Anticipate and Communicate for IRBs: Ethical Management of Incidental and Secondary Findings

October 7, 2014
1:00-2:30 PM ET

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Elisa A. Hurley, PhD
Executive Director

Welcome!

WEBINAR

The Future of Internet Research:
What We Can Learn from the Facebook
Emotional Contagion Study

Thursday, October 30, 2014 | 1:00-2:30 PM ET

PRIM&R PUBLIC RESPONSIBILITY IN MEDICINE AND RESEARCH

Mary L. Gray, PhD, and **Christian Sandvig, PhD**, will discuss the Facebook emotional contagion study and focus on some of the commonly raised questions pertaining to internet and social media research.

Elizabeth Buchanan, PhD, will moderate this discussion.

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Anticipate and Communicate for IRBs: Ethical Management of Incidental and Secondary Findings

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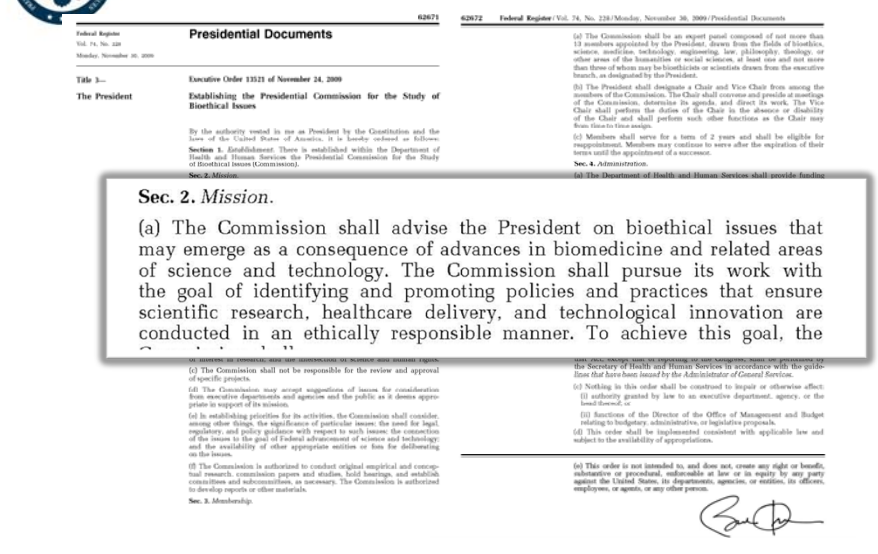
Presidential Commission for the Study of Bioethical Issues

PRIM&R Webinar, October 7, 2014

The Bioethics Commission



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Presidential Documents

Executive Order 13521 of November 24, 2009

Establishing the Presidential Commission for the Study of Bioethical Issues

Sec. 2. *Mission.*

(a) The Commission shall advise the President on bioethical issues that may emerge as a consequence of advances in biomedicine and related areas of science and technology. The Commission shall pursue its work with the goal of identifying and promoting policies and practices that ensure scientific research, healthcare delivery, and technological innovation are conducted in an ethically responsible manner. To achieve this goal, the

The Bioethics Commission

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Bioethics Commission Reports

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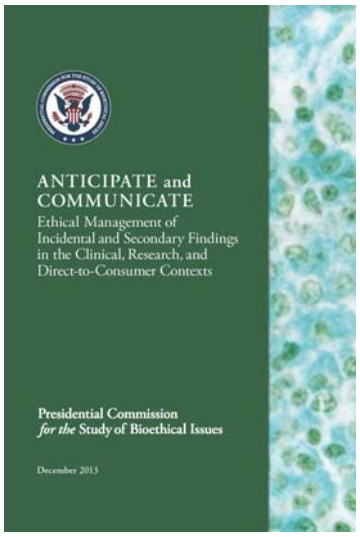
Released: December 12, 2013

11



Contrast with the Commission

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ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

