# Genomic Findings

## Developing standardised approaches for genomic findings beyond the original scope of the test

March 2024

Australian Genomics

# Acknowledgement of Country

In the spirit of reconciliation Australian Genomics acknowledges the Traditional Custodians of country throughout Australia and their connections to land, sea, and community.

We pay our respect to their elders past and present and extend that respect to all Aboriginal and Torres Strait Islander peoples today.

***Artwork by Yorta Yorta artist, Alkina Edwards, for Australian Genomics.***

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# Executive Summary

Australian Genomics

**Genomic Findings**

**Developing standardised approaches for genomic findings beyond the original scope of the test**

## Project Overview

As genomic medicine moves into mainstream healthcare, its effective integration requires understanding and application of key concepts and terms amongst all relevant healthcare professionals, patients and the public.

Agreeing on the terms used to describe genomic findings beyond the initial test indication will give patients a consistent experience and support clear communication about results, including what these findings are, what they mean, and what the next steps are.

Further, developing agreed-upon terminology will support meaningful debate about ethical management of genomic findings beyond the initial test indication. This, in turn, will support progress towards developing professional consensus guidelines.

To date, in Australia there is no national consistency in policy or clinical practice regarding how to approach the reporting or deliberate seeking of genomic findings beyond the initial test indication. There is a policy gap in this area of genomic testing in Australia and this project sought to engage with stakeholders to make progress toward consistency of approaches.

The two objectives of the project were to 1) determine appropriate terminology to describe genomic findings beyond the original scope of a clinical test, and 2) develop high level guiding principles for development of future government policy toward the management and delivery of such findings.

## Method

A scoping review of the literature was undertaken to determine what terms are being used to describe findings beyond the initial test indication (whether deliberately sought or not) and synthesise the justifications for using those terms. This work provided the evidence base to lead a discussion about Australian practice. Consultation with a broad range of Australian stakeholders through two workshops explored 1) terminology for genomic findings and 2) guiding principles for future policy for the management of genomic findings.

## Key Findings

A list of terms to describe genomic findings beyond the original scope of the test compiled as part of the scoping review included ‘incidental’, ‘secondary’, ‘additional’, ‘unsolicited’, ‘unexpected’, and ‘unanticipated’, as well as other less frequently used terms. Four main themes arose from synthesising the justifications for or reasons against using these terms: 1) expectedness of the finding, 2) effective communication, 3) relatedness to the original test indication, and 4) how the genomic information was generated.

In the consultation workshops, participants were most comfortable with the term ‘additional’ as an overall term for findings beyond the initial test indication. This was the case for both findings identified unexpectedly and those deliberately sought. Participants preferred 'additional' because they perceived it to be a neutral term and more readily understood by patients. Stakeholders developed four guiding principles for the development of policy to manage additional findings, whether deliberately sought or not. They were: patient focused, equitable, warranted, and consistent.

## Impacts

This work has reached numerous groups across the genomics community in Australia and has invigorated the discussion about appropriate and deliberate use of terminology, as well as management of genomic findings. The impacts of this project relate to developing consistency of patient experience and efficiency of healthcare across Australia.

## Recommendations

We recommend further consultation with patients, patient group representatives, and consumers in relation to terminology and the guiding principles. Publicising the guiding principles will allow us to receive feedback on this project’s output. Providing a version of this report to relevant groups could inform further government consultation activities and/or future policy development.

## Conclusion

The aims of this project were to determine appropriate terminology to describe genomic findings beyond the scope of the initial clinical test and develop high level guiding principles for development of future government policy toward the management of such findings in Australian healthcare. Despite a clear preference for using the term ‘additional’ to describe genomic findings beyond the scope of the original test, our findings suggest a need for further consultation to consider whether one term can feasibly be used across different contexts. The guiding principles inform the development of policies where patient focussed, equitable, warranted and consistent practices are achieved for managing genomic findings beyond the scope of the initial test in Australia.

## Plain Language Summary / Website Summary

Genomic findings that are outside the original reason for getting a clinical genomic test have been described as ‘secondary findings’. They can be ‘surprises’ when broad analysis of a person’s DNA is done, or they can be intentionally looked for as an ‘add on’ to testing to answer other health-related questions.

However, in Australia and globally there many different terms being used in clinical practice and genomics research to refer to these findings. There are also many ways these types of findings are being managed. For example, there is no consistent practice for whether patients should be told about 'surprise' genomic findings. In Australia, we are aiming to develop a consistent approach to these questions.

This project first reviewed the literature to find out what terms were being used, and why. The review found there were 16 different terms in common use. We looked at the justifications for use of certain terms and identified four groups of reasons used to support or oppose them. The reasons were: expectation of the finding, effective communication, relatedness to the original test requested, and how the genomic information was generated.

The 16 terms and their justifications served as background information for our two workshops, which involved a broad range of people affected by these issues. We discussed what terms we should use, and what guiding principles should inform policies about whether and how to tell patients about these findings to patients in Australia.

In the first workshop, people preferred the term ‘additional’ both for the ‘surprise’ findings and for those that were added on. The term ‘incidental’ was also considered acceptable for ‘surprise’ findings and ‘secondary’ was considered acceptable for findings that were added on.

The second workshop explored what guiding principles should inform future policy in developing a nationally consistent approach to these types of findings. The group agreed that policy development should be patient focussed, equitable, warranted, and consistent across Australia.

While this project has made progress about preferred terminology and guiding principles for policymaking in Australia, the issues are complex and further work is needed, including more engagement with groups affected by these issues.

# Background

As genomic medicine moves into mainstream healthcare, its effective integration requires a basic understanding and application of key concepts and terms amongst all relevant healthcare professionals, patients, and the public. Education and resources about genomic findings (i.e., results obtained during genomic testing) for non-genetic healthcare professionals and patients will need to include material about genomic findings that are beyond the initial test indication. The terms and accompanying definitions for such findings should be agreed upon by the genomics community, including patients.

In a clinical context, lack of clarity in terminology about genomic findings beyond the initial test indication engenders confusion and increases the likelihood of miscommunication between and among healthcare professionals and patients. Consistent, standardised terminology will facilitate effective communication between healthcare professionals as well as interactions with patients. Accessible, readily understood language is also crucial for patients to make informed decisions about testing. Agreeing on the terms used to describe genomic findings beyond the initial test indication will give patients a consistent experience and support clear communication about results, including what these findings are, what they mean, and what the next steps may be.

Further, developing agreed-upon terminology will support meaningful debate about ethical management of genomic findings beyond the initial test indication. This, in turn, will support progress towards developing professional consensus guidelines. This is important because guidelines must reflect appropriate clinical and ethical management of many different types of genomic findings and use terms that are understood by the genomics (and wider) community.

To date, in Australia there is no national consistency in policy or clinical practice regarding how to approach the reporting or deliberate seeking of genomic findings beyond the initial test indication[1] Currently, the National Pathology Accreditation Advisory Council (NPAAC) requires that laboratories "must have a policy on the reporting of genomic findings beyond the initial test indication which must be made available on request to patients and clinicians" (S1.6 p5)[2], but there is no requirement for consistent practice across laboratories.

Further, while NPAAC Standards suggest that laboratories "should consider the masking of information that is outside the scope of testing for a given patient sample", and that this "may involve masking of loci other than those targeted for analysis for a given patient" (C1.6.(ii)), there

[1] Vears DF, Sénécal K, Borry P. Reporting practices for unsolicited and secondary findings from next-generation sequencing technologies: Perspectives of laboratory personnel. *Hum Mutat*. 2017;38:905–911. https://doi.org/10.1002/humu.23259
[2] National Pathology Accreditation Advisory Council (NPAAC). Requirements for Human Medical Genome Testing Utilising Massively Parallel Sequencing Technologies. Available at: https://www1.health.gov.au/internet/main/publishing.nsf/Content/FB649C2C2A42CACDCA2580A400039643/$File/Reqs%20MPS%20Technologies%202017.pdf

are no regulatory requirements concerning deliberate searches for genomic findings beyond the initial test indication.

There is a policy gap in this area of genomic testing in Australia and this project sought to make progress toward consistency of approaches, with stakeholder input.

# Introduction

The National Health Genomics Policy Framework (NHGPF) Supplementary Information[3] indicated that a national approach to 'secondary findings' should be developed:

> *"From a service delivery perspective, a nationally consistent process on how secondary findings are approached should form part of guidance on bioethics in the context of public health policy."*

Under the previous Australian Health Ministers Advisory Committee and the Project Reference Group on Health Genomics, the Essentially Ours report[4] was commissioned to assess the regulation of the collection and use of health-related genomics information. The report outlines the issues and scope of guidance available in Australia for clinical and research genomics professional. This patchwork of policy may be interpreted in variable ways. Although acknowledging the variety of terms used, the report adopts the term 'incidental' to describe genomic findings beyond the test indication as an umbrella term for those that are a 'surprise' or deliberately sought. They do this to align with the approach used in the National Health and Medical Research Council's *National Statement* (which applies to research).

In 2017 and 2020 Australian clinically accredited genetic testing laboratories were surveyed about their practices regarding management and return of findings unrelated to the genomic test request[5]. This research found there was a lack of consensus regarding the terminology being used to describe such findings, with almost half of laboratories reporting they use a variety of terms interchangeably. A review of laboratory polices showed that reporting practices differed across testing contexts.

Though the NHGPF has lapsed, Australian Genomics' priority development (2021-2023) recognised the remaining policy gap in this area of delivery of genomic testing and progressed work on a 'secondary findings' project through its bioethics research priority area.

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[3] Australian Government. Supplementary information to the National Health Genomics Policy Framework 2018–2021. Available at: https://www.health.gov.au/sites/default/files/documents/2022/03/national-health-genomics-policy-framework-2018-2021-supplementary-information.pdf

[4] Rebekah McWhirter, Lisa Eckstein, Don Chalmers, Jane Kaye, Jane Nielsen, Margaret Otlowski, Megan Prictor, Mark Taylor and Dianne Nicol. Essentially Ours. Available at: https://www.utas.edu.au/__data/assets/pdf_file/0005/1576940/Essentially-Ours-Report-11-Final_.pdf

[5] Tudini E, Haas MA, Mattiske T, Spurdle AB. Reporting clinically relevant genetic variants unrelated to genomic test requests: a survey of Australian clinical laboratory policies and practices. *J Med Genet. 2023;60(6):609-614.* doi: 10.1136/jmg-2022-108808

## Aims

- To inform the development of nationally consistent approaches to genomic findings through academic scholarship and broad consultation with Australian stakeholders. Specifically:
    - Determine appropriate **terminology** to describe genomic findings beyond the original scope of a test.
    - Develop high level **guiding principles** for development of future government policy toward the management and delivery of such findings.

## Objectives

- To perform a **scoping review of the literature** to determine what terms are being used to describe findings beyond the initial scope of the test (whether deliberately sought or not) and synthesise the justifications for using those terms. This work provides the evidence base to lead the discussion about standardising terminology in Australian practice.
- To **consult with a broad range of Australian stakeholders** from various disciplines and the genomics community to work towards standardised approaches to terminology and developing policy for the management of genomic findings.

## Inputs

**Project Lead**: Ainsley Newson

**Project Coordinators:** Matilda Haas, Sarah Jelenich

**Working Group Members:** Ainsley Newson, Matilda Haas, Kitty-Jean Laginha, Stephanie White, Danya Vears, Clara Gaff, Gabriel Watts, Kirsten Laurendet

With additional thanks to Mary-Anne Young for advice throughout the project and Jane Tiller for valuable input into the early stages of the literature review

**External Collaborators / Contracted Services:**

- Mosaic Lab workshop facilitators (www.mosaiclab.com.au) Nicole Hunter and Keith Greaves

**Consumer Involvement:**

- Representatives of patient advocacy and support groups invited to attend consultation workshops included Genetic Support Network Victoria, Syndromes Without A Name, Rare Cancers Australia, Mito Foundation, Rare Voices Australia, Genetic Alliance, Chronic Illness Alliance.

**Engagement with First Nations Communities:**

- Aboriginal and Torres Strait Islander colleagues and Indigenous research experts were invited to attend consultation workshops. This included representatives of the Australian Alliance for Indigenous Genomics, National Centre for Indigenous Genomics, the Indigenous Genomics group at Telethon Kids Institute and Deakin University.

**Other Stakeholders:**

- Stakeholders for this project included genomics researchers, research institutions, genetics services and health professionals (both genetic and non-genetic specialists), genomics diagnostic laboratories and staff, Human Genetics Society of Australasia, Royal College of Pathologists of Australasia, other professional colleges, State/Territory and Federal Government genomics initiatives/bodies and standards organisations, international genomics initiatives/bodies including the Global Alliance for Genomics and Health, research participants, patients, patient support/advocacy groups.

**Other Resources:**

- Workshop facilitation services were provided by Mosaic Lab
- Librarian/ information technologist support was provided for literature reviews (University of Sydney and Royal Children's Hospital, Melbourne)
- Statistical support was provided for literature review (University of Sydney)

## Milestones and Timeline

| MILESTONE | TIMELINE | ACTIVITIES |
|---|---|---|
| ***Establish working group*** | *Q3-Q4 2021* | • *Define scope*<br>• *Identify stakeholders*<br>• *Appoint chair and recruit members* |
| ***Literature review*** | *Q4 2021 – Q2 2022* | • *Perform literature review*<br>• *Publish in academic journal* |
| ***Consultation*** | *Q2 2022 – Q3 2023* | • *Engagement/consultation workshops: terminology then policy* |
| ***Summary of outcomes*** | *Q4 2023* | • *Synthesise outcomes of consultations* |
| ***Report*** | *Q1 2024* | • *Report to NHMRC, government* |

**Frequency of meetings / structure of activity:**

- As the project moved through the literature review and consultation stages, team members involved in those specific activities met with high frequency (> weekly) to support the goals of the project within the timeframe of the grant.

## Budget, Expenditure and Resourcing

Personnel: Australian Genomics provided funding support for three casual Research Assistants and a part-time Postdoctoral Fellow, employed through the University of Sydney.
Publishing costs: Open Access publication in Genetics in Medicine
Consultation costs: Workshops were provided by external provider Mosaic Lab at a cost of $25,055 funded by Australian Genomics.

# Methods

**Literature Review**

A scoping review was undertaken to determine the range of different terminologies in use and the justifications for use of those terms. The literature review protocol was registered with Open Science Framework and is available at https://tinyurl.com/2kh2ca5b.

**Stakeholder Consultation**

Stakeholder consultation was carried out in the form of two online workshops:

1) Preferred terminology for genomic findings
2) Guiding principles for developing policy to manage genomic findings

The workshops were designed with Mosaic Lab during an initial co-design session (with multiple stakeholders) and in further check in sessions prior to each workshop. Mosaic Lab are community engagement practitioners and workshop facilitators who employ deliberative engagement methods to guide the exploration of issues[6].

# Results

**Scoping Review**

Following two initial exploratory literature reviews (Appendix 1), a scoping review was decided upon to systematically identify and synthesise terminology choice – and accompanying justifications - for describing genomic findings beyond the original scope of the test.

[6] https://www.mosaiclab.com.au/

The scoping review was designed to address the following research questions:

1. What justifications or reasons underlie the choice of terms used in the literature to describe genomic findings beyond the initial test indication?
2. What terms typically accompany these justifications or reasons identified in the literature?
3. What contextual factors, such as setting (e.g., clinical or research) or age/population group (e.g., paediatric or adult populations) influence justifications or terms used within the literature?

The final review included 52 eligible documents that met the inclusion criteria, from 3571 records originally screened. Four main themes emerged from the justifications: 1) expectedness of the finding, 2) effective communication, 3) relatedness to the original test indication, and 4) how genomic information was generated. The full findings can be reviewed in the publication in the journal *Genetics in Medicine* (Appendix 2).

The scoping review facilitated the compilation of a list of terms that have been used to describe findings beyond the original test indication, as well as providing a framework for considering the appropriateness of terms based on the justifications others have given to support or oppose each term. This provided a foundation for subsequent consultation activities for this project. This list of terms is reproduced in Appendices 2 and 3.

**Terminology for genomic findings beyond the initial test indication (Workshop 1)**

The list of terms used to describe genomic testing findings beyond the original scope of the test compiled as part of the scoping review included ‘incidental’, ‘secondary’, ‘additional’, ‘unsolicited’, ‘unexpected’, ‘unanticipated’, as well as other less frequently used terms. (Appendices 2 and 3).

The intention of the workshop was to make progress toward developing nationally consistent terminology for genomic findings beyond the initial test indication. The objectives were to share the learnings from the scoping review with stakeholders and consult with them on what term(s) they preferred, including whether different terms were needed in different contexts (Figure 1).

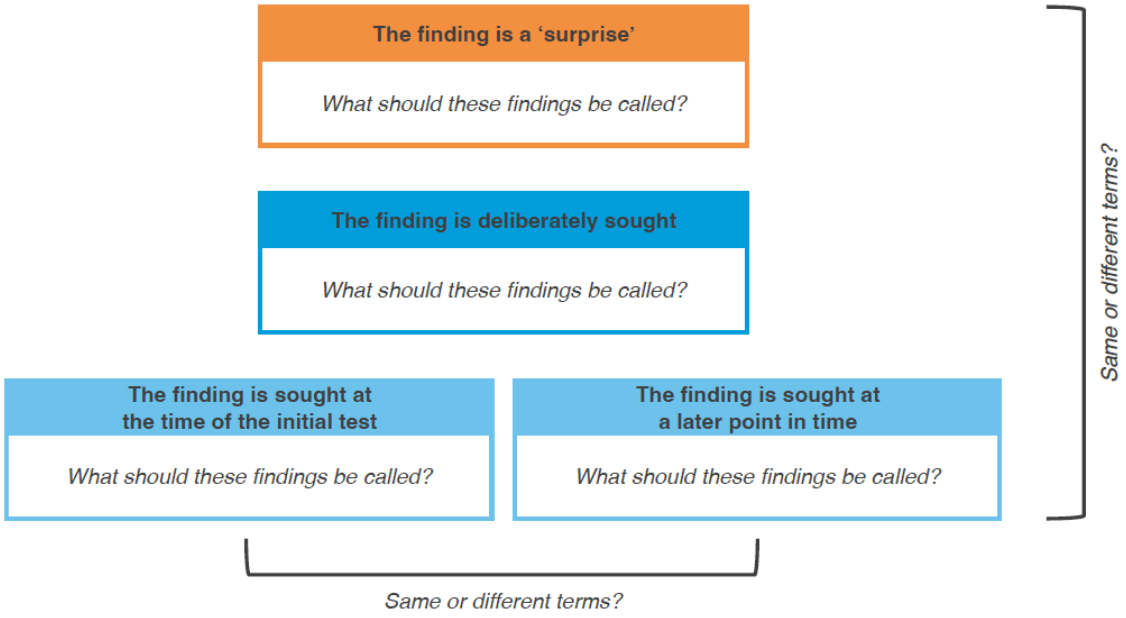


*Figure 1. Framework presented to stakeholders in Workshop 1 for consideration*

The three-hour workshop was held online on 5th September 2023. One hundred and six potential participants were invited by email to attend, with the option to instead nominate another representative. Invitees broadly represented research; genetics laboratory; ethics and policy (including Indigenous representatives); industry; patient support and advocacy; standards organisations; clinical genetics; genetic counselling; non-genetics healthcare; governments, Australian Genomics staff, and the project team. Fifty-six participants registered and 49 attended on the day.

Participants were provided with a workshop briefing paper (Appendix 3) and agenda (Appendix 4) prior to the workshop. The briefing paper outlined the following issues: why using standardised terminology is important, the contexts in which these issues arise, and a summary of work to date. The briefing paper presented a comprehensive table outlining the main terms used and reasons 'for' and 'against' the use of each of those terms.

During the workshop, Mosaic Lab led participants through the agenda, which began by exploring the terms, prioritising a set of terms for further discussion, and discussing pros and cons of each of the terms in small groups. Participants then individually ranked each term. A 'what was said' report was provided to Australian Genomics after the workshop (Appendix 5).

The workshop highlighted the complexities of establishing consensus on terminology use. Participants' overall 'comfort levels' with different terms are shown in Figure 2, which suggests strong support for the term 'additional'. However, we note that this is a high-level summary figure and not a nuanced view.

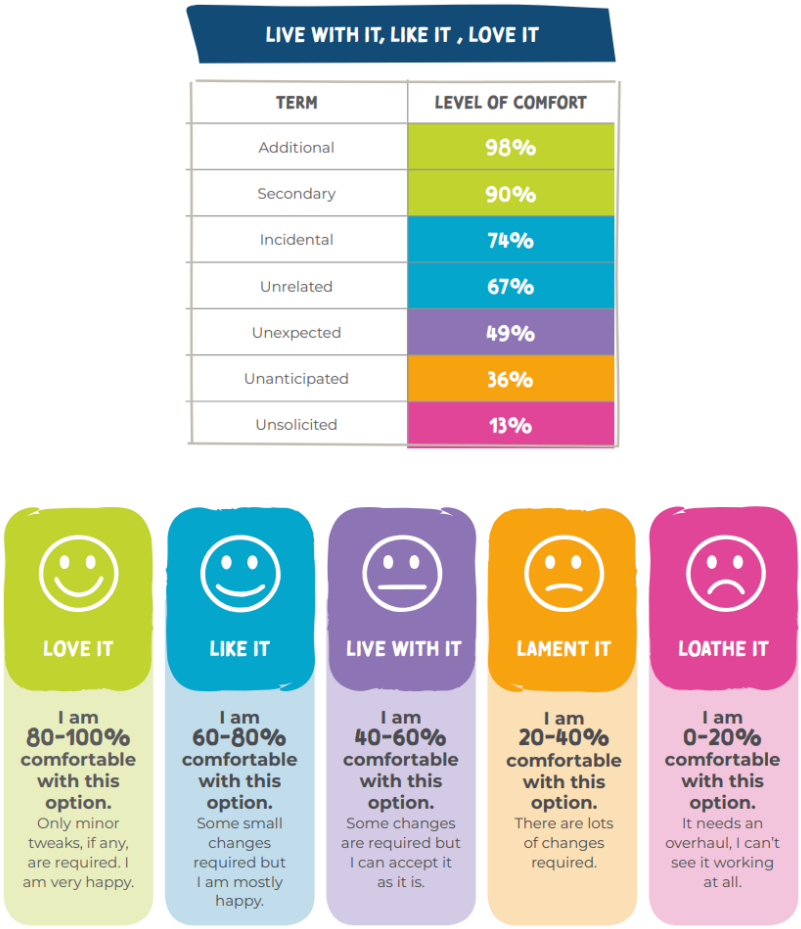


*Figure 2. Overall findings on comfort levels with the different terms. This question measured comfort with each term independently, expressed as the percentage of respondents whose comfort level with the term exceeds 40%. The percentages in the table represent the number of respondents willing to, at minimum, 'accept' the use of a term in all contexts.*

A more detailed summary of participants' terminology preferences from Workshop 1 is below. The full data can be reviewed in Appendices 5 and 6.

*Table 1. Detailed summary of Workshop 1 participants' terminology preferences*

| ***Term*** | ***Comfort level*** | ***Context*** |
|---|---|---|
| ***Endorsed terms:*** | | |
| **Incidental** | 74% (29/39) voters could "live with" "like" or "love" this term | 81% (30/37) thought it was best used in the context of 'surprise' findings |
| **Secondary** | 90% (35/39) voters could "live with" "like" or "love" this term | 54% (21/39) thought it was best used for deliberately sought findings<br><br>51% (20/39) thought it was best used for deliberately sought findings regardless of timing of offer to receive those findings (both with the initial test or sometime later) |
| **Additional** | **98% (38/39) voters could "live with" "like" or "love" this term** | **67% (26/39) thought it was best used in all contexts** |
| ***Terms not endorsed:*** | | |
| **Unsolicited** | 13% (5/39) could "live with" "like" or "love" this term<br><br>72% (28/39) voters loathed the term | 81% (25/31) thought it was best used in the context of 'surprise' findings |
| **Unexpected** | 49% (19/39) could "live with" "like" or "love" this term | 82% (28/34) thought it was best used in the context of 'surprise' findings |
| **Unanticipated** | 36% (14/39) voters could "live with" "like" or "love" this term | 83% (29/35) thought it was best used in the context of 'surprise' findings |
| **Unrelated** | 67% (26/39) voters could "live with" "like" or "love" this term | 59% (22/37) thought it was best used in all contexts |

The design of the data collection activities and tools may have influenced the outcomes. For example, participants could choose as many options as they wished, and the order of options may also have influenced both decision-making and level of detail provided about their perspectives in free text fields.

