle IFs with their participants.
Table 2. Elements for further research and consideration

| Participants empowerment | Researchers | Common | Clinician-researchers |
|-------------------------|-------------|--------|-----------------------|
| Consent forms           | Respect what is expressed by participant | Broaden consent forms | Prioritize patient well-being |
|                         |             | Respect participant autonomy (choice at consent) |                        |
|                         |             | Avoid paternalistic tone |                        |
| Communication           | Limited to the scope of the study | Patient as partner (patient participation in decision making) | Researcher should contact treating physician |
|                         | Address the variability in genetic comprehension | Ensure participants are equipped to deal with information |                        |
|                         |             | Educate the public (genetics) |                        |
|                         |             | Clear language and explanations |                        |
|                         |             | Avoid a one-size-fits-all model |                        |

Infrastructure and guidelines

| Resources               | Address need for genetic counselors | Address the lack of resources: WHO will be responsible for covering the added costs to the health care system? |
|-------------------------|-------------------------------------|----------------------------------------------------------------------------------------------------------|
|                         | Address the distinction between research and clinic | REBs to provide guidance and set out clear procedural outline (REB approved disclosure) |
| Guidelines and policy   | Address lack of clear guidelines/policies and lack of agreement (need an international standard) | Multidisciplinary team approach |
|                         | Engage stakeholders | Address the need for legal protection for genetic information (Canada) |
|                         | Need an awareness of national and provincial laws | |

REB, research ethics board; WHO, World Health Organization.
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Supporting Information

Additional supporting information may be found in the online version of this article at the publisher’s web-site.

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