AMERICAN MEDICAL ASSOCIATION

U.S. Preventive Services Task Force

American Cancer Society®

ACPM
American College of Preventive Medicine

ACR
AMERICAN COLLEGE OF RADIOLOGY

Taxonomy of Findings

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TYPE OF RESULT DISCOVERED	DESCRIPTION	EXAMPLE
Primary Finding	Practitioner aims to discover A, and result is relevant to A	In a child with unknown vaccine history, a test done to determine a child's immunity status before the chickenpox vaccine is administered
Incidental Finding: *Anticipatable*	Practitioner aims to discover A, but learns B, a result known to be associated with the test or procedure at the time it takes place	Discovering misattributed paternity when assessing a living kidney donor and potential recipient who believe they are biologically related
Incidental Finding: *Unanticipatable*	Practitioner aims to discover A, but learns C, a result not known to be associated with the test or procedure at the time it takes place	When a DTC genetic testing company identifies a health risk based on a newly discovered genetic association not knowable at the time a previous sample was submitted
Secondary Finding	Practitioner aims to discover A, and also actively seeks D per expert recommendation	ACMG recommends that laboratories conducting large-scale genetic sequencing for any purpose should actively look for variants underlying 24 phenotypic traits
Discovery Finding	Practitioner aims to discover A through Z by employing a test or procedure designed to detect a broad array of results	A "wellness scan," a whole body computed tomography (CT) scan, is intended to discover any abnormal finding throughout the body

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Review

Question 1: In which of the following cases would discovery of a BRCA mutation be considered an anticipatable incidental finding?

a) When conducting whole genome sequencing for the purpose of discovering any variant of significance ("tell me everything").

b) When conducting genetic testing for an unrelated disorder, and clinical practice guidelines suggest also looking for BRCA mutations.

c) When conducting genetic testing for the express purpose of discovering a BRCA mutation.

d) When conducting whole genome sequencing for research about the genetic cause of an unrelated disease.

Modalities

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Certain types of tests are unlikely to give rise to incidental and secondary findings.

- Discrete tests: produce only the particular results sought (e.g., pregnancy tests)
- Broad diagnostic tests: meant to find any abnormality (e.g., full body scans)

Tests for which practitioners obtain both the information sought and additional information potentially give rise to incidental and secondary findings.

Modalities

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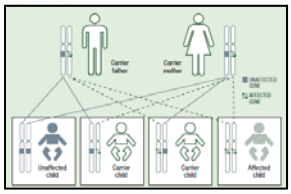
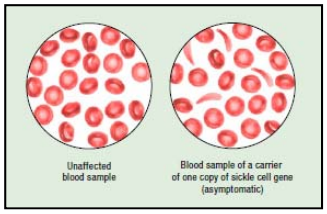
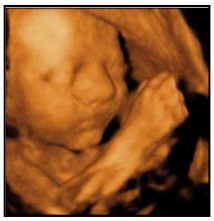


Large-scale Genetic Sequencing



Testing of Biological Specimens



Imaging

Modalities

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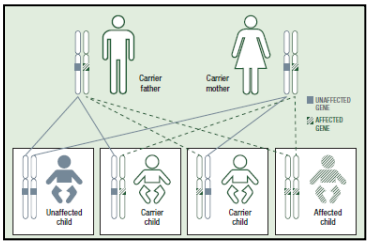
Large-Scale Genetic Sequencing

- Encompasses whole genome sequencing, whole exome sequencing, and other next-generation genomic analyses
- Potential to yield large numbers of incidental and secondary findings.
- Much of what is discovered is of unknown or uncertain medical value
- Implications for biologically-linked family members



Genetic Research

Modalities

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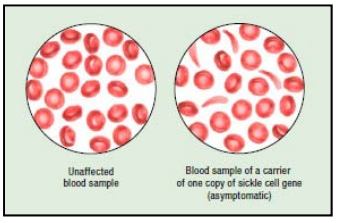
Testing of Biological Specimens

- Includes testing of blood, urine, or other tissues
- Incidental and secondary findings could definitively indicate a health issue of concern, or could require additional diagnostic tests to determine any health implications



Incidental Finding of Sickle Cell Trait

Modalities

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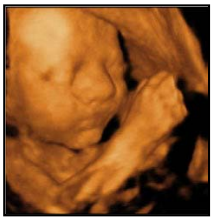
Imaging

- Includes magnetic resonance imaging (MRI), computed tomography (CT) scans, X-rays, neuroimaging, and ultrasounds
- Imaging products report results of the entire field of view (e.g., a CT scan of the abdomen can include images of the kidneys, liver, adrenal glands, and pancreas, with the possibility of discovering incidental and secondary findings in those organs)
- The likelihood of encountering incidental findings using imaging techniques is high, even among asymptomatic individuals



3-D Fetal Ultrasound
Taken by a DTC Company

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Review

Question 2: Which of the following is an example of a test or procedure that could give rise to incidental findings?

a) A test measuring blood glucose levels in diabetics.

b) A CT scan of the abdomen.

c) A test for strep throat.

d) A genetic test for Huntington's disease.