Given the ambiguity of these initial results, a follow-up questionnaire was emailed shortly after the workshop to both participants and those who were invited but did not attend. The intention of this survey was to obtain greater clarity about which terms are preferred in which contexts (e.g. 'surprise' findings versus those that are deliberately sought). Thirty-two participants completed the follow-up questionnaire, and the most popular choices of terms are summarised in Table 2 (full data provided in Appendix 7). However, it should be noted that the project team observed through responses and email communications that the follow-up questionnaire itself may also have caused some confusion, reinforcing again the inherent complexity in this dialogue. Confusion was related to similarity between questions and the notion that any genetic testing and analysis ordered by a healthcare professional was "in scope" information. However, the follow-up questionnaire did reinforce some aspects of the data collected in Workshop 1, including that 'additional' was a preferred term across the different genomic testing contexts.

*Table 2. Follow-up questionnaire results summary. Votes are expressed as a percentage with the number of votes out of total votes shown in brackets.*

| ***Type of context*** | ***Preferred term*** | ***Votes*** |
|---|---|---|
| *When the finding is a **'surprise'** we should say...* | *Additional* | *54% (22/41)* |
| *When the finding is **deliberately sought** we should say...* | *Additional* | *50% (16/32)* |
| *When the finding is **sought at a later point in time** we should say...* | *Additional* | *91% (29/32)* |
| *When the finding **is sought at the time of the initial test** we should say...** | *Additional* | *53% (16/30)* |

**Indicates the question participants expressed they had difficulty interpreting.*

***In summary, at the end of Workshop 1, participants were most comfortable with the term 'additional' as an overall term for findings beyond the initial test indication. This was the case for***

***findings identified unexpectedly and those deliberately sought. Participants preferred 'additional' because they perceived it to be a neutral term and more readily understood by patients[7].***

For findings discovered unexpectedly (i.e., 'surprise' findings), while most participants preferred the term 'additional', they were also willing to use the term 'incidental'. Support for 'incidental' stemmed from the entrenchment of this term in clinical practice, not only in genomic medicine but in medical practice more widely (e.g., medical imaging). It is also well-established in the literature[8].

For findings beyond the initial test indication that are identified through deliberate searching (with consent and analysis taking place either at the time of testing or later), most participants indicated they would be comfortable using the term 'additional'[9]. However, there was similar support for the term 'secondary'[10].

**Guiding principles for policy about managing genomic findings (Workshop 2)**

The objective of Workshop 2 was to develop high-level guiding principles which could contribute to shaping future Australian policy for additional findings in genomic testing. Note that in Workshop 2, the project team had started to test the use of the term 'additional' to describe these findings, following support for the term in Workshop 1. In the briefing paper for Workshop 2, we used the combination terms additional/incidental to describe 'surprise' findings, and additional/secondary to describe findings that were deliberately sought (Appendix 6).

Workshop 2 was conducted with a smaller participant group. We invited stakeholders that had attended the first workshop, been pre-briefed, or were otherwise familiar with the issues for discussion, and had an interest in policymaking in this area. The workshop was initially planned to be held in person, however, due to feedback from invitees and low registration rates, it was changed to an online workshop format and held a few weeks later than initially planned. This approach potentially improved attendance numbers and promoted a more equitable mix of represented groups. The three-hour workshop was held on 28th November 2023. From approximately 58 invitations, there were 30 registrations and 25 attended on the day.

Participants were provided with a briefing paper (Appendix 6) and agenda (Appendix 8) prior to the workshop. Because the outcomes of Workshop 1 were not ultimately clear to the project team, Workshop 2 began with a short summary of outcomes of the terminology workshop (see above) and a final vote for preferred terminology (Table 3).

[7] MosaicLab. *Australian Genomics – Terminology for Genomic Findings: Workshop 1 Report*. 5 September 2023:23-4.
[8] Workshop 1 Report:19-20.
[9] Workshop 1 Report:23-4.
[10] Workshop 1 Report:21-22.

*Table 3. Testing the terminology – final vote for Workshop 2 participants*

| ***Type of context*** | ***Votes*** |
|---|---|
| **How comfortable are you using additional in both contexts** (for 'surprise' and deliberate findings)? | 83% (19/23) of voters could "live with" "like" or "love" this term |
| **Do you think we need two distinct terms for the two different contexts** (for 'surprise' and deliberate findings)? | 67% (16/24) Yes<br>33% (8/24) No |
| If you had to choose between **additional and incidental** for **'surprise' findings**… | 54% (13/24) additional<br>46% (11/24) incidental |
| If you had to choose between **additional and secondary** for **deliberately sought findings**… | 58% (14/24) additional<br>42% (10/24) secondary |

These results affirmed the preference for 'additional' in both contexts, although this was contradicted by 67% of participants (n=16/24) electing that different terms are preferred.

Guiding principles were developed collaboratively during the workshop, in response to a core remit: "What guiding principles will help shape future Australian policy for additional findings in genomic testing?" Participants brainstormed suggestions for principles that they considered important. These were then gathered into theme areas by the project team and workshop facilitators. Then participants worked in small groups to draft one or two principles, using a pre-defined template including: a short principle name, a 1-2 sentence description, and any qualifications to the use or application of the principle (3-4 bullet points). Participants were also able to provide input and feedback on key considerations toward other principles under the section "things to keep in mind whilst writing this principle" (3-4 bullet points per principle).

For the purposes of the workshop, principles were divided into three areas: 1) overall approach to additional findings, 2) principles for 'surprise' findings, and 3) principles for deliberately sought findings. At the end of the workshop, the project team further refined the drafted principles. A summary of the principles is provided here, while the full drafting of principles is available for review in Appendix 9.

The guiding principles are as follows:

**Patient focussed:** The search for and reporting of additional findings is patient focussed, within the bounds of what the health system can sustainably support. Appropriately informed and flexible

consent to deliberate searches is of paramount importance, and any reporting of additional findings aims to empower patients to make autonomous medical decisions in line with their considered preferences.

**Equitable**: The search for and reporting of additional findings must be equitable. Health systems – inclusive of laboratories, clinical genetic services and downstream clinical services (including non-genetic services) – must support individuals/families who receive additional findings in a manner that considers equity of access to services, including information provision and appropriate medical management.

**Warranted**: The search for and reporting of additional findings must be warranted. Considerations include (but are not limited to) medical relevance, individual, familial and community implications, potential benefits and harms, clinical context (e.g. paediatric/adult), and patient capacities. Reporting of additional findings must be appropriate for the patient, considering (but not limited to) age, education, primary language, and cultural or ethnic background.

**Consistent**: The search for and reporting of additional findings must be nationally consistent. Services ought to mitigate the discovery of additional/incidental findings through the design of nationally consistent testing processes (e.g. blinding of genes outside the scope of the test). Deliberate searches for additional/secondary findings must follow a nationally consistent gene/variant list. This encompasses shared standards for types and quality of results, consent requirements, and evaluation of clinical actionability. Such standards ought to account for differences in state legislate frameworks and local health network guidelines, as well as differences between adult and paediatric populations.

## Outcomes

| MILESTONE | OUTPUTS | COMMENTS TOWARDS PROGRESS / COMPLETION DATE |
|---|---|---|
| ***Establish working group*** | Members recruited | Completed |
| ***Literature review*** | Publication in Genetics in Medicine | Completed |
| ***Consultation*** | Workshops held on 5th September and 28th November 2023 | Completed |
| ***Summary of outcomes*** | Report submitted 15th March 2024 | Completed |
| ***Report*** | Submitted 31st March 2024<br>Report includes all project documents submitted to Australian Genomics | Completed |

- **Sharing of knowledge/engagement:**
    - **Consumer involvement**
    - **Engagement with First Nations communities**

The project team acknowledges the limited attendance at workshops by consumer and First Nations community representatives. This, as well as the pace of some workshop activities and further exploration of consultation questions means that further engagement is required. Any further engagement and consultation should extend to all stakeholder groups, but patients and First Nations people should be specifically engaged with in this process.

Future engagement options could include:

- Developing a consultation version of this report and seeking written feedback on its findings or holding focus groups or workshops.
- Developing education and resources about genomic findings for patients and non-genetic healthcare professionals.
- Developing a project brief for broad distribution.
- Seeking further opportunities for sharing the research findings, such as presentations at conferences or to relevant committees.
- Consultation on the guiding principles.

- **Collaborative projects/activities**: none identified
- **Other project outputs/outcomes**: see appendices

# Discussion

This project set out to work toward developing nationally consistent terminology and approaches to management of genomic findings beyond the original scope of a clinical test. The approach was unique to other issues previously explored by Australian Genomics in that systematic review of previous research and commentary on the issues was built upon with broad engagement and consultation activities.

**Terminology for findings beyond the scope of the original test**

Across all consultations on terminology, the term 'additional' was the most preferred, applying to both contexts of 'surprise' findings and those deliberately sought. Participants of the first workshop agreed in majority that they were comfortable using the term 'additional' across all contexts (67%), while in the second workshop the same percentage of participants indicated that they thought there needed to be two distinct terms (67%). This was one of the most notable contrary outcomes between the two workshops, but it should be noted that there were fewer participants in the second workshop (less than half), and that the first workshop was designed to specifically focus on terminology while the second was not.

Whether it is feasible to use the term 'additional' in both contexts remains to be tested. In the context of communicating with patients, it was considered the most easily understood term by our workshop participants, and there are data to support 'additional' being the preferred term by patients[11]. However, there are some distinctions between genomic findings beyond the scope of the test when they arise as a 'surprise' compared to when they are deliberately sought. For example, deliberately sought findings could be analysed through a pre-determined list of genes known to cause various health conditions, while the types of 'surprise' findings would vary with the mode of testing and could potentially be much broader in their scope and related health conditions. Whilst offering further analysis according to a gene list is not yet common practice in Australia, it has been done by a few laboratories in the past[5]. A distinction between the two may be necessary in future if analysis of a pre-determined set of genes is routinely offered as an addition to what is being done for the patient's clinical presentation. If such services are introduced, it will be important to obtain specific and separate consent for any additional analyses and to be clear whether there is a cost to the patient. Therefore, using one umbrella term for patients may not be straightforward if this kind of service is introduced in future.

Issues may also arise when clinical and laboratory professionals are communicating with each other about genomic findings. Confusion could arise from using one term to describe different types of genomic findings across the genomic testing pipeline, from consent and test request to reporting

[11] Tan N, Amendola LM, O'Daniel JM, Burt A, Horike-Pyne MJ, Boshe L, Henderson GE, Rini C, Roche MI, Hisama FM, Burke W, Wilfond B, Jarvik GP. Is "incidental finding" the best term?: a study of patients' preferences. Genet Med. 2017 Feb;19(2):176-181. doi: 10.1038/gim.2016.96. Epub 2016 Aug 4. PMID: 27490114; PMCID: PMC5291803.

results back to patients or research participants. However, decisions made by the patient to accept return of 'surprise' findings or request additional analyses for deliberate findings should be well documented as part of the test consent process, such that the nature of these findings is distinguishable. Though, as discussed above, whether such a distinction is necessary may depend on the scope of genetic testing services routinely offered in future.

Therefore, while there was broad consensus that 'additional' was the most preferred term, further consideration should be given to whether separate terms are needed for the different contexts. While there was reasonable support for existing terms 'incidental' and 'secondary', interestingly, throughout this project there has been no suggestion that there is scope for coming up with new terms. This may be because stakeholders feel that there is already a saturation of terms, which is supported by our finding of at least 16 terms in widespread use.

One observation from the workshop was that participants had clear views about the terms they preferred and why they used them. Their reasons often aligned with the justification themes identified in the scoping review. If we are to achieve nationally consistent use of terms in Australia, there will need to be significant change in the practices of stakeholder groups, which is where clear and direct policymaking will play an important role. However, we consider that on the issue of terminology, there will always remain some diversity in Australia due to the lack of international consensus. We should focus on Australian stakeholders but participate in international discussion when required.

**Guiding principles**

Terminology for genomic findings and their management is subject to ongoing discussion. Therefore, currently it is too early to either determine national policy or draft recommendations. As an initial step, guiding principles can provide a 'bridge' between academic research and stakeholder opinion and future policy. The guiding principles resulting from the collaborative development approach were titled: patient focussed, equitable, warranted, and consistent. Workshop participants have not yet had the opportunity to review the guiding principles as presented in this report.

The principles developed from this exercise could be applied more broadly across the different contexts (refer to Figure 1) and so four overarching guiding principles were finally developed. From fifty initial suggestions for guiding principles put forward by the group in Workshop 2, these were combined into themes resulting in four principles. This process demonstrated the consistent views of stakeholder groups as to the key areas of importance for developing policy in this area.

The guiding principles highlight the areas or values considered of highest importance by our stakeholders when developing policy about these types of genomic findings. These principles can be applied to the development of a policy framework and policy actions, which can then be implemented at the health services level.

The Health Technology and Genomics Collaboration, a national committee responsible for all aspects of new health technologies, are in the process of refreshing the National Health Genomics Policy Framework. This report will inform the management of genomic findings beyond the initial scope of the test, and our aim is to convey the importance of developing policy in this area. The new NHGPF and its implementation outcomes will directly inform the development of genomic testing policy, guidelines and standards by all relevant organisations.

## Impacts

**Significance of the project:**

- Developing consistency of patient experience across Australia.
- Developing consistency and efficiency of healthcare.
- To ensure consent is correctly explained and given by the patient.
- Importance of including patient voices. Upon identifying the literature gap related to patient voices in the scoping review, we sought to include patient voices through direct engagement in our workshops.

**Key impact(s):**

- White S, Haas M, Laginha KJ, Laurendet K, Gaff C, Vears D, Newson AJ. What's in a name? Justifying terminology for genomic findings beyond the initial test indication: A scoping review. Genet Med. 2023 Nov;25(11):100936. doi: 10.1016/j.gim.2023.100936. Epub 2023 Jul 13. PMID: 37454281.
- Stephanie White, Matilda Haas, Kitty-Jean Laginha, Kirsten Laurendet, Clara Gaff, Danya Vears, Ainsley J. Newson. What's in a name? A scoping review of justifications for terms to describe (incidental) genomic findings. Australasian Society of Genetics Counsellors Special Interest Group (poster). Melbourne, 17-18th November, 2023.
- Australian Genomics National Steering Committee presentations.
- Availability of this report for future policy briefs / recommendations, etc.

**Implementation plans: sustainability or longevity of the project and its output(s):**

- Though further consultation is recommended, this project has reinvigorated a national conversation about terminology for genomic findings and these can be applied to other projects and policy development. Our work can be applied to other projects and policy settings:
    - Finalising the choice of language for the National Clinical Consent Package project.
    - Engagement with the Australian Commission on Safety and Quality in Healthcare (ACSQHC) to make a case for them to reconsider the terminology for genomic findings used in *Requirements for medical testing for human genetic variation 3rd Edition*.

## Limitations

- Limited patient, patient group and consumer involvement in consultation activities.
- The project did not reach a clear consensus on terminology. While the data mostly supports that stakeholders prefer to use the term 'additional' across contexts, it is yet to be tested whether this would work in practice.
- The design of data collection tools and ambiguity in responses.

## Recommendations and Future Directions

- Further consultation with patients, patient group representatives and consumers on both terminology and the principles.
- Publication of the guiding principles on the Australian Genomics website as a policy output.
- Provision of a version of this report to inform further government consultation activities and/or future policy development.

# Conclusion

The aim of this project was to inform the development of nationally consistent approaches to genomic findings by combining academic scholarship and broad consultation with Australian stakeholder groups. Specifically, our objectives were to determine appropriate terminology to describe genomic findings beyond the scope of the initial clinical test and develop high level guiding principles for development of future government policy toward the management and delivery of such findings in Australian health care. Despite clear preference for use of the term 'additional' to describe genomic findings beyond the scope of the original test, our findings also support the need for further consultation to consider whether one term can be feasibly used across different contexts. The guiding principles speak to the development of policies where patient focussed, equitable, warranted, and consistent practices are achieved for managing genomic findings beyond the scope of the initial test in Australia. This work has reached numerous groups across the genomics community in Australia and has invigorated the discussion about appropriate and deliberate use of terminology, as well as management of genomic findings.

# Appendices



**Appendix 1. Exploratory literature reviews**

Initially a review of 169 published journal articles already compiled in the Melbourne Genomics Additional Findings reference library was undertaken by MH and JT. This review focussed on terms used and the definitions provided with the use of those terms, as well as focussing on summary statistics like the country of origin of publications, geographical and temporal trends in use of different terms.

Next a literature review guided by a librarian was conducted by MH and KL. This review was undertaken with more stringent search terms and inclusion/exclusion criteria, and focussed on terms and their meanings, but also gathered information about approaches and considerations about disclosing such findings. This review began with 465 articles returned from a MEDLINE search and resulted in 22 articles which met inclusion criteria. Eleven articles focussed on the terminology debate.

Resources related to these reviews are available on request.

**Appendix 1**

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# REVIEW

# What's in a name? Justifying terminology for genomic findings beyond the initial test indication: A scoping review

Stephanie White[1,2,3], Matilda Haas[2,4], Kitty-Jean Laginha[1,2], Kirsten Laurendet[1,2], Clara Gaff[2,4,5,6], Danya Vears[2,4], Ainsley J. Newson[1,2,*]

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ABSTRACT

Genome sequencing can generate findings beyond the initial test indication that may be relevant to a patient or research participant's health. In the decade since the American College of Medical Genetics and Genomics published its recommendations for reporting these findings, consensus regarding terminology has remained elusive and a variety of terms are in use globally. We conducted a scoping review to explore terminology choice and the justifications underlying those choices. Documents were included if they contained a justification for their choice of term(s) related to findings beyond the initial genomic test indication. From 3571 unique documents, 52 were included, just over half of which pertained to the clinical context ($n = 29$, 56%). We identified four inter-related concepts used to defend or oppose terms: expectedness of the finding, effective communication, relatedness to the original test indication, and how genomic information was generated. A variety of justifications were used to oppose the term "incidental," whereas "secondary" had broader support as a term to describe findings deliberately sought. Terminology choice would benefit from further work to include the views of patients. We contend that clear definitions will improve ethical debate and support communication about genomic findings beyond the initial test indication.



## Introduction

Advances in genomic sequencing technologies have enabled the routine generation of vast amounts of genetic data and information, including findings beyond the initial test indication.[1] This phenomenon is not new to clinical or research settings.[2,3] In both settings, an array of terms are used to describe these types of genomic findings. Aside from

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"incidental," descriptors include "secondary," "unsolicited," "unexpected," "unsought for," and "additional," to name a few. These terms are used interchangeably and inconsistently in the literature and in practice, often with little clarification or justification.[4]

Much of the original debate about terminology was prompted by the publication of the American College of Medical Genetics and Genomics (ACMG) 2013 guidelines on the reporting of incidental findings, as they were called at the time. The ACMG stipulated that any clinical genomic test be accompanied by intentional analysis of 56 "clinically important" genes.[5] Following publication, extensive discussion ensued regarding the appropriateness of using "incidental" to describe deliberately sought findings. The ACMG later adopted "secondary" in a subsequent version of the policy.[6]

It is now a decade since the initial publication of the ACMG guidelines. Yet, inconsistent use of terms for these findings continues.[7] This lack of consensus within the genomics community as to the naming and designation of findings impedes constructive discussion about how they ought to be managed.[7] Reasons underlying the choice of terms are often unclear but may reflect differences in the perception and prioritization of underlying definitional concepts.[8] A lack of clarity engenders confusion, increases the likelihood of miscommunication between stakeholders and hinders progress toward professional consensus guidelines.[9] As integration of genomics into routine medicine advances, developing agreed-upon terminology is crucial to deliberate meaningfully about ethical management of genomic findings beyond the initial test indication.[10]

To inform a consistent approach to the management of such findings, it is first necessary to explore existing reasons given in the literature for terminology choice. We therefore undertook a scoping review to systematically identify and describe the justifications ascribed to various terms for genomic findings beyond the initial test indication. We sought to answer three research questions:

1. What justifications or reasons underlie the choice of terms used in the literature to describe genomic findings beyond the initial test indication?
2. What terms typically accompany these justifications or reasons identified in the literature?
3. What contextual factors, such as setting (eg, clinical or research) or age/population group (eg, pediatric or adult populations) influence justifications or terms used within the literature?

## Materials and Methods

We conducted a scoping review guided by the Joanna Briggs Institute evidence synthesis manual, which builds upon the scoping review framework set out by Arksey and O'Malley.[11] We selected a scoping review over other methods of evidence synthesis because we aimed to explore justifications for terms, rather than evaluate their effectiveness.[12] Reporting items align with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement for scoping reviews.[13] No similar reviews were identified on International Prospective Register of Systematic Reviews, Joanna Briggs Institute Systematic Review Register, Medline, or Cochrane Reviews. An a priori review protocol is available on the Open Science Framework (https://tinyurl.com/2kh2ca5b). The original protocol included an objective to develop a position statement about terminology use. However, the justifications identified in this review had varying degrees of soundness. We concluded that an evaluation of these justifications, in view of developing a position, would require separate analysis and evaluation with broad stakeholder input. Additionally, we initially planned to assess the role of geography in terminology choice. We ultimately removed this from our aims because (among other reasons) the review was designed to primarily capture justifications rather than provide a representative illustration of global terminology use.

### Eligibility criteria

Using the population, concept, and context criteria, we sought documents that defined and justified terms related to genomic findings beyond the initial test indication (see Supplemental Information for full details).[12] Briefly, we included documents that provided reasons for and/or against terms (ie, a justification for the choice of a particular term) and pertained to the clinical or translational research context. Documents published before 2010 were excluded because the likelihood of generating genomic findings beyond the aim of the initial test was low before the mainstream uptake of comparative genomic hybridization that occurred around this time.[14]

### Search strategy and information sources

In consultation with an information scientist, we searched MEDLINE, EMBASE, Web of Science, and Google Scholar. Medical Subject Heading terms and keywords were combined with Boolean operators, such as "incidental*" or "secondary finding," "human genetics" or "genomics," and "terminology as topic" (see Supplemental Information for full search strategy). The aim of our search was to explore the literature for justifications accompanying terms in use. Therefore, we did not limit the review to any particular terms. Results were limited to the English language. The search was last run on June 6, 2022. Forward and backward searching was performed on all documents meeting eligibility criteria. Using Web of Science, we generated a list of citations that included (1) references that had cited eligible documents and (2) references in the bibliographies of eligible documents.

### Eligibility screening

Citation files were downloaded from databases into the reference management tool, Zotero, and deduplicated.[15]

Eligibility criteria were piloted by two reviewers (S.W. and K.L.) on 20 randomly selected documents. Minor refinements were made, such as specifying that documents related to prenatal genomic testing were eligible.

### Title and abstract screening

Citations were uploaded into Covidence (systematic review software) for title and abstract screening.[16] Documents were deemed eligible if they met inclusion criteria, required further reading to determine eligibility, or had missing or ambiguous information. Two reviewers (S.W. and K.L.) independently screened 20% of the documents in tandem. A Cohen's kappa statistic of 0.88 was achieved before the reviewers independently screened the remainder.[17]

### Full-text screening

Citations were downloaded from Covidence into Microsoft Excel. Three reviewers (S.W., M.H., and K.L.) independently screened 10% of the full-text documents in tandem. A Fleiss-kappa statistic of 0.87 was achieved before each reviewer continued to screen independently.[18] Disagreements about eligibility were resolved through discussion among the core review team (S.W., M.H., K.L., and A.J.N.).

## Data items and charting

Predetermined data items were charted in Microsoft Excel (see Supplemental Information for the full list of data items). Briefly, we charted documents details (eg, author, title, year, and country), setting (eg, clinical, translational research, or unspecified research), and age/population group (eg, pediatric, adult, and prenatal). We extracted the justifications used for terms verbatim. Two reviewers (S.W. and M.H.) piloted the data charting workbook with 25% of eligible documents, resulting in removal of items that were not consistently reported (eg, whether there was mention of the pathogenicity or actionability of variants). After piloting, one reviewer (S.W.) charted independently, and these were checked for accuracy by another reviewer (K.-J.L.).

## Data mapping and synthesis

We inductively mapped the justifications used for and against terms and conducted a narrative synthesis.[19] We developed a preliminary synthesis by organizing data into tables that grouped together the same preferred term. For example, all documents supporting the term "incidental" were grouped with the various justifications noted alongside. A second set of tables combined the same or similar justifications with the accompanying terms and contextual factors (ie, setting and age/population group) noted alongside. Tables captured justifications for and against terms.

We then explored relationships within our data by visualizing the number and type of justifications and terms, as well as determining whether there were dominant contextual factors for the justifications. We defined a dominant contextual factor as appearing in >50% of the same group of justifications and incorporated these observations into the narrative synthesis. Because our review was designed to explore justifications and accompanying terms, we did not apply statistical analyses to the observed justifications, terms, or contextual factors.

Justifications were grouped into similar concepts (eg, "expectedness of the finding" or "effective communication"), and these groupings were used to organize the narrative summary. In addition, the narrative synthesis involved iterative and collaborative critical reflection. Regular meetings among the core review team provided an opportunity to discuss our interpretations of the data by drawing on our multidisciplinary knowledge, which included ethical, legal, and social issues in genomics, evidence synthesis methodology, policy, genetic counseling, and philosophy.

# Results

Fifty-two documents were included (Figure 1). Many of these were from the United States ($n$ = 18, 35%), set in the clinical context ($n$ = 29, 56%), and applied to both adult and pediatric populations ($n$ = 26, 50%). Almost half were normative documents ($n$ = 25, 48%), defined here as conceptual, nonempirical papers that "provide arguments in support of [a]… preferred view of how things ought to be."[20] Of the empirical articles reporting primary data ($n$ = 10, 19%), one reported patients' perspectives about terminology and one reported clinicians' perspectives.[21,22] In the remaining majority ($n$ = 50, 96%), justifications for terminology were based on the authors' views and beliefs. Table 1 summarizes the document characteristics.

We identified justifications for and against a variety of terms. A high degree of overlap meant that in many cases, the same justification was used to argue for or against different terms and the same terms were ascribed to different justifications (Table 2). Four main concepts capture the justifications: "expectedness of the finding," "effective communication," "relatedness to the original test indication," and "how genomic information was generated."

## Expectedness of the finding

A prominent concept invoked in justifications for and against a variety of terms was whether results can be expected or anticipated. Most commonly, "incidental" was opposed because genomic technologies are known to generate findings beyond the initial test indication.[23-34] "Unexpected,"[23,31,35,36] "unsought for,"[37-39] "unanticipated,"[37,40] "chance findings,"[35] and "secondary"[31] were also opposed on this basis. "Unanticipated" was specifically opposed in one document on the basis that the frequency of

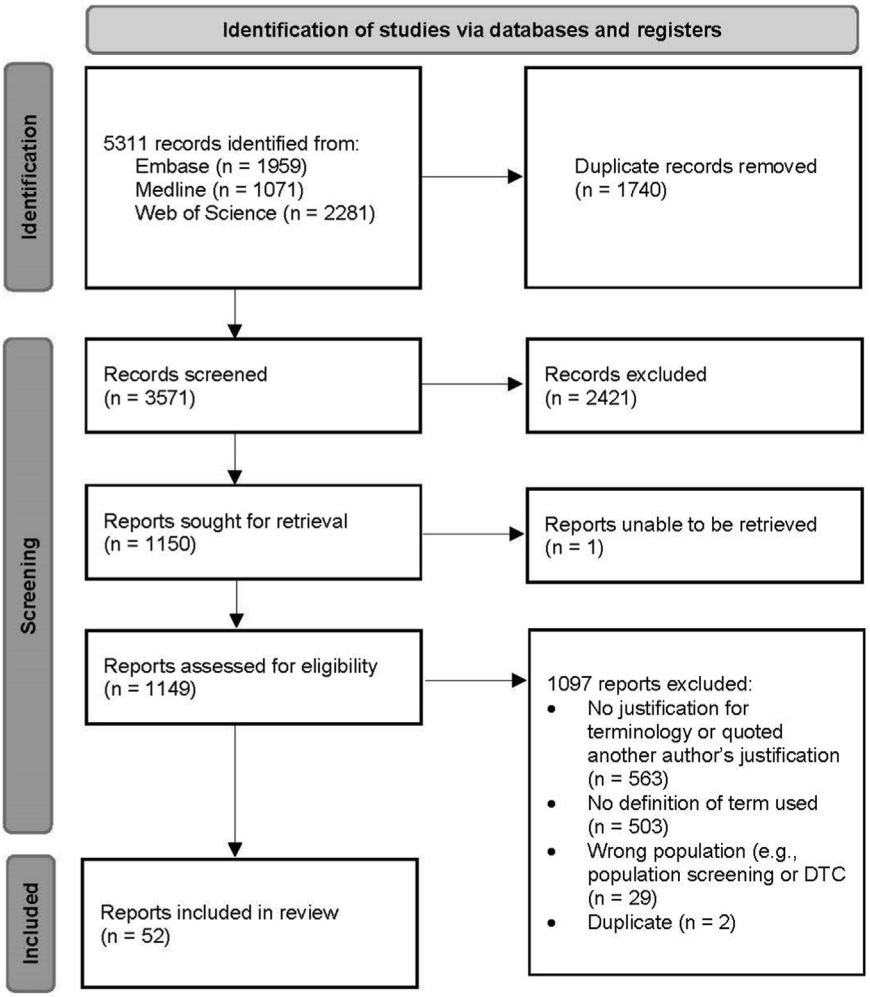


**Figure 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart.[13] From 3571 unique records, 52 were included in this review. DTC, Direct-to-consumer.

some findings can be estimated based on population frequency.[37] Further opposition to "unexpected" was based on the variable extent to which different genomic findings can be expected[41] and that the term could cast doubt on the clinician's competency.[37] A prominent argument, often given in response to the 2013 ACMG guidelines on incidental findings,[5] was that "incidental" is ill-suited to describe findings that are actively and intentionally sought.[6,26,27,29,37,39-52]

Instead, many documents proposed that terms should convey our ability to anticipate genomic findings that are beyond the initial test indication. Supported terms included "secondary,"[22,53] "unsolicited,"[23,28,31,39,54] "additional,"[23,29,34,55] "known unknowns,"[30] and "unanticipated."[25] There was prevalent support for "secondary" findings to describe results arising from the deliberate effort to uncover pathogenic variants outside of the original test indication.[6,29,42,53,56-58]

Some suggested "incidental"[42,43,58] and "individual genomic result"[27] as umbrella terms to broadly refer to findings that could and could not be anticipated. A minority supported terms to describe findings from genomic testing that could not be reasonably anticipated, including "incidental,"[22,43,53] "unsolicited,"[57] and "off-target results."[37] In the prenatal setting, "incidental" was applied to findings identified in parents because "incidental," it is argued, means "a diagnosis found unintentionally."[60]

## Effective communication

Some documents were guided toward developing widely accessible terminology. For example, "incidental" was commonly justified on the basis that it is the most often used and universally understood term.[40,48,62,63] A term not being well recognized (eg, "secondary"[59] or "unrelated"[40]), having a negative connotation (eg, "opportunistic"[40]), or having potential to cause confusion (eg, "incidental"[21,32,57,60] or "unrelated"[37]), were cited as reasons to avoid their use. Others supported terms such as "unanticipated"[26] and "additional"[21,41] because of their familiarity to patients. Several authors opposed terms such as "unrelated,"[40] "incidental,"[48] and "unexpected"[41] because the term was unable to fully capture the concept they were trying to convey.

**Table 1** Article characteristics ($N = 52$)

| Article Characteristic | *n* | % |
|---|---|---|
| First author country | | |
| United States | 18 | 35 |
| The Netherlands | 9 | 17 |
| United Kingdom | 7 | 13 |
| Belgium | 6 | 11 |
| Canada | 5 | 10 |
| Germany | 4 | 8 |
| France | 2 | 4 |
| Japan | 1 | 2 |
| Setting | | |
| Clinical | 29 | 56 |
| Both clinical and research | 14 | 27 |
| Translational research | 6 | 11 |
| Unspecified research | 3 | 6 |
| Methodology | | |
| Normative | 25 | 48 |
| Qualitative | 5 | 10 |
| Guideline | 5 | 10 |
| Nonsystematic review | 5 | 10 |
| Quantitative | 4 | 7 |
| Meeting report | 4 | 7 |
| Systematic review | 2 | 4 |
| Mixed-methods | 1 | 2 |
| Case study | 1 | 2 |
| Age/population group | | |
| Both adult and pediatric | 26 | 50 |
| Not specified | 16 | 31 |
| Adult | 6 | 11 |
| Prenatal | 3 | 6 |
| Pediatric | 1 | 2 |
| Primary focus on terminology | | |
| No | 44 | 85 |
| Yes | 8 | 15 |

Another common reason used to justify terms was their inclusion in guidelines relevant to the authors' context.[6,28,40]

In both clinical and research settings, authors argued against terms they thought misrepresented the importance of genomic findings to patients or research participants. For instance, "incidental"[21,32,37] and "secondary"[40] were thought to minimize the significance of a genomic finding. Terms such as "unrelated,"[37] "unanticipated,"[37] and "incidental"[61] were rejected because they do not help patients or research participants understand what kind of results they may receive. Furthermore, "unexpected" was deemed inappropriate because of patients' expectations that anything of clinical significance be communicated to them.[37] Conveying the importance of a genomic finding to patients or research participants was thought to be achieved with "additional,"[21] "unsolicited,"[57] and "unanticipated."[26] Some preferred "additional" because they thought it did not convey a positive or negative value.[21,41]

## Relatedness to the original test indication

A common justification for terminology choice, often in the clinical setting, was the ability to convey the finding as unrelated to the patient's clinical presentation or test indication. Many authors justified their terminology choice on this basis, highlighting that "incidental,"[60,64] "unsolicited,"[33,39,54,57] "additional,"[41,55] "unexpected,"[51,60,61] and "unanticipated"[25] all fulfilled this criterion.

Some authors thought that a term's ability to establish a link between the primary result and the finding beyond the initial test indication was important. Terms such as "secondary"[37] and "additional"[21] were supported on this basis, whereas "unsought for"[37] and "unexpected"[41] were rejected. Others rejected terms such as "primary" and "secondary," arguing that selecting terms based on establishing a relationship between findings is irrelevant.[49]

## How genomic information was generated

Justifications based on how genomic findings were generated were used to argue both for and against terms. For example, terms such as "unsought for"[37,38] and "incidental"[26] were rejected on the basis that they did not convey the amount of effort required to identify and interpret a genomic variant. "Unanticipated" was offered as a term that did not belittle the clinician's or researcher's expertise or effort required to generate a finding beyond the initial test indication.[26]

In the earlier years of its clinical application, some commentators conceived of genomic testing as a form of screening, rather than simple diagnostic testing. To reflect this distinction, "unsolicited"[33,39] and "genome-wide screening with a diagnostic indication"[35] were offered as appropriate terms.

Others wanted to move away from terms that emphasized the way findings were generated and focus instead on the result at hand. Support for "individual genomic result" was thought to achieve this because this term does not communicate the primary intention of the clinician or researcher.[27] Meanwhile, "incidental" was thought to place too much emphasis on the clinician's or researcher's intention, rather than the nature of result.[27,38] Others supported terms that simply describe a finding that should be disclosed, suggesting "research findings" as a suitable alternative.[49]

# Discussion

In this review, we identified and described justifications for and against terms used to refer to genomic findings beyond the initial test indication. Justifications were grouped into four conceptual domains, namely the expectedness of the finding, effective communication, relatedness to the original test indication, and how genomic information was generated. Conceptual overlap was evident between domains, individual justifications, and accompanying terms.

The many and varied justifications opposing "incidental" ranged from normative arguments (eg, the idea that clinicians ought to be prepared for any possible finding)

**Table 2** Summary of justifications, terms, and citing authors

| Justification | Term |
|---|---|
| *Expectedness of the finding* | |
| Justifications against terms | |
| Inappropriate because findings can be anticipated | Incidental[23-34]<br>Unexpected[23,31,35,36]<br>Unsought for[37-39]<br>Unanticipated[35,40]<br>Chance findings[35]<br>Secondary[31] |
| The frequency of some findings can be estimated based on population frequency | Unanticipated[37] |
| The extent to which a finding is unexpected can vary widely | Unexpected[41] |
| Casts doubt on the health professionals' competency to anticipate findings | Unexpected[37] |
| Inaccurate to describe findings that are actively and intentionally sought (but outside aim of original test indication) | Incidental[6,26,27,29,37,39-52] |
| Justifications for terms | |
| Conveys that these findings can be expected (ie, that "beyond scope" results may be generated) | Secondary[22,53]<br>Unsolicited[23,28,31,39,54]<br>Additional[23,29,34,54,55]<br>Known unknowns[30]<br>Unanticipated[25] |
| Conveys that there has been a deliberate search for clinically important findings | Secondary[6,29,40,53,56-58] |
| Umbrella terms to refer to findings that can and cannot be anticipated | Incidental[42,43,58]<br>Individual genomic result[27] |
| Conveys that these findings could not reasonably be anticipated | Incidental[22,43,53]<br>Unsolicited[57]<br>Off-target results[37] |
| *Effective communication* | |
| Justifications against terms | |
| It is not well recognized | Secondary findings[59]<br>Unrelated[40] |
| Has a negative connotation | Opportunistic[40] |
| Has potential to cause confusion | Incidental[21,32,57,60]<br>Unrelated[37] |
| Minimizes importance of finding to patients and participants | Incidental[21,32,37]<br>Secondary[40] |
| Does not fully capture the concept | Unrelated[40]<br>Incidental[48]<br>Unexpected[41] |
| Does not convey what kind of results patients can expect to receive | Unrelated[37]<br>Unanticipated[37]<br>Incidental[61] |
| Inappropriate because patients expect anything of clinical significance be communicated to them | Unexpected[37] |
| Justifications for terms | |
| It is the most commonly used and understood term | Incidental[40,48,62,63] |
| It is already familiar to patients | Unanticipated[26]<br>Additional[21,41] |
| It is included in guidelines relevant to authors' context | Incidental[40]<br>Secondary[6]<br>Unsolicited[28] |
| Conveys the importance of a genomic finding | Additional[21]<br>Unsolicited[57]<br>Unanticipated[26] |
| Does not convey a positive or negative value | Additional[21,41] |

*(continued)*

**Table 2** Continued

| Justification | Term |
|---|---|
| *Relatedness to the original test indication* | |
| Justifications against terms | |
| Does not establish a link with the primary findings | Unsought for[37]<br>Unexpected[41] |
| Relationship of the finding to original test indication is irrelevant | Primary finding[49]<br>Secondary finding[49] |
| Justifications for terms | |
| Conveys that the finding is unrelated to original test indication | Incidental[58,64]<br>Unsolicited[33,39,54,57]<br>Additional[41,55]<br>Unexpected[51,60,61]<br>Unanticipated[25] |
| Establishes a link between primary result and the finding | Secondary[37]<br>Additional[21] |
| *Process of generating genomic information* | |
| Justifications against terms | |
| Belittles the effort involved in identifying and interpreting a genomic finding | Unsought for[37,38]<br>Incidental[26] |
| Emphasizes researchers' intention rather than the nature of the result | Incidental[27,38] |
| Justifications for terms | |
| Does not belittle the clinician or researcher's expertise or effort | Unanticipated[26] |
| Conveys a type of genomic screening, rather than diagnosis | Unsolicited[33,39]<br>Genome-wide screening with a diagnostic indication[35] |
| Conveys that the finding "meets criteria" for disclosure | Research findings[49] |

to issues to do with perceptions of the term itself (eg, the term minimizes a finding's significance to patients). Our review has highlighted the absence of a shared understanding of "incidental," evidenced by variation in concepts underlying justifications for or against its use. We found "secondary" was widely adopted to describe the deliberate search for genomic variants outside of the initial test indication. The interplay between "incidental" and "secondary" primarily centers around the expectedness of the finding, with "incidental" deemed inappropriate because of the known capability of genomic testing to produce findings beyond the initial test indication. Meanwhile, "secondary" was accepted for its ability to convey that these findings would not only be expected but deliberately sought. However, our results may reflect the high proportion of documents pertaining to a North American context; in other regions, deliberate searching is neither routinely endorsed by professional organizations nor commonly executed.[4,33,65,66] Professional genomics organizations could assist the genomics community as they struggle to agree on the meaning of "incidental" and "secondary" by including clear definitions. Alternatively, some organizations have moved away from "incidental" and "secondary,"[33] and this could be influencing clinicians' and researchers' choice of terms.[28] Ensuring that we have a shared understanding of these commonly used terms is critical for future clinical practice, research, and policy guidance.

Inconsistency and ambiguity in the way terminology is used and justified may be explained by the variety of settings within which genomic testing is offered.[67] Different motivations, perspectives, and priorities of stakeholders are underpinned by myriad internal and external expectations of clinicians and researchers. For example, research genomic testing may be aimed at identifying variants with unknown or unclear effects. In contrast, clinical genomic testing is aimed at identifying pathogenic variant(s) in a gene known to be associated with the patient's phenotype. Communicating the relatedness of a finding to the initial purpose of testing may be more important in clinical than research settings. Our review found that terminology choices in the research setting were justified by simply appealing to the term's capacity to describe what was found, as opposed to the clinical setting, where terms tended to be justified based on their relatedness to the primary purpose of testing or how the genomic information was generated.[27,38,49] Indeed, the concept of relatedness to the initial test indication was more prevalent in discussions of naming genomic findings in documents from the clinical rather than research context. It is likely clinicians prioritize terms that help to set patients' expectations by differentiating the possible results from genomic testing.[9] A primary function of pretest genetic counseling is to facilitate client-centered discussions about the implications of genomic testing, including discussions that elicit preferences and facilitate shared decision making about disclosing findings beyond the initial test indication.[68]

Therefore, to help patients navigate consent discussions, terminology that distinguishes between results related to the purpose of testing, and other possible results may help patients to provide informed consent.

An unintended finding of our review was the absence of literature reporting patients' and research participants' perspectives about terminology. Most justifications arose from the perspectives of the document authors, rather than primary data. Although some commentators offered justifications for or against terms based on hypotheses about patients' or research participants' interpretations of terms, only one study obtained and reported empirical data on patients' perspectives.[21] Notably, this study identified a discordance between terms typically used by the genomics community ("incidental") and patients' preferences ("additional"). Balancing the views of expert stakeholders with the voices of patients and research participants is in line with emerging priorities within the genomics community, namely diversity, equity, and inclusivity.[69] In future, studies exploring the impact of genomic findings upon patients and research participants could specifically ask about the perceptions and impact of terminology. Comparing and synthesizing the definitions of terms describing genomic findings would complement this review of justifications. Developing a shared understanding will support the goals of genetic counseling, including effective communication, education, and support in interpreting genomic information.[68]

### Strengths and limitations

The concepts described in this review are inter-related, exhibiting some degree of overlap, meaning that justifications may have been synthesized differently by a different team of reviewers. We managed this by critically reflecting upon our assumptions and holding regular team meetings. In addition, the heterogeneity of terms means that it is possible some documents were missed in this review.[7] Because of resourcing, we were only able to include documents written in English but acknowledge that similar and important debates are taking place globally. Justifications for terminology in languages other than English may have provided additional insights. Our search methods were limited to the specified academic databases. As such, except for forward and backward searching, some types of materials (such as book chapters or gray literature) may not have been identified. The review is strengthened by the expertise of our interdisciplinary team and by conducting the review in accordance with established evidence synthesis guidelines.

### Conclusion

Our review has highlighted an abundance of justifications used to support and oppose a variety of terms to describe genomic findings beyond the scope of the original test. Justifications were synthesized into four overarching concepts: "expectedness of the finding," "effective communication," "relatedness to the original test indication," and "how genomic information was generated." Our review identified broad opposition to using "incidental" in the genomics context, although reasons for opposing its use vary widely. Different terms may be suited to clinical and research contexts respectively because of their distinct goals and priorities. Future research could use these findings as a conceptual map for stakeholder consultations, which should amplify patients' voices. Developing widely agreed-upon terminology will support effective communication as we move toward a consensus on ethical management of genomic findings beyond the initial test indication.

## Data Availability

Data are available upon request by contacting the corresponding author.

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## Ethics Declaration

Ethical approval was not sought because this was a secondary analysis of published data. No human or animal participants were involved in this review.

## Conflict of Interest

The authors declare no conflicts of interest.

## Additional Information

The online version of this article (https://doi.org/10.1016/j.gim.2023.100936) contains supplemental material, which is available to authorized users.

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Appendix 3

# Briefing Paper: Terminology for genomic findings beyond the original test indication

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*September 2023*

Australian Genomics

## What is the issue?

An inherent aspect of genome sequencing is that it can generate findings beyond the initial test indication. These findings may be relevant to a patient or research participant's health, and generate three key questions:

1. What should such findings be called? Should terminology vary between settings or contexts?
2. What should be done with such findings when they arise unexpectedly?
3. Should such findings be deliberately searched for? If so, under what conditions?

Australian Genomics is addressing these questions over the course of two workshops.

In *Workshop 1* we will address the first question. Consensus regarding terminology used to describe these findings has remained elusive, with a variety of terms in use globally. Aside from 'incidental', descriptors include 'secondary', 'unsolicited', 'unexpected', 'unsought for' and 'additional', to name a few. The interchangeable and inconsistent use of these terms in research, clinical practice, and the literature impede our progress toward their ethical management.

In *Workshop 2* we will address the second and third questions. To date in Australia there is no national consistency in policy or practice regarding how to approach the reporting or deliberate seeking of such findings. *information about the second workshop will be provided soon.*

## Why is terminology for these findings important?

As genomic medicine moves into the mainstream, its effective integration requires a basic understanding of key concepts and terms amongst all relevant healthcare professionals, patients and the public. Education and resources about genomic findings for non-genetic healthcare professionals and patients will need to include information about genomic findings that are beyond the initial test indication. The terms, and accompanying definitions, should be agreed upon by the genomics community, including patients.

In a clinical context, lack of clarity in terminology about genomic findings engenders confusion and increases the likelihood of miscommunication between and among healthcare professionals and patients. Consistent, standardised terminology will facilitate effective communication between healthcare professionals as well as in interactions with patients. Accessible, readily understood language is crucial for patients to make informed decisions. Agreeing upon the terms used to describe genomic findings will give patients a consistent experience, and support clear communication about results, including what these findings are, what they mean, and what the next steps are.

Further, developing agreed-upon terminology will support meaningful debate about ethical management of genomic findings beyond the initial test indication. This, in turn, will support progress towards developing professional consensus guidelines. This is important because guidelines must reflect appropriate clinical and ethical management of many different types of genomic findings and use terms that are understood by the genomics (and wider) community.

# Where does the issue arise?

The question of what to call findings beyond the initial genomic test indication arises in a variety of settings:

- In **clinical care (including clinical care delivered under a research protocol)**, a finding unrelated to the test indication could arise when, for example, an exome sequence is performed with the aim of identifying the underlying cause of developmental delay in a child. Here, a finding unrelated to the clinical indication could arise while analysing the exome data. A pre-determined set of genomic findings beyond the initial clinical indication could also be deliberately sought.

- In population health and basic research, a finding beyond the initial test/sequencing indication can also arise.
    - While genomics is not yet in routine use in population screening in Australia, projects to model what this might look like are underway. Decisions about reporting or deliberately searching for findings beyond the scope of the screening program or screening test will need to be made as part of the design of any screening offer.
    - In basic research, including cohort studies, findings may be discernible from data interrogation by bioinformaticians, or data could be reinterpreted to offer a selection of results to study participants. There is some guidance on such findings in the NHMRC's *National Statement on Ethical Conduct in Human Research*.

**While we acknowledge that population health and basic research are important areas, please note that the two workshops will focus on the clinical care setting only.**

# What has happened to date?

## Justifications for terms used

We have recently published a scoping review that reports on the justifications used for and against terms:

White S, Haas M, Laginha KJ, Laurendet K, Gaff C, Vears D, Newson AJ. What's in a name? Justifying terminology for genomic findings beyond the initial test indication: a scoping review. *Genet Med. 2023;25(11):100936.* *doi: 10.1016/j.gim.2023.100936*

## Practices in Australia

Laboratory policies and practices have been surveyed by Tudini and colleagues:

Tudini E, Haas MA, Mattiske T, Spurdle AB. Reporting clinically relevant genetic variants unrelated to genomic test requests: a survey of Australian clinical laboratory policies and practices. *J Med Genet. 2023;60(6):609-614.* *doi: 10.1136/jmg-2022-108808*

## Australian policy context

The Commonwealth Department of Health and Aged Care is keen to explore a consistent policy position regarding both terminology and the approach to genomic findings beyond the initial test indication.

- The *National Health Genomics Policy Framework* (2018-present) includes the following:

> - **Secondary findings**
>
> Secondary findings are gene variants that are identified during testing, but are unrelated to the patient's clinical presentation and the primary investigation for which the genomic test is performed. With the rapid increase in genomic testing, the prevalence of secondary findings has grown. Secondary findings can be complex and sensitive because of the potential to impact other members of the family.
>
> There is currently no national agreement on what constitutes a best practice approach to secondary findings, with arrangements differing between states and territories. There is also no agreed position on whether there is a responsibility for existing genomic information to be reanalysed as new genomic knowledge emerges.
>
> ***The secondary findings challenge***
>
> Whilst secondary findings offer an opportunity to proactively engage with medical conditions, they also present policy challenges in relation to community literacy and service delivery.
>
> Engaging with secondary findings will depend largely on how well-informed patients are and how consent processes are structured. From a service delivery perspective, a nationally consistent process on how secondary findings are approached should form part of national guidance on bioethics in the context of public health policy. Guidance is also required to clarify the roles and responsibilities of medical professionals in presenting secondary findings.
>
> A further complex policy consideration is around data retention and the responsibility or expectation that those patients that have consented will have their records retested against new genomic knowledge to uncover health conditions. This may mean that in the future it will be necessary to develop an agreed national position on those conditions for which there is sufficient evidence that existing genomic data should be reanalysed.

*See: NHGPF Supplementary Information, p14*

- The National Pathology Accreditation Advisory Council (NPAAC; now overseen by the Australian Commission on Quality and Safety in Health Care) requires laboratories to have a policy about such findings. See:
  - Requirements for human medical genome testing utilising massively parallel sequencing technologies (First Edition 2017)
  - Requirements for medical testing for human genetic variation (Third Edition)

  NPAAC uses the terms 'incidental' in the 2017 MPS guidelines, and 'unsolicited' in the 2023 human genetic variation guidelines.

# What terms have been put forward? What justifications – both for and against – have been offered?

Our scoping review of justifications for and against terms used to describe findings beyond the initial test indication identified that **at least 17 terms** have been used since 2010. The following table presents these, with justifications for and against. For a full synthesis, please see our recent *Genetics in Medicine* paper (linked to above).

***Table 1*** *- Justifications of Terms*

| Term | Reasons For | Reasons Against |
|---|---|---|
| ***Incidental*** | • Conveys that findings from genomic testing could not be reasonably anticipated<br>• Can convey an unintentional diagnosis (for example, a diagnosis in parents in the prenatal setting)<br>• The term itself is commonly used in the relevant literature | • Ill-suited to describe findings that are actively and intentionally sought<br>• May cause confusion for patients as the term is uncommon/ unfamiliar<br>• May cause confusion as the term is used inconsistently in the literature<br>• May minimise the significance of the finding<br>• May be misleading as genomic technologies are known to generate findings beyond the initial test indication<br>• Does not convey meaningful information to patients<br>• May trivialise the amount of time or degree of effort required to identify and interpret a genomic variant<br>• Emphasises intention rather than the nature of the result |

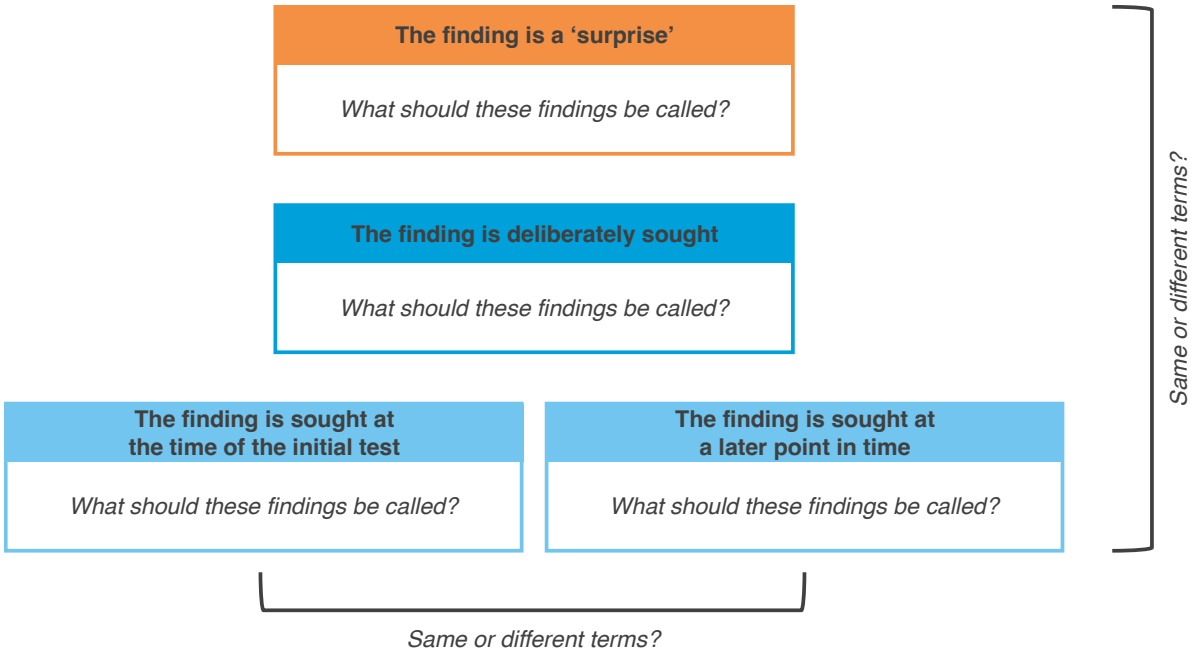
| Term | Reasons For | Reasons Against |
|---|---|---|
| ***Secondary*** | • Appropriate when used to describe results arising from the deliberate effort to uncover pathogenic variants outside of the original test indication – e.g., ACMG guidelines<br>• Establishes a link between the primary result and the finding beyond the initial test indication<br>• Conveys that these results can be expected from genomic sequencing | • May imply that the finding is unexpected or accidental, whereas genomic technologies are known to generate findings beyond the initial test indication<br>• May minimise the significance of the finding<br>• Already has another meaning in medicine (e.g., secondary infertility)<br>• May not be a well-recognised term in some parts of the world |
| ***Additional*** | • Familiar to patients<br>• Does not convey a positive or negative value of the result<br>• Establishes a link between the primary result and the finding beyond the initial test indication<br>• Conveys the importance of the finding | • No specific criticisms identified |
| ***Unsolicited*** | • Where findings from genomic testing could not be reasonably anticipated<br>• Conveys that findings may be unsought for whilst being anticipatable/ expected due to the nature of genetic testing technologies<br>• The term is already used in some relevant guidelines | • Predominantly used in Europe |

| Term | Reasons For | Reasons Against |
|---|---|---|
| ***Unexpected*** | • Beyond the initial test indication<br>• Appropriate because the extent to which genomic findings can be expected may vary<br>• Conveys that the result is unrelated to the primary reason for testing | • Genomic technologies are known to generate findings and thus may cast doubt over clinician competency<br>• Does not fully capture the types of results patients may receive/ does not convey meaningful information to patients<br>• Gives impression nothing of clinical significance will be conveyed<br>• Does not establish a link with the primary findings |
| ***Unanticipated*** | • Familiar to patients<br>• Does not belittle clinicians' expertise or minimise the effort required to generate a finding beyond the initial test indication | • Genomic technologies are known to generate findings beyond the initial test indication<br>• May be misleading as the frequency of some findings can be estimated based on population frequency<br>• Does not explain the types of results patients may receive |
| ***Others**** | • May be useful where a finding could not be anticipated | • These umbrella terms do not convey the primary intention<br>• Some may cause confusion and or have a negative connotation (e.g. 'opportunistic findings')<br>• Some may not explain type of result that will arise<br>• Some may not convey the effort required to identify and report genetic variants |

**e.g. unsought for, individual genomic result, known unknowns, off-target results, chance findings, unrelated, opportunistic, genome-wide screening with a diagnostic indication, primary finding, research findings*

# What is the task for Workshop 1?

We are aiming to define preferred terminology for these findings for clinical practice in Australia. The following diagram may help us in our decision-making:



Appendix 4

mosaicLAB

# Australian Genomics: terminology for genomic findings

## WORKSHOP 1 AGENDA

5 September 2023

| LOGISTICS | |
|---|---|
| Location | Zoom https://us02web.zoom.us/j/81584766988<br>Passcode: 389742 |
| Date and time | Tuesday 5 September 12-3pm |
| Facilitators | Nicole Hunter and Keith Greaves, MosaicLab |

| PURPOSE AND SUCCESS | |
|---|---|
| Purpose | To agree on consistent terminology to describe genomic findings beyond the original test indication |
| What does success look like? | The workshop will provide an opportunity to:<br>• share learnings from the project's research<br>• agree on consistent terminology for genomic findings under different contexts<br>• outline next steps |

## WHAT SHOULD WE CALL GENOMIC FINDINGS BEYOND THE INITIAL TEST INDICATION, AND WHAT SHOULD WE DO ABOUT THEM IN AUSTRALIA?

| TIME | NOTES | OUTCOMES |
|---|---|---|
| 11:45am | Arrivals and tech checks | |
| 12:00pm | Getting Started<br>Purpose of the session, agenda, introductions and a chance to share the experiences and hopes we are bringing to the session today. | Participants feel prepared to begin |
| | An introduction by Ainsley/Matilda<br>Background to the project, where we are up to in the process and a sense of the scale of the challenge ahead. | Understand the background |
| | Discussion on outcomes of our work to date<br>What stands out? What is apparent? What questions are still emerging? Whether terms should differ with the context in which they are used? | Questions answered and ready to explore key terminology |
| | Exploring the possible terms<br>Review and add to the list of terms to consider today | Have a clear list of possible terms to discuss and assess |
| 1:20pm<br>(15 mins) | BREAK | Step away from the desk and get some air! |
| | Assessing the terms (Step 1)<br>In smaller groups we will discuss what is for and against each of these terms under different contexts | We are clear on what each terms pros and cons are |
| | Assessing the terms (Step 2)<br>Under each context individuals will then rank the terms and provide reasons. As a group we will explore results and understand what it means. | Clarity on which terms are preferred under what contexts |
| | Taking stock, check out and next steps<br>How did we go? What is unresolved and where to next? | Clear about next steps – workshop 2 and what it will aim to do |
| 3:00pm | Workshop ends | |

Appendix 5

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# AUSTRALIAN GENOMICS TERMINOLOGY FOR GENOMIC FINDINGS

## WORKSHOP 1

What was said report

5 September 2023

# TABLE OF CONTENTS



*What should we call Genomic findings beyond the initial test indication, and what should we do about them in Australia?*

# INTRODUCTION

## OVERVIEW

On September 5th, 50 key stakeholders from various sectors across Australia, including policy makers, clinicians, genetic counselors, researchers (both in genetics and bioethics), population health experts, representatives from patient experience groups and interested observers, participated in a three-hour online workshop hosted by the Australian Genomics project team and facilitated by MosaicLab facilitators Nicole Hunter and Keith Greaves.

The primary focus of the workshop was to address the question:

*What should Australian Genomics call genomic findings beyond the initial test indication?*

This first session was to agree (or find super majority acceptance) of a term/s to be used in different contexts. A four-hour in-person meeting will follow this online workshop, culminating in finalising some principles for implementation of this terminology in Australian policy.

## WORKSHOP PURPOSE

The session gave participants an opportunity to agree on consistent terminology to describe genomic findings beyond the original test indication. The workshop provided an opportunity to:

- Share learnings from the projects research
- Agree on consistent terminology for genomic findings under different contexts
- Outline next steps

# PARTICIPANTS

Representatives from over 15 different organisations attended the session. Attendees are listed below with a 'category' identified for their main area of expertise/interest.

| NAME | ORGANISATION |
|---|---|
| **Sarah Jelenich** | *Australian Genomics* |
| **Sophie Bouffler** | *Australian Genomics* |
| **Bronwyn Terrill** | *Australian Genomics (genetic education)* |
| **Amanda Willis** | *Clinical and genetic counselling* |
| **Belinda Creeighton** | |
| **Jenny Eaton** | *Clinical and genetic counselling (NZ rep)* |
| **Kirsten Boggs** | *Clinical and genetic counselling* |
| **Zornitza Stark** | *Clinical and genetic counselling* |
| **Jennifer Borowsky** | *Clinical and genetic counselling* |
| **Julie McGaughran** | *Clinical and genetic counselling* |
| **Michelle de Silva** | *Clinical and genetic counselling* |
| **Amy Nisselle** | *Ethics and policy* |
| **Caitlin Howley** | *Ethics and policy* |
| **Jane Nielsen** | *Ethics and policy* |
| **Lisa Dive** | *Ethics and policy* |
| **Melissa Martyn** | *Ethics and policy* |
| **Carolyn Johnston** | *Ethics and policy* |
| **Dianne Nicol** | *Ethics and policy* |
| **Alice McCarthy** | *Ethics and policy (Indigenous)* |
| **Kaashifah Bruce** | *Ethics and policy (Indigenous)* |
| **Louise Lyons** | *Ethics and policy (Indigenous)* |
| **Breanna Gallagher** | *Government (Commonwealth - policy)* |
| **Neil Everest** | *Government (Commonwealth - policy)* |
| **Saras Menon** | *Government (State/Territory)* |
| **Sadia Afrin** | *Government (Commonwealth - policy)* |
| **Ari Horton** | *HCP (non-genetics)* |
| **Lucy Fox** | *HCP (non-genetics)* |

| NAME | ORGANISATION |
|---|---|
| **Kishore Raj Kumar** | *HCP (non-genetics)* |
| **Bryony Thompson** | *Laboratory research* |
| **Gladys Ho** | *Laboratory research* |
| **Peter Kaub** | *Laboratory research* |
| **Sebastian Lunke** | *Laboratory research* |
| **Ben Lundie** | *Laboratory research / standards* |
| **Chiyan Lau** | *Laboratory research* |
| **Eric Lee** | *Industry* |
| **Jeremy Kenner** | *NHMRC* |
| **Lauren Hunt** | *HGSA (standards)* |
| **Vanessa Cameron** | *RCPA (standards)* |
| **Falak Helwani** | *Patient representative/group* |
| **Monica Ferrie** | *Patient representative/group* |
| **Ainsley Newson** | *Project team* |
| **Clara Gaff** | *Project team* |
| **Danya Vears** | *Project team* |
| **Gabriel Watts** | *Project team* |
| **Kirsten Laurendet** | *Project team* |
| **Matilda Haas** | *Project team and AG* |
| **Stephanie White** | *Project team* |
| **Amanda Spurdle** | *Research* |
| **Samantha Croy** | *Research* |
| **Yassine Souilmi** | *Research* |

# WORKSHOP AGENDA

| TIME | NOTES | OUTCOMES |
|---|---|---|
| 11:45AM | **Arrivals and tech checks** | |
| 12:00PM | **Getting Started**<br>Purpose of the session, agenda, introductions and a chance to share the experiences and hopes we are bringing to the session today. | *Participants feel prepared to begin* |
| | **An introduction by Ainsley Newson**<br>Background to the project, where we are up to in the process and a sense of the scale of the challenge ahead. | *Understand the background* |
| | **Discussion on outcomes of our work to date**<br>What stands out? What is apparent? What questions are still emerging? Whether terms should differ with the context in which they are used? | *Questions answered and ready to explore key terminology* |
| | **Exploring the possible terms**<br>Review and add to the list of terms to consider today | *Have a clear list of possible terms to discuss and assess* |
| 1:20PM (15 MINS) | **BREAK** | *Step away from the desk and get some air!* |
| | **Assessing the terms (Step 1)**<br>In smaller groups we will discuss what are the reasons for and against each of these terms under different contexts | *We are clear on what each terms pros and cons are* |
| | **Assessing the terms (Step 2)**<br>Under each context individuals will then give a sense of their level of comfort with the terms and provide reasons. As a group we will explore results and understand what it means. | *Clarity on which terms are preferred under what contexts* |
| | **Taking stock, check out and next steps**<br>How did we go? What is unresolved and where to next? | *Clear about next steps – workshop 2 and what it will aim to do* |
| 3:00PM | **Workshop ends** | |

# RESULTS

## HOPES & ADVICE

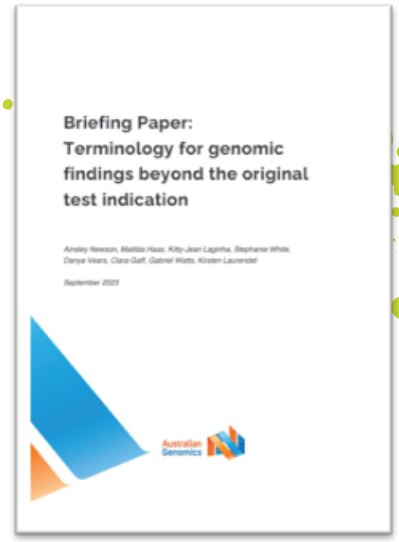
In preparing for the day, participants were invited to consider what hopes and advice they had for each other to stay focused on the clinical setting of the session.


*...continued overleaf*


National agreement
Aim to achieve equity in access to and standard of care
Provide a positive space to talk about this result
Learning perspectives from all parts of the sector
It would be good to have consistency with international as well as national approaches
Consider that several terms have racist roots (eugenics) or originated in research on model organisms. E.g., ancestry, admixture, etc.
Culturally safe, end to end genetic health pathways
I hope we stay focused on the way we communicate to patients
Consistency of terms across lab and clinic, using terms that make sense to the patient/client
Achieve consistency for patients, clinicians, and others
Developing a consistent approach
Culturally appropriate resources for Aboriginal and Torres Strait Islander people
Consistent + layered national approach for labs, Drs, and patients
Incidental finding can be grey - is a finding really different from patient's presentation, or just lack of clinical information
Facilitating patient understanding of pathology results
Find a term that minimises patient confusion about what this offer is compared to diagnostic
Focused reason for testing in the first place
Focus on communication and engagement with patients

# INSIGHTS FROM BRIEFING PAPER

Participants were asked to review the briefing paper "Terminology for Genomic Findings Beyond the Initial Test Indication," and reflect on notable insights and any lingering questions. The questions raised by participants have been loosely themed.




## INSIGHTS FROM THE PAPER

The differing contexts are important - the spoken language used with the patient/family, the written language in the consent form, the formal reporting language on a lab report

Had not considered the "surprise" aspect associated with terms like incidental.

Critical to ask community members their thoughts

| THEME | QUESTIONS | COMMENTS |
|---|---|---|
| **Categories and Distinctions** | Are there three categories rather than two? E.g., primary, secondary, additional/unanticipated/ incidental ... | We will know later today |
| | clarifying difference between expected from technical perspective (wider panel, doing chromosome work) versus expected from patient/clinical perspective (indication for testing)? | Linked to question about "terms for a patient" |
| | The terms need to be contextualised to the test purpose- what is the intended primary purpose, a secondary purpose, a research question. Then use a term (not a single word) per setting? | Are these categories clearly distinct or do they have some overlap |
| | Is the distinction between deliberately sought or not relevant when talking to patients? In my experience, this kind of delineation is not so important when returning the result? | |
| | When seeking additional findings i.e., reproductive screening following primary analysis, is this secondary or is this just an alternative primary investigation? | |

*...continued overleaf*

| THEME | QUESTIONS | COMMENTS |
|---|---|---|
| **Categories and Distinctions** | What would be the utility in differentiating between surprise vs deliberately searched, and at initial test vs later reanalysis? | |
| **Consistency and Analysis** | Is there an iterative terminology process required? | We should be clear that we are not denying people their voice |
| | Do we focus on "clusters" of terms that fit the context? | This is part of the conversation after the break. |
| | Why is predominant use in Europe a reason against use of 'unsolicited'? | Reason that was critiqued in the literature. Most European policy documents take a conservative approach compared to America. There were terms that had critique in the literature. |
| | Was there any analysis regarding which kind of document the term was found in? For instance, was the term incidental findings more often seen in research related documents? | Didn't focus on the analysis but there was variety |
| | All six proposed terms (other than 'others' are relative. Therefore, don't we need to have consensus on the term with which each term contrasts as part of this process? E.g. primary, secondary, expected, unexpected, intended, incidental, sought, unsolicited, indicated, additional, anticipated, unanticipated. | |
| **Context and language Use** | Can we use different terms in different contexts? It seems to me that perhaps the most relevant term for patients is 'additional', but in the lab it may be necessary to keep the distinction between secondary and incidental | Primary driver for the testing and where is the testing taking place? |
| | How do we ensure terms are appropriate in different cultural groups | |
| | How do we ensure that clinician is using same language with patients/consumers as laboratories - consistency? | |
| **Probabilistic vs Deterministic Language** | How do we move away from deterministic language to probabilistic (e.g., strata of risk/ chance) as that is what the technology/science is giving us as a result? | |

*...continued overleaf*

| THEME | QUESTIONS | COMMENTS |
|---|---|---|
| **Terminology Appropriateness and Impact** | How do we account for patients understanding terms differently? Not all clinicians will spend time with patients to explain what the term means or discuss the patient's understanding of the term. Receiving a diagnosis/finding is such an emotional and pivotal experience for patients. Ensuring that patients understand the meaning of the terms used is incredibly important. | We realise patients voice has not been used much to date and this is a reason to do this nationally |
| | Is there a need to have one term for the patient. i.e. the way the finding was found may be irrelevant, but the outcome is that something that doesn't explain my condition has not been found. Alternatively, there may be a reason to define the difference between sought vs unsought findings in the laboratory for policy reasons. | Relates to another question that clarifies the stakeholder |
| | How to ensure terminology is succinct and accurate in a short space so truncation of lengthy terms doesn't happen or doesn't cause issues to clinicians or patients | Agree |
| | Can this be considered a 'screening test' (i.e., European suggestion) | |
| **Utility and comparative Analysis** | What is the key driver of the terminology decision? Technical correctness, comprehensibility, both, others? | It could be all these things depending on the stakeholder. We might prioritise different ideas depending on who you are. |
| | When the term "surprise" is used, who is this a surprise for? The lab, the patient, the doctor? | All the above but not at the same time. Do not get to hung up on the term 'surprise'. It was explaining the context. |
| | Is it counterproductive to 'solve' the issue with respect to the clinical context without reference to the research contexts (multiple) when we may want consistency between the multiple contexts (if that is possible)? | |
| | Importance of consistent terminology in consent vs the results | |
| | Is there evidence that any one term is better or less harmful than another? | |

# EXPLORING POSSIBLE TERMS

In small groups, participants reviewed the possible terms to describe genomic findings beyond the original scope. They decided to add the term 'unrelated' to the original list of six key identified terms, considering it an important addition to enhance the terminology options for the deeper dive sections of this workshop.

## KEY IDENTIFIED TERMS FOR DEEP DIVE

### Unexpected

GC in our group mentioned that they would often use this with patients. Primary/Secondary less relevant to patients in this GC's experience (but obviously need to ask patients too). So long as explanation clear, don't really mind the word.

Often makes sense to patient.

Intended? Inadvertent (might be less widely understood).

Unexpected and expected for 'surprise' and deliberate - two sides.

Most things can be expected from a technical perspective.

### Additional

Again, noting alignment with international standards/lab practices, also this is helpful to both labs and patients - it doesn't diminish the purpose of the original genetic test

Consider as an umbrella term that makes sense colloquially, while on the lab/ clinical side there could be delineation between those actively sought or not, etc.

Encapsulates all the terms simplistically for all.

Has neutral connotations and is easily understood.

### Unsolicited

Of the yellow 6, I think this would be the most challenging for a patient to understand.

Not patient friendly.

### Unanticipated

The same as unexpected.

### Incidental

Parallel with use in non-genomics areas of health care (e.g., radiology).

### Unrelated[1]

Like other comments ad not related to primary reason.

I think this is a good term to communicate with patients.

Could be used as part of a definition.

I like it.

### Secondary

[1] N.B. 'Unrelated' was added by the participants as a term which should be included in the deeper dive sections of this workshop.

# OTHER TERMS

### Primary finding

Is this relating to the primary result of the test or a 'surprise' result?

Seems logical to include this - isn't it important for the patient.

Has to be included.

Lab person in our group mentioned they tend to use this from a lab point of view rather than a patient point of view.

### Known unknowns

Would be VERY difficult to explain this to a patient.

Too many political connotations.

Very confusing.

### Off-target results

Good.

Potential for confusion with targeted therapy? But note 'on target' and 'off target' are prob well understood by the general public.

### Unsought for

More patient friendly than unsolicited.

Thinking from patient perspective, anything that 'diminishes' the original reason for testing is quite confusing. So 'unsought for' raises confusion about the purpose. Perhaps again, slightly different terms on lab reports vs test results/patient reports?

### Chance findings

Good alternative to "incidental finding", this is often language I would use to describe what an incidental finding actually is when discussing with patients.

Could raise mistrust? how did you find something by chance?

### Research findings

If the work is in research program, then GC might use it. But this would not be for clinically validated test in clinically validated lab. A research finding (and ability to act on it) would be distinct from primary finding or clinical finding. If a research finding can't act on it - so distinction is drawn with patient.

**Individual genomic result**

**Opportunistic**

**Genome-wide screening with a diagnostic indication**

# ASSESSING THE TERMS REASONS FOR & AGAINST

In small groups, participants discussed and listed the reasons for and against each of the seven key identified terms.

| TERM | REASONS FOR | REASONS AGAINST |
|---|---|---|
| **Additional** | Allows for future adjustment in reporting approaches without changing the terminology | Can have a positive connotation - additional findings sounds like a good thing<br>*(Could you clarify? I think the OP (not me) is saying that this term itself implies that these findings should be sought, or reported when found, i.e., presupposing the next step, c.f. having a term that is more neutral as to whether such findings should always be sought/reported/returned etc.)* |
| | Can be used for multiple contexts and to support discussion about the implications of the finding with patients | Could connote lack of consent ("you've done additional tests that haven't been consented to"). |
| | Conveys the importance of the finding | Could diminish importance of finding |
| | Does not convey a positive or negative value of the result | Doesn't differentiate between actively sought vs incidental finding |
| | Establishes a link between the primary result and the finding beyond the initial test indication | Makes it difficult to differentiate between the primary reason for testing and the 'additional' finding. Additional would need some further explanation (e.g., that we weren't expecting it, that it is related/unrelated to the primary reason for testing) |
| | Familiar to patients | Potential for confusion that the "additional" finding is still related to primary patient presentation |
| | Largely neutral statement, less emotional inference | Very bland / beige - does it convey significance? |
| | Least problematic if a bit beige/woolly | Would need some further explanation. Additional to what? |
| | Most plain language of all options | |
| | Takes away value judgement | |

*...continued overleaf*

| TERM | REASONS FOR | REASONS AGAINST |
|---|---|---|
| **Incidental** | Alignment with ACMG guidelines | Conveys a negative connotation for a finding that in all likelihood (with the appropriate reporting procedures) is important for the person/family |
| | Also used in other medical contexts e.g., radiology, so brings some familiarity | Does not convey meaningful information to patients |
| | Can convey an unintentional diagnosis (for example, a diagnosis in parents in the prenatal setting) | Emphasises intention rather than the nature of the result *(sounds hard to explain to a patient, and negative connotations - sounds like it should be used to explain a mistake)* |
| | Conveys that findings from genomic testing could not be reasonably anticipated *("some findings"?)* | If we are reporting critical but off target results in all individuals this is not incidental - it is important public health information about known risks associated with a result that have interventions to reduce risk and improve quality and or quantity of life in the patient and potentially many family members |
| | Term is in use in other health domains, e.g., radiology | Ill-suited to describe findings that are actively and intentionally sought |
| | The most widely used | Infers a lack of consequence, but this may not be always true |
| | The term is commonly used internationally | internet search suggests that incidental means less important |
| | The term itself is commonly used in the relevant literature | May be misleading as genomic technologies are known to generate findings beyond the initial test indication |
| | | May cause confusion as the term is used inconsistently in the literature |
| | | May cause confusion for patients as the term is uncommon/ unfamiliar |
| | | May minimise the significance of the finding |
| | | May trivialise the amount of time or degree of effort required to identify and interpret a genomic variant |

*...continued overleaf*

| TERM | REASONS FOR | REASONS AGAINST |
|---|---|---|
| **Incidental** *...continued* | | Most widely used but may not be adequately descriptive. |
| | | Outdated term that implies desire to avoid these findings and ties us into the notion that these should be avoided |
| | | Term not widely understood by non-professionals |
| | | There is a difference between not (technically) anticipated and an unwillingness so see/deal with these variants. |
| | | Widely understood by medical professionals but not plain language for patients |
| | | Works better in research context |
| **Secondary** | Alignment and definition in ACMG guidelines | Already has another meaning in medicine (e.g., secondary infertility) |
| | Appropriate when used to describe results arising from the deliberate effort to uncover pathogenic variants outside of the original test indication e.g., ACMG guidelines | May imply that the finding is unexpected or accidental, whereas genomic technologies are known to generate findings beyond the initial test indication |
| | Consistent with US | May minimise the significance of the finding |
| | Conveys that these results can be expected from genomic sequencing *(Using this would be consistent with ACMG/AMP which labs in Australia use as the main reference.)* | May not be a well-recognised term in some parts of the world |
| | Establishes a link between the primary result and the finding beyond the initial test indication | Suggests aiming for it from the outset. (So may not work with 'surprise' findings) |
| | Explains what is happening | Works best as part of a three-part structure with primary-secondary-unanticipated/incidental |
| | Good complement to 'primary' *(How many labs are actually using "primary finding" on their reports or in other material?)* | |

***...continued overleaf***

| TERM | REASONS FOR | REASONS AGAINST |
|---|---|---|
| **Secondary** *...continued* | Understandable for patients | |
| | Widely used | |
| **Unanticipated** | Does not belittle clinicians' expertise or minimise the effort required to generate a finding beyond the initial test indication | Does not explain the types of results patients may receive *(Was this a deliberate move into the 'for' column?)* |
| | Easier for people that don't speak English as first language | Frames it in a negative light |
| | Familiar to patients | Genomic technologies are known to generate findings beyond the initial test indication |
| | | Harder to grasp c.f. unexpected. Unanticipated is a more complex term |
| | | May be misleading as the frequency of some findings can be estimated based on population frequency |
| | | Sounds like lab don't know what they are doing, as if found by accident |
| | | The implied surprise is unnecessary |
| **Unexpected** | Appropriate because the extent to which genomic findings can be expected may vary | Could create distrust between clinician and patient |
| | Beyond the initial test indication | Does not establish a link with the primary findings |
| | Conveys that the result is unrelated to the primary reason | Does not fully capture the types of results patients may receive/does not convey meaningful information to patients |
| | Familiar word to patients | Element of surprise is misleading if appropriate counselling provided and depending on how the lab process is structured |
| | For testing *(Would this be the most useful to cover unexpected in terms of mixed samples etc?)* | Emotive undertone |

***...continued overleaf***

| TERM | REASONS FOR | REASONS AGAINST |
|---|---|---|
| **Unexpected** *...continued* | | Frames it in a negative light |
| | | Genomic technologies are known to generate findings and thus may cast doubt over clinician competency |
| | | Gives impression nothing of clinical significance will be conveyed |
| | | Has implications on prevalence |
| | | not a neutral term |
| | | Same as 'unanticipated' but more negative connotations, so unanticipated is preferable |
| | | Some results, although not 'primary' may be reasonably expected |
| | | Sounds like lab don't know what they are doing, as if found by accident |
| **Unsolicited** | Conveys that findings may be unsought for whilst being anticipatable/ expected due to the nature of genetic testing technologies | "Sought by means of an invitation or request". Raises questions as to who requested it - not the patient, surely. |
| | The term is already used in some relevant guidelines | Difficult to understand and conveys value judgement |
| | Where findings from genomic testing could not be reasonably anticipated | Frames it in a negative light |
| | | Hard to use with patients |
| | | Has negative connotation - implies unasked for or unwanted |
| | | Just don't like how it sounds |
| | | Legalese |
| | | Meaning is 'asked for |
| | | Predominantly used in Europe |

***...continued overleaf***

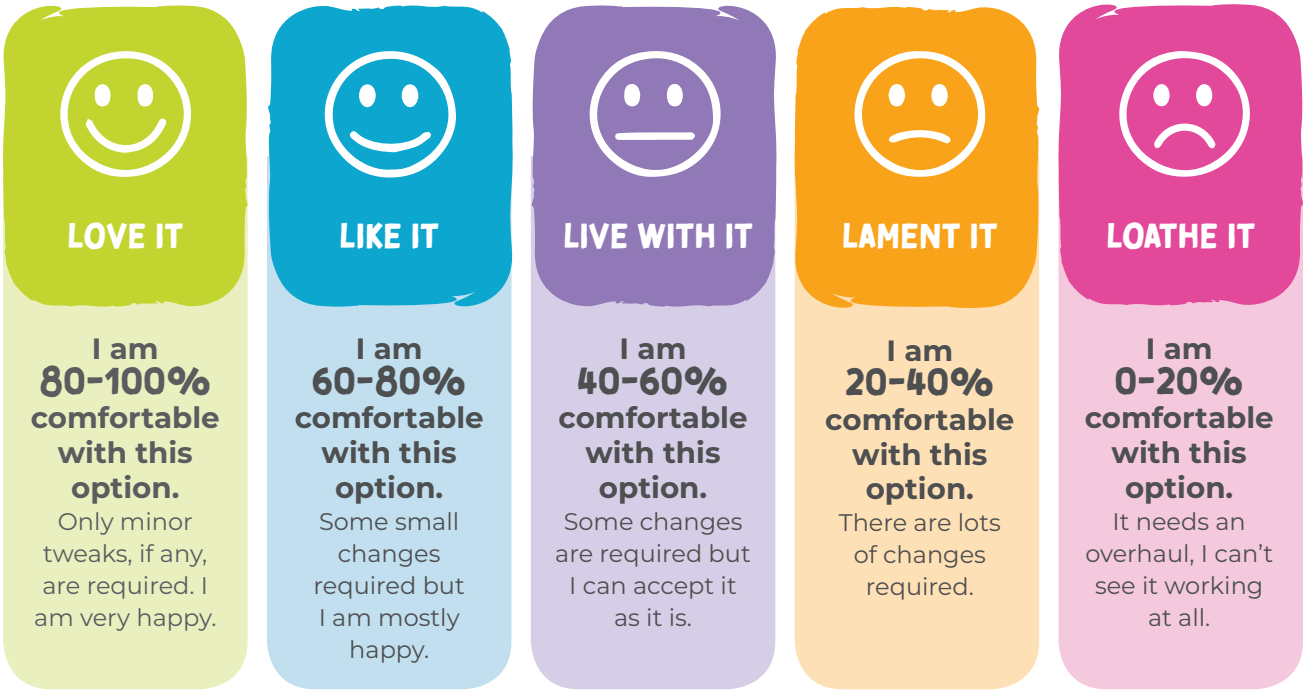
| TERM | REASONS FOR | REASONS AGAINST |
|---|---|---|
| **Unsolicited** *...continued* | | Sounds like a behaviour of an unwanted and illegal kind |
| | | Unclear meaning, word has negative connotations |
| **Unrelated** | Can easily be used as a descriptor in consent forms. If not selected, may still be useful as an explainer for an alternate term. | Ambiguous |
| | Helps to define or separate the possible test results | Context of relatedness in genetics/ genomics in terms of family - could be confusing |
| | In line with how a lab might report a result? Describes what's going on | Could this potentially be confusing given the familial context of many genetic tests |
| | Neutrality | It may not always easy to be tell if it is definitely related or unrelated |
| | Simplicity for both patients & clinicians | More ambiguous and open to interpretation. Unrelated to what? |
| | | So many assumptions underpinning these for and against |
| | | Unrelated to what? |

## ‘TERMS’ OVERALL LEVEL OF COMFORT

Participants were given time to look at and reflect on the previous feedback for each ‘term’. Individually, participants discussed and noted down their levels of comfort around each ‘term’. Results are shown below. This is how the levels of comfort were scaled:

**LIVE WITH IT, LIKE IT , LOVE IT**

| TERM | LEVEL OF COMFORT |
|---|---|
| Additional | 98% |
| Secondary | 90% |
| Incidental | 74% |
| Unrelated | 67% |
| Unexpected | 49% |
| Unanticipated | 36% |
| Unsolicited | 13% |

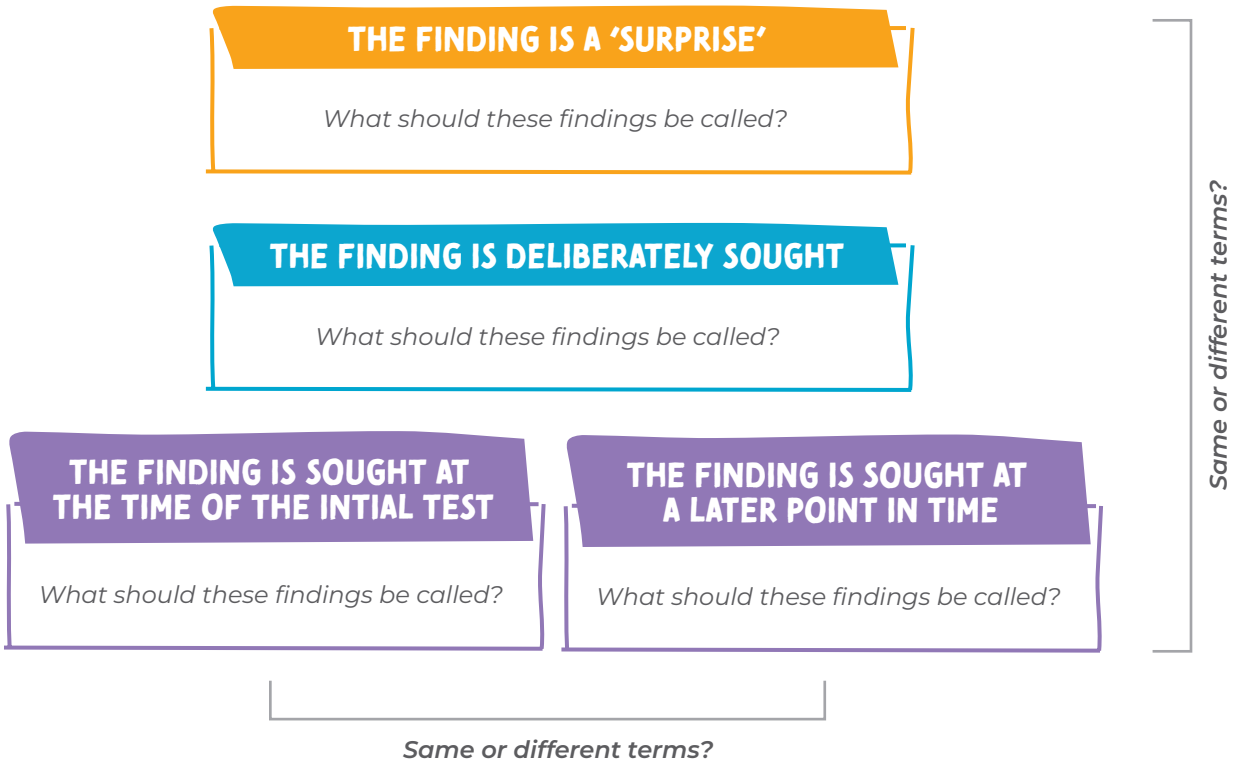


Each term below shows the overall levels of comfort consolidated for all participants. To find our 'super majority' we combine the results for those that can 'live with it', 'like it', and 'love it'.

This consolidated super majority result is identified like this in the results below.

67%

All the terms were also considered in terms of which 'context' they were best suited. The second graphs refer to the below diagram:

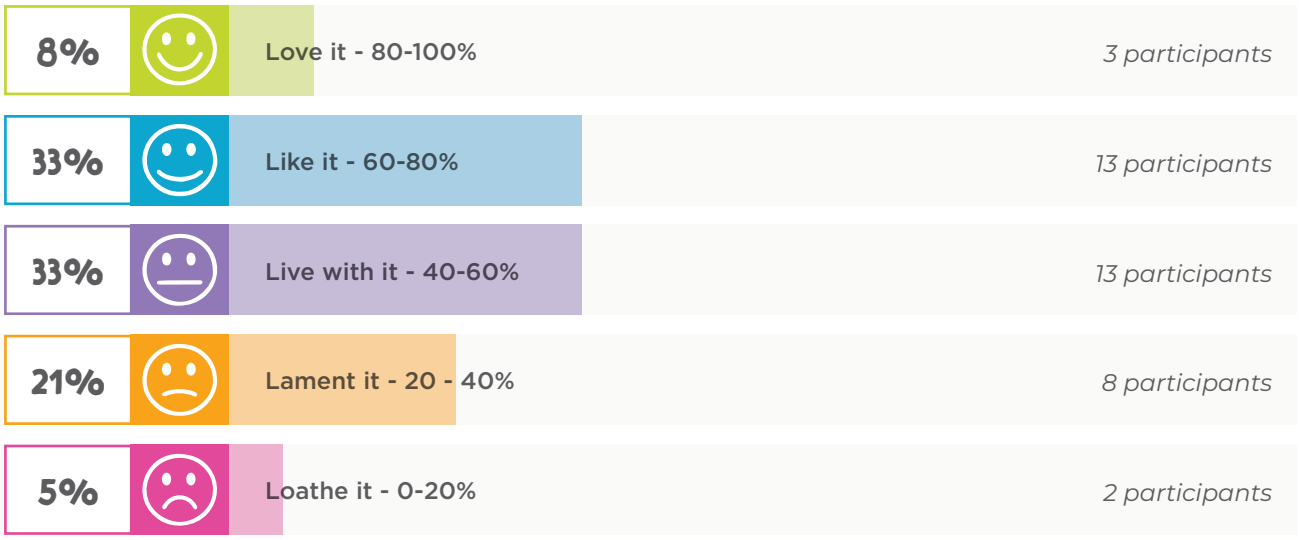



Each term was assessed against these contexts and an 'all' context was also offered as an option. For those people who didn't like the term ('loathe it' or 'lament it') they would have chosen not to pick any of the contexts. Therefore, the context graph is a percentage of those people who could 'live with' the term or higher.

# INCIDENTAL

## HOW COMFORTABLE ARE YOU WITH THE TERM – INCIDENTAL?

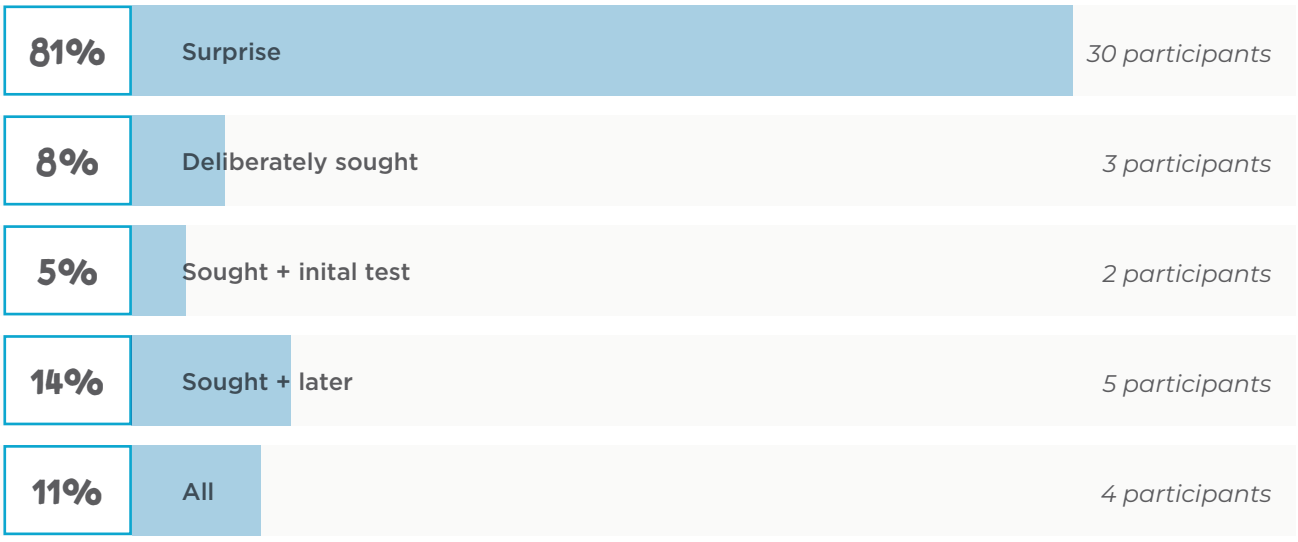
*39 out of 74 participants answered this question*




## UNDER WHICH CONTEXT ARE YOU MOST COMFORTABLE WITH THIS TERM?

74%

*37 out of 74 participants answered this question*



## What are your reasons for your level of comfort?

1. So entrenched already.

2. Consistent with use in other clinical domains (e.g., radiology); BUT should only be used for surprise findings.

Should be for mistakes only - def not something that is sought

Only appropriate for 'surprise' results, but again, the potential for these is raised during consent, so to me not really appropriate in the context of genomic testing.

Commonly used word in genetics, e.g. on current clinical genetic testing consent forms. however, the word 'incident' has negative connotations. also does not accurately describe 'sought' findings

Does imply some surprise and a potential negative value but for a truly "surprise" finding is the most descriptive.

Already often used in genomics and other areas of medicine; reasonable acronym; but can be challenging to understand and internet search suggests lesser.

Familiar, but not relevant in all contexts.

'Incidental' diminishes the significance and importance of the findings. It makes it sound as though the findings are accidental and has negative connotations. It is also unsuitable for findings that are deliberately sought.

Used internationally and has meaning but do not like in non-surprise context. At later date it is never incidental.

Current lab use, aligned with ACMG in this usage, clinical genetics knows what we mean.

Already used in medical practice for 'surprise' findings from medical investigations.

Commonly used internationally. Differentiates between accidental versus deliberately sought findings.

It is a widely used term and I think it makes sense in the context of surprise (but only that).

Longstanding.

Not simple enough.

Incidental has connotations of a tangential importance, however that which is sought later seems most likely to be actually incidental to the purpose of the initial test.

Suggests that this is less important than the 'primary' finding.

Commonly used, universally understood, has no negative connotations. There might be an argument it downplays the importance of a particular finding, but I think further explanation from a lab or clinician could overcome this.

Terminology known to scientists and researchers as well as clinicians dealing with reports.

For lay people this isn't easy to understand.

Understood in the professional community (but not by patients).

Difficult to understand from patient / lay person perspective and is not sought for and implies that the finding is not sought for and / or not important which may not be the case.

This term is used in other areas of medicine and has a clear meaning.

Well known in science and medicine. Not well understood by public. Could suggest it's not as important.

Well-established in the literature; specifically describes findings that were not sought.

Widely used and largely well understood.

Due to its use in other areas of medicine, and its widespread use.

From a patient perspective it makes it seem unimportant. From a lab perspective it takes effort to identify and curate variants and this term makes it sound accidental.

I think any of the terms presented are okay as long as we have a clear definition of what they mean. With patients, I would not stick to any one term, but be guided by what they are comfortable using.

This relies so much on a great consent process which may take place months in advance of results - the word on its own is meaningless to patients.

Not perfect, but usable.

It's seems to be used a lot, but might not be widely understood by lay people, especially people whose first language is not English.

I don't see how any finding can be incidental. If you have picked a set of genes or a gene specifically to be tested for a suspected condition, then all possible findings should be expected.

Outdated, implies undesirable result that should have been avoided and doesn't fit with the changing notion of what to do with these findings, and their importance.

Familiar with this term as it has been used in the projects I've worked on. Not particularly easy to understand in plain language. Doesn't really convey the seriousness of some of the conditions that could be found.

Though it is widely used, the negatives outweigh this.

Easily understood by most healthcare professionals, not sure that all patients would understand this term though in relation to why they had their testing done in the first place.

# SECONDARY

## HOW COMFORTABLE ARE YOU WITH THE TERM – SECONDARY?

*39 out of 74 participants answered this question*

| | | |
|---|---|---|
| 8% | Love it - 80-100% | *3 participants* |
| 56% | Like it - 60-80% | *22 participants* |
| 26% | Live with it - 40-60% | *10 participants* |
| 8% | Lament it - 20 - 40% | *3 participants* |
| 3% | Loathe it - 0-20% | *1 participant* |

## UNDER WHICH CONTEXT ARE YOU MOST COMFORTABLE WITH THIS TERM?

90%

*39 out of 74 participants answered this question*

| | | |
|---|---|---|
| 15% | Surprise | *6 participants* |
| 54% | Deliberately sought | *21 participants* |
| 54% | Sought + inital test | *21 participants* |
| 51% | Sought + later | *20 participants* |
| 36% | All | *14 participants* |

## What are your reasons for your level of comfort?

'Secondary' when deliberately searching and asking at the time of the initial test doesn't make sense to me. I am less interested in doing what the US does (c.f. comment in prior session).

Commonly used and well understood for genetic reporting internationally. consistent with international trends (ACMG/AMP used int).

Could work across all but feel that the difference between primary and secondary would need to be explained for patient understanding. Downside is it may downplay the clinical importance of the information.

Could work as way of describing a result that is not the primary reason for the test.

Neutral value and relates to the primary findings that were sought. Would perhaps need additional explaining during counselling though.

ACMG, links between primary result.

Easy to understand.

This term is easily understood and provides context without introducing negative or positive connotations. However, I prefer 'additional' because 'secondary' could.

Has value attached to the wording.

ACMG definition exists and consistent with this use.

Confusing for patients. Confused use already in the literature and more generally.

Commonly used internationally. Differentiates between accidental versus deliberately sought findings.

As with incidental, it is commonly used and makes sense in these contexts (perhaps in combination with incidental for surprise).

No meaning.

A simpler word than incidental and aligns with guidelines.

Any finding that is sought, yet additional to the primary test indication is well described as a secondary finding.

Okay to use when considering as the secondary reason for referral; otherwise conveys that the results are less important when they are a 'surprise'.

Again, I think it's familiarity with the term that makes me lean towards it. It implies a finding that wasn't initially sought, but in no way diminishes its importance. It's just secondary to the primary clinical reason for testing.

Non emotive word, easy to understand.

I like this wording but think their could be some confusion for different population groups about what this means.

Can be used to mean 'other than primary but intended' OR 'other than primary/intended and unanticipated'.

I think good for use when findings are deliberately sought, complements primary and relatively easy to understand (though implies that the finding is less significant than the primary finding which may not be true).

Uncertain meaning.

Understandable to patients. Distinguished itself from the primary result. But it will always need clarifying, the term doesn't stand alone.

Widely established, currently used for labs; seems most appropriate for findings that could be anticipated (i.e. not surprise), but are beyond indication for testing.

Simple, largely well understood.

Widely used, explains its an extra finding. Could be misunderstood as a surprise finding.

From a pt perspective could make it seem unimportant when it might not be (so -ve). But 'secondary' is a good counter to 'primary' i.e., the reason for the test so I could live with it.

Fine to use as long as the definition is clear, so we all know what we're talking about when we use it.

If we have secondary, surely, we must have primary? This is also meaningless as stand on its own terminology for patients - secondary to what and implication is of less value or unimportant.

Good for secondary testing phases.

I think it may be at risk of somewhat diminishing the clinical significance of the result.

Reasonably neutral but still somewhat devalues importance of finding. Seems to be used in contrast to "primary" but not all/ many labs actually use "primary result" in their report or consent materials. Seems mainly based on clinician comfort/ terminology.

Easy to understand, fits with previous literature and ACMG guidelines so internationally consistent.

I think it would only be useful to describe deliberately sought findings, regardless of time point. There are some issues with it conveying a reduced significance of the finding, but I don't think the connotation is as strong as some of the other terms.

I believe most stakeholders would understand this term in relation to test results being conveyed.

# ADDITIONAL

## HOW COMFORTABLE ARE YOU WITH THE TERM – ADDITIONAL?

*39 out of 74 participants answered this question*

| | | |
|---|---|---|
| 44% | Love it - 80-100% | *17 participants* |
| 44% | Like it - 60-80% | *17 participants* |
| 10% | Live with it - 40-60% | *4 participants* |
| 3% | Lament it - 20 - 40% | *1 participants* |
| 0% | Loathe it - 0-20% | - |

## UNDER WHICH CONTEXT ARE YOU MOST COMFORTABLE WITH THIS TERM?

98%

*39 out of 74 participants answered this question*

| | | |
|---|---|---|
| 18% | Surprise | *7 participants* |
| 28% | Deliberately sought | *11 participants* |
| 23% | Sought + inital test | *9 participants* |
| 26% | Sought + later | *10 participants* |
| 67% | All | *26 participants* |

## What are your reasons for your level of comfort?

Patients like it; makes sense.

Might be preferable for patients. but for intentionally sought only.

The most plain language term, to me has no implied meaning that may cloud patients perception of the result. Could work across all contexts. Lab reports almost always have some interpretive/tech info included this term could be paired with more detail.

Not an accurate way of describing findings from an initial test. If you use to describe findings from an initial test, it could imply testing was done in addition to what was consented to.

Has a neutral value to even positive value. To me feels fairly understandable to all involved.

Explains any results that are separate.

Can be positive; difficult to misunderstand. However, does require explanation re context.

Straightforward language.

Neutral connotations, easily understood and explained!

It suggests it is separate to the true purpose of the test but does not attract value or have negative connotations. Explanation can show this additional finding has important impact to an individual and family.

Useful as an umbrella term to include incidental and secondary findings.

Clearer for patients than 'secondary' More chance of this being widely understood and accepted as it is not a contested term meaning.

Doesn't differentiate between accidental versus deliberately sought findings. Often used to lump the two.

I think it is the best term to cover all three options (but not 'deliberately sought' - perhaps this should just be called 'findings').

Simple and effective.

Broad enough to allow context to be built around it. Plain English - may help translation.

Additional is the best catch-all term and probably the most widely comprehensible. Secondary is more appropriate to describe deliberately sought additional findings, but these are nevertheless additional.

Less emotive, whilst still indicative of finding beyond primary reason for testing.

It's a catch-all term, it's easily understood, it seems the most patient-focussed of all the terms. It holds no ambiguity whereas terms like 'incidental' and 'secondary' might.

Non-emotive, very easy to understand for anyone reading reports etc.

Neural language, easy to understand for lay people and those from different ethnic backgrounds, translates easily.

Most flexible, but also a bit ambiguous and not as useful in technical contexts.

Easiest to understand from a lay perspective, doesn't imply lesser significance like 'secondary does' - if one term were to be used for both intentionally and not intentionally sought then I think additional would be the most all-encompassing term.

Uncertainty regarding what this term means.

Familiar term, and translatable for those who don't have English as first language. Does not apply emotion/judgement Can be used in all contexts, and the term is understood without further clarification being needed.

Works well as a potential umbrella term (across categories like incidental/secondary) to describe any findings not related to indication for testing; transferrable to various contexts including patient conversations because it is descriptive, colloquial.

Simplest for patients, may not convey significance but later text describing the finding should be able to do this.

Fairly neutral, especially good when sought later.

We've used this and found reasonable acceptance of it by patients. Slight concern that some patients don't understand this is an 'add on' and believe/hope (?) that it's new analysis for the primary condition.

I think this is the most neutral and stands up on its own - also does rely on the context on the consent process to make clear what the test is seeking and what it is not.

Most neutral and flexible of 3 options.

It's an accessible, everyday word.

I think out of all the terms is probably best able to describe any other finding that may not be directly related to the suspected condition the testing was done for.

Easiest to understand, and while somewhat ambiguous it is highly amenable to a still developing environment without conferring a priory value judgement.

Simple and easy to understand word. Conveys that it is on top of the original test quite nicely. Doesn't feel biased to good or bad. Only hesitation is that it can be confusing when no diagnosis is made, so then it's not really additional to anything.

I know it is a term preferred by patients, so could live with it. But I do think it is a term that will need an extended explanation because it doesn't get across some of the key concepts.

Term easily understood by all but may lose some of its clinical importance in relation to initial test being requested.

# UNSOLICITED

## HOW COMFORTABLE ARE YOU WITH THE TERM – UNSOLICITED?

*39 out of 74 participants answered this question*

| | | |
|---|---|---|
| 0% | Love it - 80-100% | - |
| 5% | Like it - 60-80% | *2 participants* |
| 8% | Live with it - 40-60% | *3 participants* |
| 15% | Lament it - 20 - 40% | *6 participants* |
| 72% | Loathe it - 0-20% | *28 participants* |

## UNDER WHICH CONTEXT ARE YOU MOST COMFORTABLE WITH THIS TERM?

13%

*31 out of 74 participants answered this question*

| | | |
|---|---|---|
| 81% | Surprise | *25 participants* |
| 0% | Deliberately sought | - |
| 0% | Sought + inital test | - |
| 0% | Sought + later | - |
| 23% | All | *7 participants* |

## What are your reasons for your level of comfort?

Technically correct; able to be used across different types of findings.

Term hard to understand.

Really negative connotations, implies it wasn't asked for and perhaps not wanted. not at all appropriate in the context of a test where the possibility of additional findings is raised as part of consent.

Word has negative connotations. There are multiple other words to use which are preferable.

Sounds too much like legalese and is not immediately understandable. Has a negative value.

Interpretation is that it is unwanted.

Not plain language.

Doesn't seem fitting for genetic testing.

This term is not easily understood. The definition is 'not asked for or not sought for'. It implies that these are unwanted findings, and that the patient almost did not have autonomy/control over receiving them.

Has dangerous associations of lack of consent or violation of consent.

Has a negative connotation.

I'm not really comfortable with its use in any context, but just felt I should tick one of the boxes! I just think it has bad connotations - suggesting that it is done without consent.

Endorsed in pathology.

May not be broadly understood. Negative connotations.

Too many negative connotations. Think unsolicited advice, unsolicited advance, etc.

Connotation of word is very negative, suggests unwantedness of results, downgrading their perceived importance.

Don't like the term at all. It makes it sound almost like it was an unwanted finding. Has negative connotations.

To me this means unwanted.

Loaded term, don't think it reflect that it wasn't the primary indication for the test.

Makes logical sense, but problematic connotations and a more university-level term.

Hard to understand, implies a negative connotation (i.e., that something was sought for against the will of the patient).

Uncertainty what this term means.

Poorly understood by public and suggests it was not wanted / consented for. Add negative connotations.

Sounds like unintentional, possibly a mistake; opposite is "solicited" - is that what genetic tests do?

Patients won't understand, sounds negative and like someone has done something wrong.

For all the reasons the group came up with.

Solicitation is a word that would not be familiar to many and has a specific negative connotation with prostitution.

Like this least. It sounds like something you did not look for and did not want to find.

This is a totally inaccessible term for patients and suggestive of a legal context.

Legalese sounding, implies lack of care in finding.

It has a negative connotation and suggests the findings are unwanted.

I don't patients will relate to this at all.

Hardest to understand, sounds like we did something we shouldn't have.

Not patient friendly at all.

It is a loaded and complex term.

Sounds like the test was performed 'just for the fun of it'.

# UNEXPECTED

## HOW COMFORTABLE ARE YOU WITH THE TERM – UNEXPECTED?

*39 out of 74 participants answered this question*

| | | |
|---|---|---|
| 0% | Love it - 80-100% | - |
| 18% | Like it - 60-80% | *7 participants* |
| 31% | Live with it - 40-60% | *12 participants* |
| 38% | Lament it - 20 - 40% | *15 participants* |
| 13% | Loathe it - 0-20% | *5 participants* |

## UNDER WHICH CONTEXT ARE YOU MOST COMFORTABLE WITH THIS TERM?

49%

*34 out of 74 participants answered this question*

| | | |
|---|---|---|
| 82% | Surprise | *0 participants* |
| 0% | Deliberately sought | - |
| 3% | Sought + inital test | *1 participant* |
| 3% | Sought + later | *1 participant* |
| 18% | All | *6 participants* |

## What are your reasons for your level of comfort?

Really only works as an alternative to 'incidental', and 'incidental' is better.

This could be used to cover laboratory error and/or really unexpected/usual findings like consanguinity etc that labs have to legally report out.

The opposite term is expected, which is never used in the context of testing and may set unrealistic expectations about the likelihood of results for the 'primary' test indication. Again, conveying result could not have been anticipated seems inappropriate.

This term best goes with a 'surprise' result.

Has a negative value. I think for describing these findings the words used need to empower the patient rather than imply they are victims. To me, regardless of whether the finding is medically actionable, all have the potential to have personal utility.

Word used more widely in everyday language and indicates result was a surprise.

Challenge in confidence.

Implies poor understanding of the testing being conducted.

Seems inaccurate, given the capability of genomic testing to produce findings beyond the initial indication. Also has negative connotations and diminishes importance of the findings by implying that they are almost shocking/surprising.

It has value judgement attached

It's meaning should be clear to patients but prefer a term that is in use.

Not inflammatory/anxiety provoking.

I'm mildly comfortable with use of this term in the context of surprise. But it might suggest to a patient a lack of competence on the part of the clinician or lab.

Not accurate.

Not neutral.

Only applicable to surprise results.

Only for surprise findings, easier to understand than unsolicited or unanticipated in conversation, but question the need of a qualifier.

I don't think this term would fit unless a finding was not in any way sought. It's ok but there are other terms that convey more clearly the nature of these sorts of findings that arise during NGS.

Shock factor.

If patients have been adequately counselled before the test any results should not be unexpected.

Offers no benefit over 'unanticipated' and has a slightly problematic connotation.

Implies a lack of competent for the clinician, also may not be necessarily unexpected (e.g., if the patient's family has a history of a certain genetic condition / predisposition).

Uncertainty what this term means.

Term understood by public and indicates its meaning independently. But could have more negative emotive associations.

Sounds like the clinician/ lab could not have anticipated such a result, possibly there was an error.

VERY happy in spoken language to patients, more reserved when it comes to laboratory reports as may imply some kind of failure in the laboratory.

Its use could be too narrow - if kept for when truly unexpected findings arise.

Implies accidental finding but variant curation requires effort. Pts shouldn't get 'unexpected' results if they have been counselled to expect results from an extra/wider analysis.

I use not expected with patients often, but in terms of it not being associated with the reason for doing the test.

Again, where clarity and understanding is achieved at consent, there is clarity around what this means. Does have a negative/shock connotation to it.

Works at a mechanical lab level, but emotive that may imply surprise to patient.

It's a familiar word.

Again, I don't truly believe that any result should be unexpected. If you a have picked a gene or a set of genes to best tested, then all possible results should be expected.

Implies that we don't know what we are doing or don't understand our technology/approaches. Could encourage legal challenges in context of undesired disclosure.

Easy to understand, could be used in most contexts.

It doesn't make sense that we would talk about something being unexpected, when we know these findings may arise.

I prefer other terms but could cope with this one.

# UNANTICIPATED

## HOW COMFORTABLE ARE YOU WITH THE TERM – UNANTICIPATED?

*39 out of 74 participants answered this question*

| | | |
|---|---|---|
| 3% | Love it - 80-100% | *1 participant* |
| 5% | Like it - 60-80% | *2 participants* |
| 28% | Live with it - 40-60% | *11 participants* |
| 49% | Lament it - 20 - 40% | *19 participants* |
| 15% | Loathe it - 0-20% | *6 participants* |

## UNDER WHICH CONTEXT ARE YOU MOST COMFORTABLE WITH THIS TERM?

36%

*35 out of 74 participants answered this question*

| | | |
|---|---|---|
| 83% | Surprise | *29 participants* |
| 3% | Deliberately sought | *1 participant* |
| 3% | Sought + inital test | *1 participant* |
| 3% | Sought + later | *1 participant* |
| 17% | All | *6 participants* |

## What are your reasons for your level of comfort?

As above for unexpected, perhaps slightly better because the term sounds more neutral.

Alternative term for unexpected as described above - lab error and or other unusual finding.

Could work, but only for 'surprise' results - though discussion of 'surprise' or uncertain significance results is now a routine part of genetic testing, so to me any term that conveys surprise/that a result could not have been anticipated is inappropriate.

Longer word than unexpected. more complex.

Negative value. Is not correct, many of these findings are indeed anticipated, they are often not sought though. Makes it seem that we don't know what we're doing.

Does describe the result but word may still be too technical for patient.

Long. potential source of distrust and misplaced surprise.

Sounds like the lab doesn't know what they're doing.

Same reasons as unexpected.

We can anticipate knowing family history and population prevalence.

Not inflammatory/anxiety provoking.

As with unexpected, I'm mildly comfortable with use of this term in the context of surprise. But it might suggest a lack of competence on the part of the clinician or lab.

Not accurate.

Negative.

You can deliberately search for something yet not anticipate finding it, so it covers both surprise and deliberate, which could be vague.

More difficult word for non-native English speakers, again for surprise findings only.

It would only be appropriate to describe findings that arise completely unexpectedly.

Similar to unexpected.

As above, implied patient hasn't been adequately prepared for this type of result.

Most useful and non-problematic term for this context but works best as third category accompanying primary/intended and secondary/additional.

Implies level of surprise which may not be applicable in all circumstances.

Unclear meaning.

More complex term for public to understand.

Same as unexpected - if such a result could not have been anticipated, was there a mistake?

VERY happy in spoken language to patients, more reserved when it comes to laboratory reports as may imply some kind of failure in the laboratory.

complicated. Will become less relevant as more is known about the genome.

Anticipated' is a more advanced word than 'expected'. Same criticisms apply as for unexpected.

I don't use it, but I think it's fine.

I think falls into the same category as unexpected. They are very similar in what response they receive.

Implies lack of technical capability/ knowledge but does describe how it was unearthed, potential health consequences.

More complicated way of saying 'unexpected'.

Same reason for unexpected.

Implies that we don't know what we are doing or don't understand our technology/approaches. Could encourage legal challenges in context of undesired disclosure. Only a little better than unexpected.

Not particularly plain language.

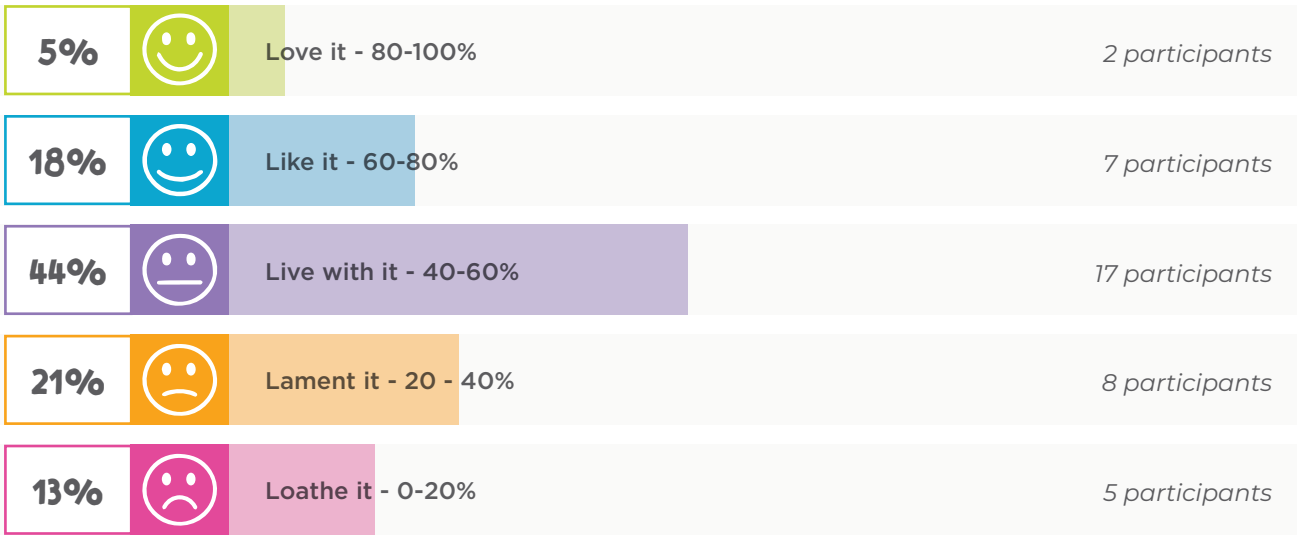
It doesn't make sense that we would talk about something being unanticipated, when we know these findings may arise.

I don't believe all stakeholders would comprehend this term in relation to a test finding.

# UNRELATED

## HOW COMFORTABLE ARE YOU WITH THE TERM – UNRELATED ?

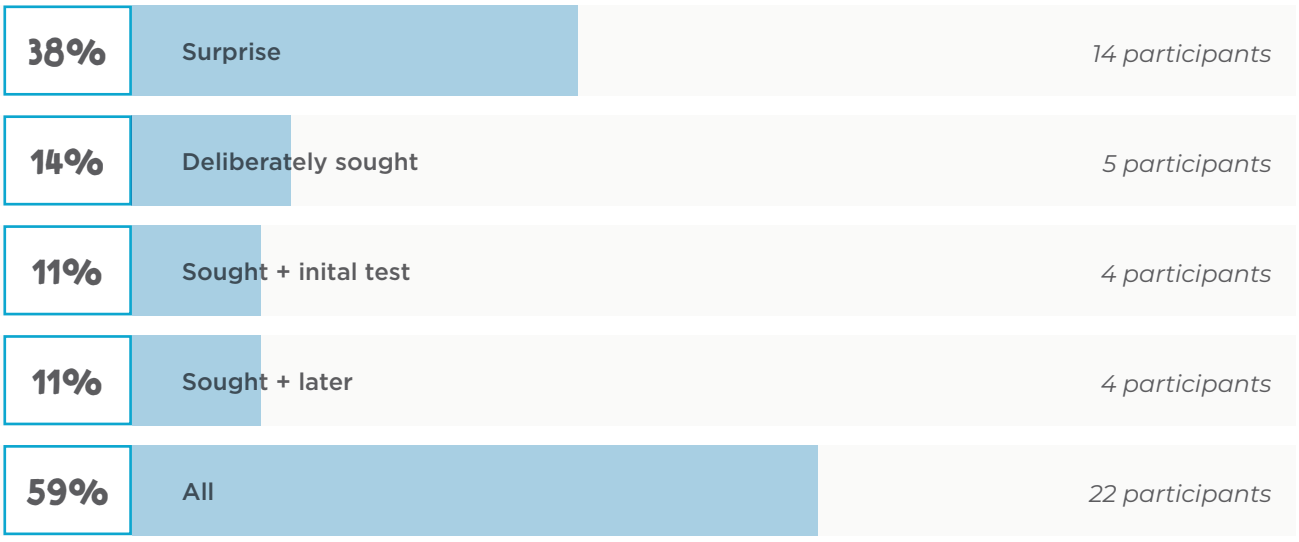
*39 out of 74 participants answered this question*




## UNDER WHICH CONTEXT ARE YOU MOST COMFORTABLE WITH THIS TERM?

67%

*37 out of 74 participants answered this question*



## What are your reasons for your level of comfort?

The comments about its ambiguity seem important to me. And it carries an inherent meaning in relation to other terms, i.e., a comparison.

this term on its own does not work - it has to be part of a sentence - I think it could be useful in a description - unrelated to original test indication.

To me, begs the question 'unrelated to what?' May not be related to the test indication, but could still be related to family history, and likely definitely related to health. Tricky in familial context of genetic testing, could be misinterpreted.

Related' has another meaning in genetics i.e., your relatives, people that are related to you. So, using this work in another context is needlessly confusing.

Has a slight negative value but of all the "un" words, is the least emotive. If used it would need some explanation about what it is unrelated to so that these findings are not minimalised.

Neutral term to explain results found.

Grammatically unrelated to what is key.

Some unambiguity but could be consistent with lab reporting practices.

Has connotations with relatedness of individuals which is not ideal.

Useful as umbrella term; meaning of word directly allows distinction from primary finding.

May be useful for the deliberately sought findings unrelated to the primary reason for testing. But could get confusing.

Minimises the potential relevance for the patient.

It might work in the context of surprise, but it doesn't work beyond this.

Not accurate.

Simple neutral English. But may be more ambiguous than additional.

Too vague.

Once additional findings are sought, there's a specific request for this information, so they are related to a request, though not clinical phenotype.

It does cover the full gamut of scenarios, but raises the question, 'unrelated to what?'. If I were a patient that would be my first question. And the fact is it may not be completely unrelated.

It is tricky for this word to fit in as it needs a disclaimer. Unrelated to what.

Confusing terminology when discussing a test that will likely have implications for other family members.

Deeply problematic - related to what and in whose mind?

Useful for the purpose of explaining to patients i.e., for consent purposes - explaining that it is unrelated to the primary test purpose (though may not be true in circumstances where there is some connection to the primary diagnosis).

This term is not clear.

Non emotive. But harder for public to understand and needs context around it for public.

Not preferred, but it does position the findings in relation to the initial indication for testing; agree it could be useful as part of a definition or as a way of explaining the finding to a patient, but perhaps not as the key term itself.

Maybe difficult to define/know what is definitely related and what is unrelated.

explains separate result to the test indication. But agree could cause confusion about familial relationships.

Related to what' may present some challenges in terms of precision of language but it does clarify for patients that it's unrelated to the primary reason for testing.

This is quite useful to use in any context. A finding unrelated to the clinical indication for testing.

I like this term but also think that it is problematic as it relies on a very clear understanding of what is related. Interesting to explain this would require the use of the other words so this one probably would be redundant anyway.

Most neutral term and descriptive of meaning to patient i.e., not related to original presenting reason.

Think this one would cause confusion for patients.

I think this could be utilised as well as additional for the same reason listed above under additional.

Unrelated to what? Most labs only report things relevant to, and therefore related to, an individual's health. Non-intuitive and could be misunderstood in context of familial relationships.

Could be confusion given 'related' is a term normally associated with family in the genetics/genomics context.

I like this term because it helps to structure the conversation around possible outcomes of testing with patients. It takes the pressure of the front end of testing (e.g., technical differences, expectedness etc) and focuses on the nature of the result.

I prefer other terms but could cope with this one.

# LIKE, WISH, WONDER

To conclude the workshop, participants were invited to share their reflections on the session. They were asked for one thing they liked, one thing they wished for and one thing they are left wondering about. Responses appear below:

## I LIKE...

- The technology used was so easy - great workshop.
- GroupMap was great for real time feedback - certainly helped with discussion.
- Hearing so many diverse views.
- Great facilitation, tech actually enhanced the workshop.
- Very skilful and pleasant facilitators.
- The curiosity and respect everyone brought to the discussions.
- GroupMap is great - easy to use.
- Excellent workshop, no butcher's paper, no being picked on to present group views!
- Great workshop!
- Fast process to get many perspectives.
- Great facilitating!
- Very thought provoking.
- The format.
- Really slick facilitating today, great to hear everyone's views.
- Different vehicles/ mechanisms for capturing people's perspectives.
- Very smooth process.
- The interactivity.
- Hearing everyone's diverse perspectives.

## I WISH...

- We had more chances to hear from more voices - it was nice to discuss in the small groups where everyone had a say, but we may not be exposed to all the nuances. Group Map was good, but not every point of discussion made it there.
- We could eventually discuss standardisation of individual test request and resulting terms. From an electronic information exchange perspective, tests/panel names should be less than 40 characters in total - genomic requesting/resulting terms are sooooo long!
- We had stepped through the deliberate vs surprise a bit more (but as Nicole said, this should come out in the data).
- There was a little more time to write reasons for our ratings.
- Each component could have been sped up a bit, to condense the time. None of the breakout discussions changed the poll options.
- I would have like maybe a proponent of each term providing their justification for why they think it is the best one.
- We had a teeny bit more time to deliberate at the step where we decided if there were any more terms to include.

## I WONDER...

How to best tie in international standards vs national perspectives.

How we will get patient/consumer input on this as they are the end users of this.

How easily laboratory information systems / clinical information systems will be able to implement these changes.

Technical and other distinctions very important to resolve.

If patients will have different views.

How this will be viewed by other stakeholders.

What the general public thinks/ wants/understands, we're a small and very biased group!

The tension between the usability of the term and lab technical aspects was a good call out and something I noticed - I wonder if this can be resolved.

What the wider reaction to additional will be.

How we are going to keep everyone happy!

# CONCLUSIONS

From these results it was clear that the term 'Additional' was the most preferred in nearly all contexts. This seems to be the most preferred and acceptable term going forward.

The reasons for this choice include:

- It's the most easily understood
- The most neutral, and
- The best umbrella term

# NEXT STEPS

Workshop number two will be conducted **in-person, Tuesday 31st October 2023, 12:30-4:30pm.**

The focus of this workshop will be to determine some principles and ideas for implementation of this term into policy in Australia.

**PLEASE NOTE:**

This report has been prepared by MosaicLab on behalf of and for the exclusive use of Australian Genomics. The sole purpose of this report is to provide Australian Genomics with materials produced at the workshop on the 5 September 2023.

This report has been prepared in accordance with the scope of services set out by Australian Genomics. In preparing this report, MosaicLab has relied upon the information provided by the participants at the workshop. Australian Genomics can choose to share and distribute this report as they see fit. MosaicLab accepts no liability or responsibility whatsoever for or in respect of any use of or reliance upon this report by any third party.

*MosaicLab is a Victorian-based consultancy that specialises in community and stakeholder engagement, facilitation, negotiation, strategic planning and coaching.*

**REPORT PREPARED BY:**

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Appendix 6

# Briefing Paper (Workshop 2): Principles for genomic findings beyond the original test indication

*Gabriel Watts, Matilda Haas, Stephanie White, Danya Vears, Clara Gaff, Ainsley Newson*

# What is the issue?

An inherent aspect of genome sequencing is that it can generate findings that go beyond the initial test indication, but which may be relevant to a patient's health.

- In *Workshop 1* we considered questions of terminology regarding such findings: what should they be called? Are different terms appropriate for different contexts?
- **In *Workshop 2*, our aim is to generate high-level principles regarding the identification and management of such findings.**

The outcomes of both workshops will inform future national policy regarding the management of such findings.

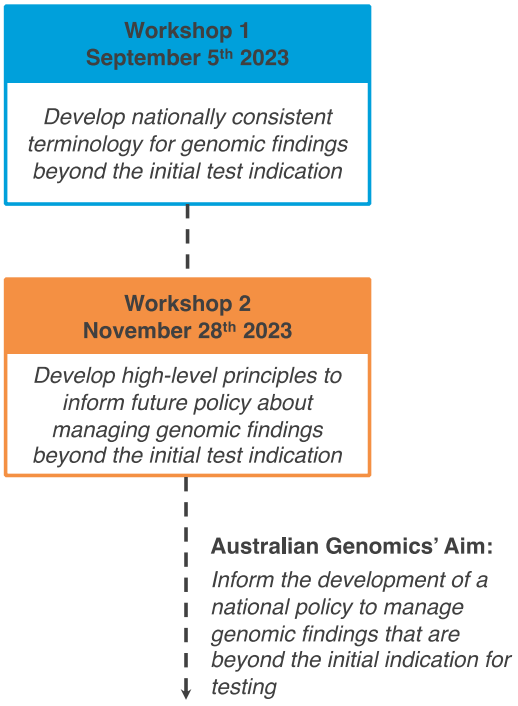


***Figure 1 -*** *Genomic Findings Project process*

# Outcome of Workshop 1

In *Workshop 1*, participants were most comfortable with the term 'additional' as an overall term for findings beyond the initial test indication. This was the case for both findings identified unexpectedly and those deliberately sought (see Appendix 1: Table 1). Participants preferred the term 'additional' because of its perceived neutrality and the view that it is likely to be more readily understandable by patients.[1]

For **findings discovered unexpectedly** (i.e., 'surprise' findings), while most participants preferred the term 'additional', they were also willing to use the term 'incidental' (see Appendix 1: Tables 2, 3). Support for 'incidental' stemmed from the entrenchment of this term in clinical practice, not only in genomic medicine but in medical practice more widely (e.g., imaging). It is also well-established in the literature.[2]

For findings beyond the initial test indication that are **identified through deliberate search** (with consent and analysis taking place either at the time of testing or later), most participants indicated they would be comfortable using the term 'additional' to describe such findings.[3] However, there was similar support for the term 'secondary' for deliberate searches (see Appendix 1: Tables 1, 3).[4]

[1] MosaicLab. *Australian Genomics – Terminology for Genomic Findings: Workshop 1 Report*. 5 September 2023:23-4.

[2] Workshop 1 Report:19-20.
[3] Workshop 1 Report:23-4.
[4] Workshop 1 Report:21-22.

# Plans for Workshop 2

In *Workshop 2* we will build upon the results of *Workshop 1* to develop initial **guiding principles** in response to two further questions regarding additional genomic findings initial test indication:

1. **What should be done with additional/incidental findings when they arise unexpectedly?**
2. **Should additional/secondary findings be deliberately searched for? If so, under what conditions?**

To date in Australia there is no national consistency in policy or clinical practice regarding how to approach the reporting or deliberate seeking of additional findings.[5] Currently, the National Pathology Accreditation Advisory Council requires that laboratories "must have a policy on the reporting of incidental findings which must be made available on request to patients and clinicians" (S1.6 p5)[6], but there is no requirement for consistent practice across laboratories.

Further, while NPAAC Standards suggest that laboratories "should consider the masking of information that is outside the scope of testing for a given patient sample", and that this "may involve masking of loci other than those targeted for analysis for a given patient" (C1.6.(ii)), there are no regulatory requirements concerning deliberate searches for additional findings.

***The initial guiding principles we develop in this Workshop will help inform future Australian policy on how additional findings should be managed in clinical practice. Ultimately, we hope that Australian policy can set clear and ethically considered expectations for both laboratories and clinicians, and that Australian patients have the same opportunity no matter where they live.***

[5] Vears DF, Sénécal K, Borry P. Reporting practices for unsolicited and secondary findings from next-generation sequencing technologies: Perspectives of laboratory personnel. *Hum Mutat*. 2017;38:905–911. https://doi.org/10.1002/humu.23259

[6] National Pathology Accreditation Advisory Council (NPAAC). Requirements for Human Medical Genome Testing Utilising Massively Parallel Sequencing Technologies. Available at: https://www1.health.gov.au/internet/main/publishing.nsf/Content/FB649C2C2A42CACDCA2580A400039643/$File/Reqs%20MPS%20Technologies%202017.pdf

# Guiding Principles

## What is a guiding principle?

A guiding principle is a **high-level statement** that both **expresses an ideal or value** (e.g., equality, justice, autonomy, etc.) and should be **actively pursued as a goal**. In an ethical sense, guiding principles serve as explicit statements for morally good actions, as well as providing reasons to inform governance of ethical best-practice.

Guiding principles seek to inform actions at a high level. Unlike codes of conduct, professional rules, and mandates, they leave room for judgement in their application. This enables stakeholders to account for different contexts, settings, resources, and needs.

Guiding principles are also distinct from guidelines. Such principles do not seek to merely regulate behaviour in a consistent manner. Their purpose is to promote consistent and transparent **rationales** for action (including policy development), establish expectations for ethical behaviour, express commitments required for best practice, and resolve conflicts.

While guiding principles are high-level statements, their practical application often requires that they be sufficiently specific to indicate when and why they ought to be applied. For instance, guiding principles pertaining to deliberate searches for additional findings ideally ought to indicate the conditions that would need to be met for deliberate searching to occur, and why it is appropriate or necessary (or if not, why not).

An example related to genomics are the 'Underlying Principles' from the recent Western Australian genomics strategy, *WA Genomics Strategy 2022–2032: Towards precision medicine and precision public health*:

### Underlying principles

To achieve the vision of the Strategy, the implementation of the strategic initiatives will need to be underpinned by the strong principles outlined below.

**Principle 1:** The application of genomic knowledge to health care is equitable and informed by scientific evidence and the diverse needs of consumers, carers, families and the community.

**Principle 2:** Investment in genomic services and applications is strategically prioritised based on their value to consumers, services and the WA health system.

**Principle 3:** Individuals, families and the broader population are empowered to make decisions about the application of genomics in their health care.

**Principle 4:** Trust in the use of genomics in health care is promoted through adherence to quality and safety standards and compliance with privacy and confidentiality policies.

***Figure 2 -*** *Underlying Principles, from " WA Genomics Strategy 2022–2032: Towards precision medicine and precision public health".*[7]

[7] https://www.health.wa.gov.au/~/media/Corp/Documents/Health-for/Population-health/WA-Genomics-Strategy-2022-2032-Towards-Precision-Medicine-and-Precision-Public-Health.pdf

## Why is developing guiding principles for additional findings in genomics important?

Discussions as to how best seek and/or report additional findings, if at all, and debates over the benefits and drawbacks of actively looking for them, have been an ongoing feature of genomic policymaking over the last decade.[8]

Despite this, there remains significant variation in global policy and practice regarding their identification and management. Guidelines in some jurisdictions, such as Europe, explicitly state that steps should be taken to *avoid* the discovery of additional findings.[9] For example, ESHG guideline concerning 'opportunistic screening' (2021), explicitly emphasise "a cautious approach to opportunistic screening."[10] In contrast, the American College of Medical Genomics recommends that laboratories actively search for causative variants in a list of 56 (now 81) genes known to cause 24 (now 38) conditions.[11]

In Australia, there is uncertainty about what can or should be done. There is a need to articulate our position in order to contribute to ongoing global debate. The development of initial guiding principles can also serve as a useful indicator of what a future national policy should contain.

## Principles: points for consideration

In *Workshop 2* will we seek to develop guiding principles in three contexts:

1) the **overall** approach to additional findings;
2) the reporting and management of **'surprise'** additional/incidental findings; and
3) **deliberately searching** for additional/secondary findings.

To help you think about how you would articulate your views on Australia's guiding principles for additional findings **overall** (context 1), we offer the following points for your consideration:

- What core ethical values should inform Australia's approach to additional findings?
- Do different values govern the different clinical settings (e.g. paediatric versus adult)?
- What weight should be given to:
  - Actionability?
  - Utility? (both clinical and personal)
  - Severity?
  - Evidence of pathogenicity (including in diverse groups)?
  - Age of onset?
  - Resourcing?

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[8] See 'Further Reading' below.

[9] van El CG, Cornel MC, Borry P, et al. Whole-genome sequencing in health care. Recommendations of the European Society of Human Genetics. *Eur J Hum Genet*. 2013;21 Suppl 1(Suppl 1):S1-5. PMID: 23819146; PMCID: PMC3660957. Available from: https://doi.org/10.1038/ejhg.2013.46; Matthijs G, Souche E, Alders M, et al. Guidelines for diagnostic next-generation sequencing. *Eur J Hum Genet*. 2016;24:2–5. Available from: https://doi.org/10.1038/ejhg.2015.226

10 de Wert G, Dondorp W, Clarke A, et al. Opportunistic genomic screening. Recommendations of the European Society of Human Genetics. Eur J Hum Genet. 2021;29:365–377. Available from: https://doi.org/10.1038/s41431-020-00758-w

[11] Green RC, Berg JS, Grody WW, et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. *Genet Med*. 2013; 15:565-574. Available from: https://doi.org/10.1038/gim.2013.73; and Miller DT, Lee K, Abul-Husn NS, Amendola LM, et al. ACMG SF v3.2 list for reporting of secondary findings in clinical exome and genome sequencing: A policy statement of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2023;25(8):100866. Available from: https://doi.org/10.1016/j.gim.2023.100866

    - Patient preferences regarding preparedness to receive such findings?
- Who should or would be responsible reporting additional findings?
- How should issues of reanalysis and recontact be addressed?

Example considerations pertaining to context 2 - **'surprise'** additional/incidental findings include:

- Should 'surprise' findings be actively mitigated against?
- Should specific values govern the reporting and management of 'surprise' findings?
- Who is responsible for deciding whether a 'surprise' finding is reported?

Example considerations pertaining to context 3 - **deliberately searching** for additional/secondary findings include:

- Is deliberate searching for additional/secondary findings:
    - Desirable?
    - Impermissible?
    - Permissible?
    - Imperative?
- Does deliberately searching generate special responsibilities to patients?
- If deliberate searching is desirable, how do we ensure equitable access to this testing?
- How long after the initial test (for the primary clinical indication) should analysis for additional findings be able to take place?

# Further Reading

## Policy Documents/Guidelines/Recommendations

*de Wert, G., Dondorp, W., Clarke, A. et al. Opportunistic genomic screening. Recommendations of the European Society of Human Genetics. Eur J Hum Genet 29, 365–377 (2021).* https://doi.org/10.1038/s41431-020-00758-w

*Matthijs, G., Souche, E., Alders, M. et al. Guidelines for diagnostic next-generation sequencing. Eur J Hum Genet 24, 2–5 (2016).* https://doi.org/10.1038/ejhg.2015.226

*van El CG, Cornel MC, Borry P, et al; ESHG Public and Professional Policy Committee. Whole-genome sequencing in health care. Recommendations of the European Society of Human Genetics. Eur J Hum Genet. 2013 Jun;21 Suppl 1(Suppl 1):S1-5.* https://doi.org/10.1038/ejhg.2013.46

*R.C. Green, J.S. Berg, W.W. Grody, et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing Genet Med, 15 (2013), pp. 565-574,* https://doi.org/10.1038/gim.2013.73*. For the current list, see:* https://www.ncbi.nlm.nih.gov/clinvar/docs/acmg/

*Boycott K, Hartley T, Adam S on behalf of the Canadian College of Medical Geneticists. The clinical application of genome-wide sequencing for monogenic diseases in Canada: Position Statement of the Canadian College of Medical Geneticists. Journal of Medical Genetics 2015;52:431-437.* http://dx.doi.org/10.1136/jmedgenet-2015-103144

## Papers

*Vears DF, Sénécal K, Borry P. Genetic health professionals' experiences returning results from diagnostic genomic sequencing to patients. J Genet Couns. 2020 Oct;29(5):807-815.* http://doi.org/10.1002/jgc4.1209

*Vears, DF, Sénécal, K, Borry, P. Reporting practices for unsolicited and secondary findings from next-generation sequencing technologies: Perspectives of laboratory personnel. Human Mutation. 2017; 38: 905–911.* https://doi.org/10.1002/humu.23259

*Sapp JC, Facio FM, Cooper D, Lewis KL, Modlin E, van der Wees P, Biesecker LG. A systematic literature review of disclosure practices and reported outcomes for medically actionable genomic secondary findings. Genet Med. 2021 Dec;23(12):2260-2269.* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9017985/pdf/nihms-1754144.pdf

*Saelaert, M., Mertes, H., Moerenhout, T. et al. Ethical values supporting the disclosure of incidental and secondary findings in clinical genomic testing: a qualitative study. BMC Med Ethics 21, 9 (2020).* https://doi.org/10.1186/s12910-020-0452-0

*Gabrielle M. Christenhusz, Koenraad Devriendt, Kris Dierickx, Disclosing incidental findings in genetics contexts: A review of the empirical ethical research, Eur J Med Genet, Volume 56, Issue 10, 2013, Pages 529-540,* https://doi.org/10.1016/j.ejmg.2013.08.006

*Christenhusz, G.M., Devriendt, K., Van Esch, H. et al. Ethical signposts for clinical geneticists in secondary variant and incidental finding disclosure discussions. Med Health Care Philos 18, 361–370 (2015).* https://doi.org/10.1007/s11019-014-9611-8\

# Appendix 1 – Tables from Workshop 1 Report

*Table 1 - Overall Comfort Level with term (39 Respondents)*

| Term | Level of Comfort* |
|---|---|
| ***Additional*** | 98% |
| ***Secondary*** | 90% |
| ***Incidental*** | 74% |
| ***Unrelated*** | 67% |
| ***Unexpected*** | 49% |
| ***Unanticipated*** | 36% |
| ***Unsolicited*** | 13% |

**This question measured comfort with each term independently, expressed as the percentage of respondents whose comfort level with the term exceeds 40%.*

*Table 2 - Comfort levels for the term 'Additional' in various contexts (39 Respondents)*

| Context | Percentage |
|---|---|
| ***Surprise*** | 18% |
| ***Deliberately sought*** | 28% |
| ***Sought + initial test*** | 23% |
| ***Sought + later in time*** | 26% |
| ***All*** | 67% |

*Table 3 - Comfort levels for the term 'Incidental' in various contexts (34 Respondents)*

| Context | Percentage |
|---|---|
| ***Surprise*** | 81% |
| ***Deliberately sought*** | 8% |
| ***Sought + initial test*** | 5% |
| ***Sought + later in time*** | 14% |
| ***All*** | 11% |

*Table 4 - Comfort levels for the term 'Secondary' in various contexts (39 Respondents)*

| Context | Percentage |
|---|---|
| ***Surprise*** | 15% |
| ***Deliberately sought*** | 54% |
| ***Sought + initial test*** | 54% |
| ***Sought + later in time*** | 51% |
| ***All*** | 36% |

# Appendix 7

| Type of context | Terminology | Comments | Votes |
|---|---|---|---|
| When the finding is a surprise we should say... | Additional | I'm going to go with additional for most of these, on the basis that the focus is on communication with the patient. Having just returned from GA4GH I do note that most folks still use secondary and incidental together<br>Additional can be easily understood by all<br>IMO all of the other terms have a value judgement - surprise, unanticipated etc. I prefer additional. Furthermore it may very well be related so this term should be avoided.<br>I like additional. But is it worth considering 'compound' expressions? So, when a finding is a surprise it could be described as an 'additional unexpected' finding. Also, it is possible exome sequencing could reveal multiple 'surprises'?<br>I like additional because it's a neutral term, that doesn't have negative connotations. I think the same term should be used for these findings, regardless of whether they are a 'surprise' or not. This will help keep the terminology consistent. | 22 |
| | Incidental | I think this is the most accurate term for something that is a complete surprise - for whatever reason. my second choice would be unanticipated... so not something you deliberately looked for and could counsel the patient about the health implications since you felt the extra testing is worthwhile to them<br>Incidental is widely used in other areas - like radiology - when you know something unrelated to the clinical presentation could be found, but you didn't know exactly what would be identified. So easier for health professionals to adopt than a new term for the same concept. | 8 |
| | Unexpected | Seems best choice | 7 |
| | Unanticipated | | 2 |
| | Secondary | | 1 |
| | unrelated | | 1 |
| | Unsolicited | | 0 |
| When the finding is deliberately sought we should say... | Additional | I would say additional analysis<br>Additional seems like the best term of the options.<br>Using 'additional' for these findings, regardless of whether they were deliberately sought or not, would keep terminology consistent and help avoid confusion for patients.<br>Additional conveys (to me) extra information (ie not related to the indication for testing). I think it is important to use different terms for results relating to the indication for testing (particularly a dagnostic test) and those relating to future health (ACMG list) so the distinction between these is conveyed as clearly as possible | 16 |
| | Secondary | How does this differ from the initial testing? As an add on?<br>How does this differ from 'sought at the initial testing'? Or does this refer to repeat testing of the individual few years later? If the finding is deliberately sought, I would have considered an abnormality to be significant?<br>Assuming this was not primary reason for testing and these are standard add-ons that they patient can be notified of when the test is ordered<br>not sure what "sought" means | 14 |
| | Incidental | | 1 |
| | Unexpected | | 1 |
| | Unsolicited | | 0 |
| | Unanticipated | | 0 |
| | unrelated | | 0 |
| When the finding is sought at a later point in time we should say... | Additional | Analysis conducted at a later time<br>additional - with a note making it clear that this was found on later analysis.<br>Is this referring to a significant pathological mutation that was unknown/unidentified at the time of the initial testing but reported since? Or a 'surprise' finding revealed on an analysis performed at a later date?<br>Initially thought secondary or additional could be fine, but it might be tertiary or quaternary!<br>additional - noting that it was sought at a later point in time and why this was the case | 29 |
| | Secondary | no different depending on the time - the point is whether you are counselling the patient ahead of time about the extra test for extra information that might be of value for their health but not what they initially had the test ordered for<br>I think it depends on whether it is within scope of the requested test or not. For example, if the original request was for epilepsy gene sequencing but then a request came in later for preconception screening then the new findings would be primary findings for the new scope. If however the later analysis was again for epilepsy and a variant was found in a gene that causes epilepsy with one mechanism but cancer susceptibility with another mechanism then I would prefer this to be an additional finding. | 2 |
| | Unanticipated | | 1 |
| | Incidental | | 0 |
| | Unsolicited | | 0 |
| | Unexpected | | 0 |
| | unrelated | | 0 |
| When the finding is sought at the time of the initial test we should say... | Additional | I've put additional here, but I don't think any of the options really fits. If it is sought at the time of the initial test, shouldn't it just be 'the test'<br>The initial reason for the test was for .... And additionally.....<br>ddtional seems the most logical response here - it may all be an unwelcome surprise to the patient. Furthermore the additional finding may have more health impact than the primary one so secondary seems incorrect in this setting.<br>I agree - I have put additional here too, but if the finding is sought at the time of the test, then why should it be referred to differently? The term 'secondary' also seems to downgrade the importance of the findings, so I wouldn't choose that term if the naming does need to be different for these findings. | 16 |
| | Secondary | I am struggling as I feel this question does not fit the criteria in the email ' the question of what to call genomic findings that go beyond the initial reason for seeking a clinical test. '.Am I being too finiky?<br>I am in the middle of writing an email to Ainsley making much the same point :-) Only the top left panel makes any sense in relation to the question, as far as I can see.<br>Thank you<br>Not sure how this question is different to the previous one.<br>v similar to previous question - the point is if the patient can be notified ahead of time that things unrelated to their presentation/family presentation are being sought - so much wider than what they initially signed up for, you can tell them<br>secondary sounds ok, if "sought" means considered/requested | 13 |
| | Incidental | | 1 |
| | Unsolicited | | 0 |
| | Unexpected | | 0 |
| | Unanticipated | | 0 |
| | unrelated | | 0 |

Appendix 8

mosaicLAB

# Australian Genomics: principles for genomic findings

workshop 2 agenda

28 November 2023

| LOGISTICS | |
|---|---|
| **Location** | Zoom https://us02web.zoom.us/j/84166791398<br>Passcode: No passcode required |
| **Date and time** | Tuesday 28 November 1-4pm |
| **Facilitators** | Nicole Hunter and Keith Greaves, MosaicLab |
| **PURPOSE AND SUCCESS** | |
| **Purpose** | To check-in around the outcomes of workshop 1<br>To define high-level guiding principles that will help shape future Australian policy for additional findings in genomic testing |
| **What does success look like?** | The workshop will provide an opportunity to:<br>• share learnings from the project's first workshop<br>• test reactions to the final terminology<br>• start defining key principles |

What guiding principles will help shape future Australian policy for additional findings in genomic testing?

| TIME | NOTES | OUTCOMES |
|---|---|---|
| **12:45pm** | **Arrivals and tech checks** | |
| **1:00pm** | **Getting Started**<br>Purpose of the session, agenda, introductions and a chance to share the experiences and hopes we are bringing to the session today. | Participants feel prepared to begin |
| | **An introduction by Gabriel Watts**<br>Background to the project, principles and the results of workshop 1 | Understand the background |
| | **Testing levels of comfort with terms**<br>Get reactions to the final terminology | Final reactions received about the terms and what is needed |
| | **Initial ideas for principles**<br>Begin developing ideas for what would be good guiding principles | Themed ideas for the principles |
| **2:20pm**<br>**(15 mins)** | **BREAK** | Step away from the desk and get some air! |
| | **Ideas for the principles**<br>Get broader group insight into important things to remember when drafting the ideas | Clear what the teams need to include when drafting the principles |
| | Writing principles & Review<br>Participants will work in small groups to draft a principle or two for review by the group. Then the groups will review all the principles and give feedback to help inform the project team when drafting final principles. | Drafted and reviewed principles for review by the project team |
| | **Taking stock, check out and next steps**<br>How did we go? What is unresolved and where to next? | Everyone clear about next steps |
| **4:00pm** | **Workshop ends** | |

Appendix 9

mosaicLAB

# AUSGENOMICS
# – PRINCIPLES WORKSHOP

## WORKSHOP 2

What was said report

28 November 2023

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# INTRODUCTION

## OVERVIEW

On November 28, 2023 25 key stakeholders from various sectors across Australia, including policy makers, clinicians, genetic counselors, researchers (both in genetics and bioethics), population health experts, representatives from patient experience groups and interested observers, participated in a three-hour online workshop hosted by the Australian Genomics project team and facilitated by MosaicLab facilitators Nicole Hunter and Keith Greaves.

The primary focus of that workshop was to address the question:

*What guiding principles will help shape future Australian policy for additional findings in genomic testing?*

## SESSION PURPOSE

This second online session gave participants an opportunity to check-in around the outcomes of workshop 1 that was held on 5 September, as well as to define high-level guiding principles that will help shape future Australian policy for additional findings in genomic testing.

The workshop will provide an opportunity to:

- share learnings from the project's first workshop
- test reactions to the final terminology
- start defining key principles

## PARTICIPANTS

In total, 25 participants attended, representing a diverse range of groups including:

- Clinical and genetic counsellors
- Laboratory representatives
- Ethics and policy representatives
- HCP (non-genetics)
- Government
- Australian Genomics
- Project team members
- Research

** Please note that a couple of patient representatives were invited but could not attend.*

## SPEAKERS

Gabriel Watts from the AusGenomics project team gave a short presentation on the workshop 1 findings and the workshop 2 objectives, including guidance and examples of other principles.

## WORKSHOP AGENDA

| TIME | AGENDA |
|---|---|
| 12:45PM | **ARRIVALS AND TECH CHECKS** |
| 1:00PM | Getting Started: Purpose of the session, agenda, introductions and hopes. |
| | An introduction by Gabriel Watts - Background to the project, principles and the results of workshop 1 |
| | Testing levels of comfort with terms - Get reactions to the final terminology |
| | Initial ideas for principles - Begin developing ideas for what would be good guiding principles |
| 2:20PM | **BREAK** |
| 2:35PM | Ideas for the principles - Get broader group insight into important things to remember when drafting the ideas |
| | Writing Principles & Review |
| | Taking stock, check out and next steps |
| 4:00PM | **WORKSHOP ENDS** |

# RESULTS

## HOPES & ADVICE

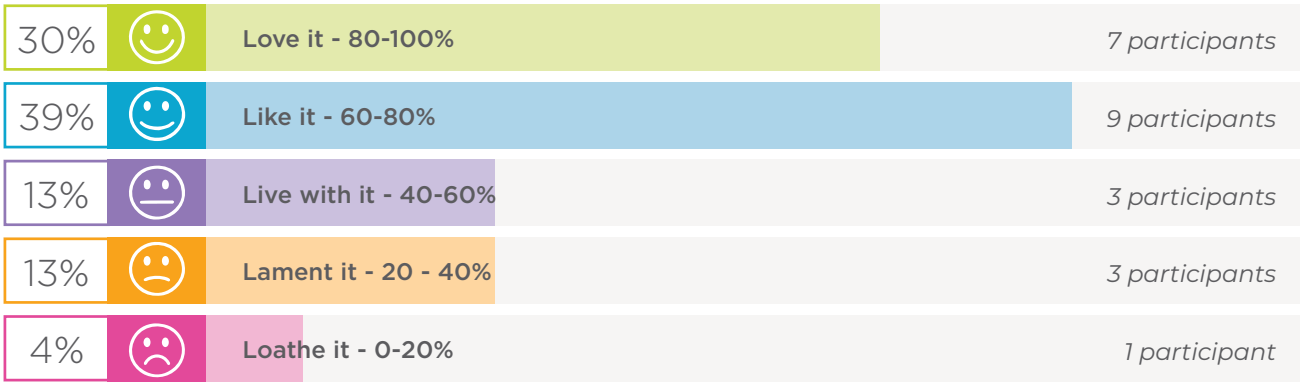
In preparing for the day, participants were invited to consider what hopes and advice they had for their time together.

# TESTING THE TERMINOLOGY

Participants were asked to review the terms chosen to describe the findings beyond the initial test indication in different contexts, that resulted from the last workshop. They were asked to test their levels of comfort and make choices according to which term resonated most in these different situations. The results are outlined below:

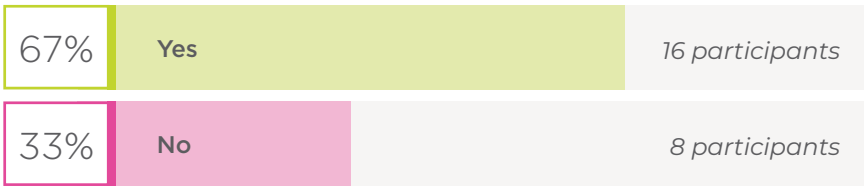
### Q1: How comfortable are you with using ADDITIONAL in both contexts (for surprise and deliberate findings)?

*23 participants answered the question.*




### Q2: Do you think we need TWO DISTINCT TERMS for the two different contexts (for surprise and deliberate findings)?

*24 participants answered the question.*




### Q3: If you had to choose between ADDITIONAL and INCIDENTAL for SURPRISE findings, which would you choose?

*24 participants answered the question.*


### Q4: If you had to choose between ADDITIONAL and SECONDARY for DELIBERATELY SOUGHT findings, which would you choose?

*24 participants answered the question.*

# WRITING PRINCIPLES & REVIEW

At first, all participants were asked to suggest 1-2 big principles under each context. These principles were then lightly clustered by the project team ready for use at the next stage of the process.

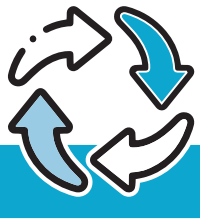
## Big Principles for when it's a SURPRISE

| INITIAL PRINCIPLE | GROUPED IDEAS |
|---|---|
| Avoid if possible (focus clinical testing on the clinical indication at hand) | |
| Client focussed findings management | Capacity for all direct stakeholders (E.g. patient, family, clinician, clinic) to manage the result.<br>A collaborative approach to identifying, issuing, supporting, managing the finding that places the best interests of the client at the centre.<br>The result is communicated (in clinic and in the report) in such a way that it reduces the chance of misinterpretation for the client.<br>Consider age-of-onset/familial implications when reporting. |
| Should be reported (with consent) when there are health benefits - actionability | |

## Big Principles for when it's a DELIBERATELY SOUGHT

| INITIAL PRINCIPLE | GROUPED IDEAS |
|---|---|
| Actionable and age-appropriate for reporting | |
| Equity of access to testing for deliberately sought findings | There should be equitable access ·Equitable access to expertise, care, testing, follow-up and resources |
| There should be a nationally consistent approach to deliberately sought additional findings | Consensus on appropriate gene lists Consensus on list of genes screened for findings |
| Upholding the autonomy of the client before deliberately searching (e.g., informed consent, option to decline) | Clear informed consent (including right not to know) |

## Big Principles OVERALL



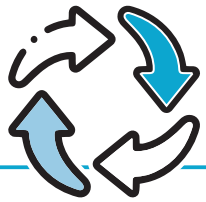
| INITIAL PRINCIPLE | GROUPED IDEAS |
|---|---|
| **Equity and consistency in practice and planning** | Equity and consistency (universal definitions, application & adoption)<br>Cannot derail primary diagnostic service. Needs to be equitable (decide whether publicly funded or not). Still need to balance benefits vs potential harm<br>National consistency in reporting of findings Equal weight is given the finding regardless of whether it is a surprise and deliberate |
| **Patient choice and autonomy** | Individuals/families undergoing testing should have a choice about receiving additional/secondary/incidental findings informed consent - clear consent process and clear lab reporting processes · ensuring patients/individuals being tested have the opportunity to opt in or opt out of receiving findings<br>Additional findings should be responsibly returned - with appropriate information and support provided<br>Patient understanding is paramount |
| **There is a clear benefit to the client / family for giving them the information** | Anything to be returned should have utility for the patient |
| **Think about the impact on the whole health system** | System in place to make decisions: balance of benefit (medical actionability) vs potential harms. Importance of liaison with referrers to manage surprise element.<br>Benefits vs harms. Consider at individual and system level (resource considerations, clinical and lab) |
| **Upholding ethical principles of non-maleficence, beneficence, autonomy, justice (maximising benefit, minimising harm, retaining patient autonomy)** | Ethical principles (see overall) |

* Please note the medical ethics principles were kept out of the next stage of the process as they were seen as overarching principles in this setting.

# FINAL PRINCIPLES

Participants worked in small teams to write the principles based on ideas offered by the whole group (from the last session). These initial principles are reproduced here as a record of the workshop. All the ideas that participants offered against each principle (to help with further writing) have been provided to the AusGenomics project team for their reference.

## OVERALL APPROACH TO ADDITIONAL FINDINGS



### DRAFT Principle 1

| | |
|---|---|
| **Heading** | Patient-centered approach to assessing benefits |
| **Description** | Results should be returned when the client/family perceives that the benefits outweigh the potential harms.<br><br>Enabling the person/family undergoing testing to decide what is actionable/ beneficial and have this reflected in their consent decisions. |
| **Qualifications or considerations for use** | Appropriate information should be given about the potential benefits and harms to support the decision<br><br>Will need to take into consideration the actionability of the findings and client/ family consent decisions for additional findings<br><br>Scope of potentially actionable findings may need to be restricted depending on resource constraints and potential health system impacts (e.g. patient may want all possible findings, but not feasible within available resources) |

### DRAFT Principle 2

| | |
|---|---|
| **Heading** | Enabling patient choice and autonomy, including dynamic informed consent and understanding lab policy |
| **Description** | Empowering the patient to make an informed decision by providing sufficient information and the opportunity for discussion. This needs to include warning about potential for additional findings. |
| **Qualifications or considerations for use** | One consideration is providing support to genetic professionals when they are aware of information but the patient has declined to know. Another consideration is adherence to policy and making lab policies known. |

## DRAFT Principle 3

| | |
|---|---|
| **Heading** | Comprehensive health system preparedness for management of additional findings |
| **Description** | Preparing the health system to support individuals/families who receive additional findings. Inclusive of laboratories, clinical genetic services and downstream clinical services to effect long term management. |
| **Qualifications or considerations for use** | Nationally consistent, equitable approach to management of individuals/families who receive additional findings e.g., clinical genetics services have different priorities, dependent on local context, state guidelines, priorities, resources. |

## DRAFT Principle 4

| | |
|---|---|
| **Heading** | Equity is underpinned by shared knowledge and resources |
| **Description** | Consistency of practice and patient experience lead to equity. There is a responsibility to share knowledge across services/labs/jurisdictions. Where possible shared infrastructure should be used (e.g. Consent, PanelApp, Shariant) |
| **Qualifications or considerations for use** | How are restrictions imposed on services (public or private) that are in position to offer more than others?<br><br>How is this prioritised in an already resource stretched health system? |

## PRINCIPLES FOR 'SURPRISE' FINDINGS

### DRAFT Principle 1

| | |
|---|---|
| **Heading** | Focus on the indication for testing |
| **Description** | Wherever possible, design test processes to minimise the detection of [name - incidental? additional?] findings. Patients/clients should know in advance that these findings may be identified and consent to or decline receipt of such findings in advance. This approach should be consistent nationally. |
| **Qualifications or considerations for use** | ◊ Balance between analysis and diagnostic yield<br>◊ Whether (and, if so, at what stage) to blind information in pipelines<br>◊ Probability a variant is pathogenic<br>◊ This may necessitate clarifying the indication for testing (better test request forms are needed!).<br>◊ How consent might be operationalised - e.g. if patient/client declines, just communication of the result? Or decline it going in the report too? |

### DRAFT Principle 2

| | |
|---|---|
| **Heading** | Findings to be managed with a client focus |
| **Description** | The provision of results should be done with the express consent of the client, utilising dynamic consent options if possible. Delivery of results should be done in an appropriate manner for the client, considering (but not limited to) age, education, primary language and cultural background. The result should be given with context to appropriate management, ongoing support, clinical and family needs. |
| **Qualifications or considerations for use** | Development of best practice guidelines for practitioners for different scenarios.<br>Development and roll out of consistent national dynamic consent for all. |

## DRAFT Principle 3

| | |
|---|---|
| **Heading** | Medically relevant incidental findings should be reported (with consent) |
| **Description** | Findings are medically relevant where there health benefit for the patient or family members from knowing the finding. Adequate informed consent should be obtained prior to testing. |
| **Qualifications or considerations for use** | Consider actionability for individual and/or family in case of paediatrics<br><br>ACMG list can be used to guide<br><br>Lab awareness of consent |

## PRINCIPLES FOR DELIBERATELY SEARCHING FOR FINDINGS

### DRAFT Principle 1

| | |
|---|---|
| **Heading** | Equity of access |
| **Description** | Consider both geographic and socio-economic equity of access to service, information and appropriate medical management |
| **Qualifications or considerations for use** | Appetite for public funding affects socio-economic equity of access |

### DRAFT Principle 2

| | |
|---|---|
| **Heading** | Ensure informed consent is obtained prior to testing |
| **Description** | Promoting autonomy through providing sufficient and multi-modal information during the consent process. Consent should be opt-in with nationally standardised processes. |
| **Qualifications or considerations for use** | Services must have appropriate resources and training to ensure autonomy is promoted during the consent process. |

## DRAFT Principle 3

| | |
|---|---|
| **Heading** | National approach to reporting additional findings |
| **Description** | Guidelines for seeking equitable and evidence-based best practice for testing and reporting of deliberately sought additional findings. |
| **Qualifications or considerations for use** | Nationally consistent recommendations for gene list inclusion and review, types and quality of results, consent requirements, including evaluation of clinical actionability, context and local regulatory requirements, e.g. adult vs paediatric, state laws, LHN guidelines. |

## DRAFT Principle 4

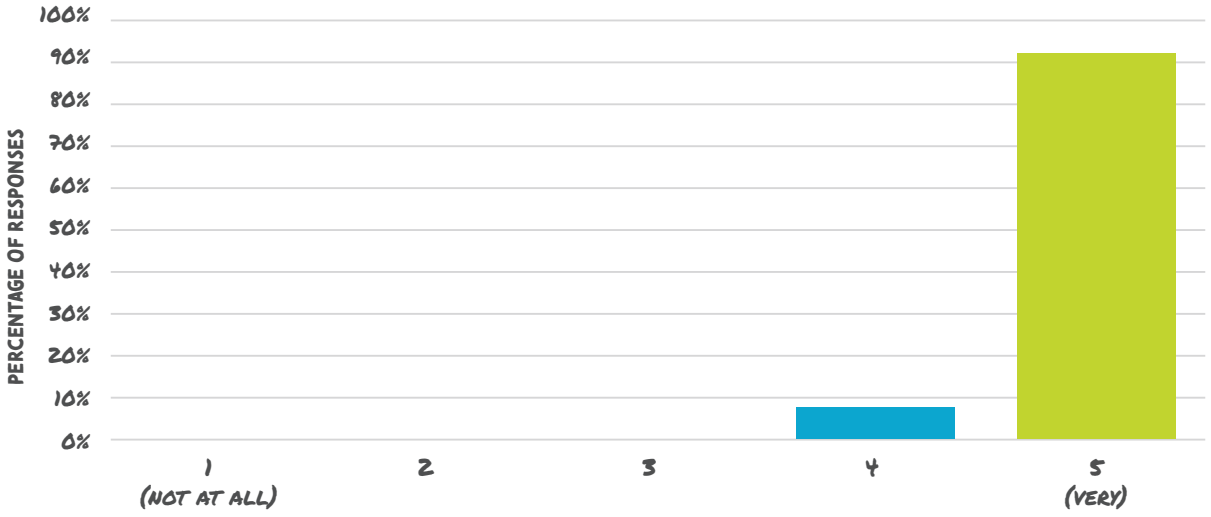
| | |
|---|---|
| **Heading** | Genes targeted in a deliberate search should be actionable and age-appropriate |
| **Description** | A standardised definition of actionability should be applied to determine the gene list analysed. This should take into account individual versus familial implications and paediatric versus adult contexts. |
| **Qualifications or considerations for use** | Any gene list applied should be consistent at a national level. |

# WORKSHOP FEEDBACK

Participants worked in small groups to draft a principle or two for review by the group. The groups reviewed all the principles and give feedback to help inform the project team when drafting final principles.

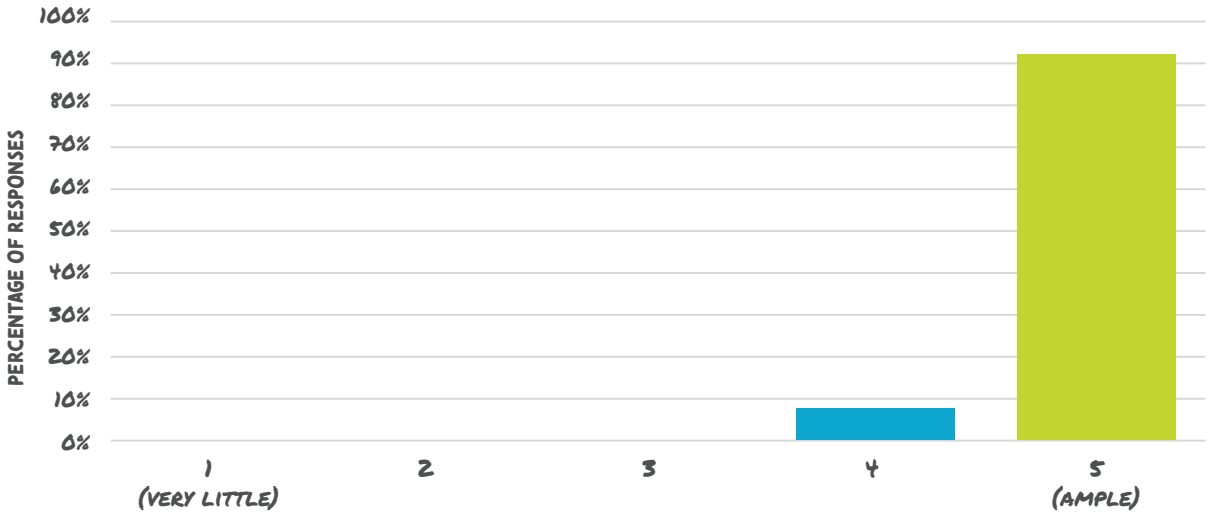
## How fair and balanced were the facilitators in their approach?

*11 participants responded*



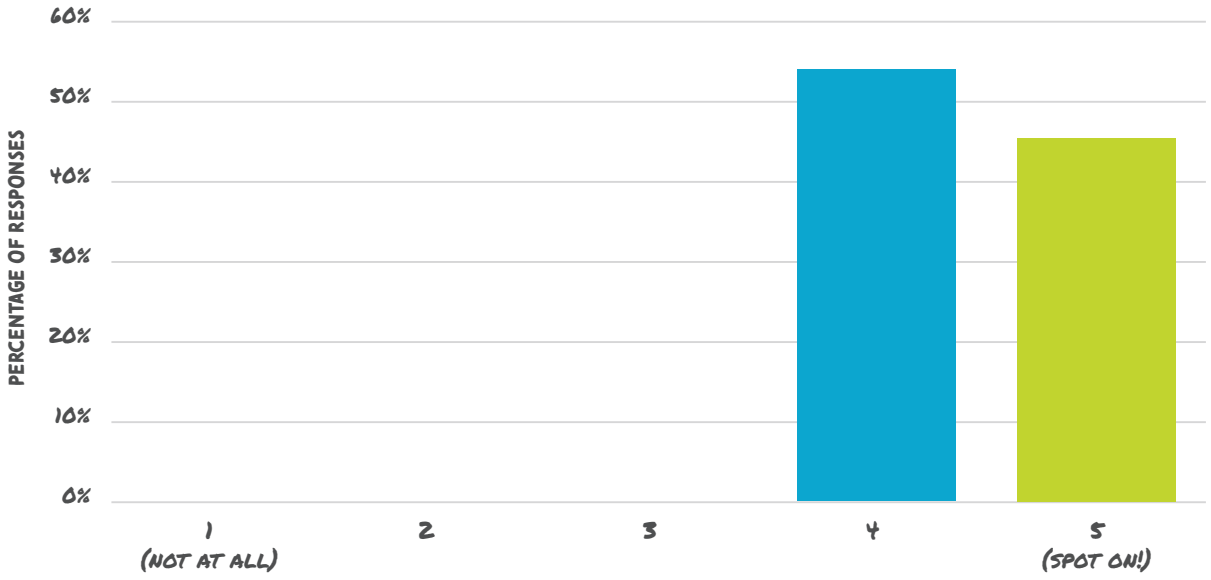

## How much opportunity did you have to contribute and be heard at this event?

*11 participants responded*



## How well did we meet the outcomes/outputs of this event together?

*11 participants responded*




## What did you like most about the event and why?

The facilitating was fantastic. It also was very evident that the Australian Genomics team had put in extensive hard work and planning to make this workshop happen. The briefing paper and agenda included a concise and clear summary to inform participants about the findings of the first workshop and let us know the aims of this second workshop.

Well facilitated, kept to time and directed the momentum where it needed to go. Very efficient use of time.

Got things done

Appreciated how engaged everyone was and the level of contribution. Also well facilitated and tech enhanced the workshop

Meeting other people and hearing their thoughts.

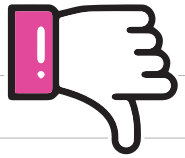
Interacting with different individuals

Got the work done

The small group sessions and interaction were great

A lot of involvement for everyone. Well done

## What did you dislike most about the event and why?



There was nothing to dislike!

Felt a bit rushed at times, to consider or flesh out points.

No dislikes

Having enough time, network speed

I understand it's important to capture current thoughts in what would be a perfect world but Australia is not ready for deliberate search for additional findings.

Tired brain at the end

## What improvements could be made for future events?

Allowing a little more time for activities like the group reflections on each principle, just to ensure that there is enough time for discussion and completing everything.

More diverse voices included.

Not sure

## Any other comments

Been surprised at both workshops about how efficient and effective this format has been. Encourage more of it for future interactions.

Very organised and great use of tools

**PLEASE NOTE:** This report has been prepared by MosaicLab on behalf of and for the exclusive use of the AusGenomics project team. The sole purpose of this report is to provide AusGenomics with materials produced at the workshop on the 28 November 2023.

This report has been prepared in accordance with the scope of services set out by the AusGenomics project team. In preparing this report, MosaicLab has relied upon the information provided by the participants at the session. AusGenomics can choose to share and distribute this report as they see fit. MosaicLab accepts no liability or responsibility whatsoever for or in respect of any use of or reliance upon this report by any third party.

*MosaicLab is a Victorian-based consultancy that specialises in community and stakeholder engagement, facilitation, negotiation, strategic planning and coaching.*

**REPORT PREPARED BY:**

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