Contexts

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Clinicians

Direct-to-Consumer Providers

Researchers

Ethical Principles

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Longstanding ethical principles ground consideration of incidental and secondary findings.

- ***Respect for Persons***: respects an individual's capacity for rational self-determination
- ***Beneficence***: calls on individuals to take actions to ensure the wellbeing of others
- ***Justice and Fairness***: calls for fair and equitable treatment of all
- ***Intellectual Freedom and Responsibility***: protects intellectual exploration while requiring that individuals take responsibility for their actions

The interpretation, application, scope, strength, and stringency of each principle varies across contexts.

The Takeaway

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Practitioners in all contexts must:

Overarching Recommendations

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Recommendation 1: Practitioners should **inform potential recipients** about incidental and secondary findings and the plan for disclosing and managing those findings.

Recommendation 2: Professional groups should **develop guidelines and best practices** for managing incidental and secondary findings.

Recommendation 3: Federal agencies and interested parties should continue to **fund research** about incidental and secondary findings.

Recommendation 4: Entities should **prepare educational materials** to inform stakeholders about incidental and secondary findings.

Recommendation 5: All individuals should have **access to quality information** about incidental and secondary findings before and after testing.

The Clinical Context

Clinical – Case Study

Carol Krucoff

- Over-hydrated during a marathon; had a seizure after crossing the finish line and fell into a coma
- An MRI revealed a small acoustic neuroma (brain tumor)
- Watched and waited for nine years
- "Had I not learned about it as an incidental finding, I would have been blissfully ignorant."

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Review

Question 3: What type of finding was Carol Krucoff's acoustic neuroma?

a) A primary finding.

b) An unanticipatable incidental finding.

c) An anticipatable incidental finding.

d) A discovery finding.

Clinical – Practical Considerations

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- Clinicians have fiduciary duties to patients (a duty to act in a patient's best interest).
- Clinicians and patients should engage in shared decision making that respects a patient's ability to make autonomous decisions.
- Clinicians should ascertain and respect patient preferences—including a patient's right *not* to know—consistent with the clinician's fiduciary duty.

"We have a bias toward doing something as opposed to doing nothing. It feels right even if it's wrong, which in many cases it surely is. And our patients almost uniformly want us to do something. Both doctor and patient are enthralled in this overwhelming medical imperative to act. Remaining still—old-fashioned watchful waiting—requires a fortitude that few doctors are able to muster."

Ofri, D., Associate Professor, New York University School of Medicine, Editor-In-Chief, Bellevue Literary Review. (2013). Incidental Findings in the Clinic. Presentation to the Bioethics Commission, April 30. Retrieved from http://bioethics.gov/node/1619.

Clinical – Recommendations

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Recommendation 6: Clinicians should **inform patients** about incidental and secondary findings and **engage in shared decision making** about next steps.

Recommendation 7: Clinicians should be thoughtful about **communicating difficult information**.

Recommendation 8: Federal agencies should study the comparative and cost effectiveness of using **discrete tests versus bundled tests or a battery** of tests.

Recommendation 9: Medical educators should continue to cultivate **"diagnostic elegance" and "therapeutic parsimony."**

Recommendation 10: Organizations should produce **evidence-based standards for screening programs** that consider incidental findings.

The Research Context

Research – Case Study

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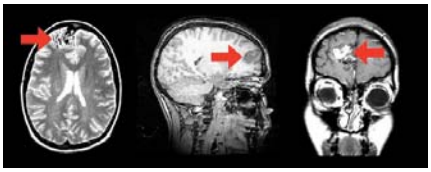
Sarah Hilgenberg

- As a student at Stanford Medicine, enrolled in a brain imaging study; participated in an fMRI test
- Researchers found an anomaly in the scan (an arteriovenous malformation); clinicians recommended removal of the mass
- Views the incidental finding as potentially life-saving



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Review

Question 4: What type of finding was Sarah Hilgenberg's arteriovenous malformation?

a) An anticipatable incidental finding.

b) A secondary finding.

c) A discovery finding.

d) An unanticipatable incidental finding.

Research – Practical Considerations

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- Researchers have obligations to participants and the creation of generalizable knowledge.
- The wide variety of research creates a challenge for developing best practices applicable to all protocols.
- Costs associated with returning incidental and secondary findings could interfere with the creation of generalizable knowledge.
- In certain types of research (e.g., research using de-identified data), returning incidental or secondary findings can be logistically difficult or practically infeasible.

"Research is the social enterprise of generating new knowledge. It serves the legitimate social purpose of supplying the information base necessary to understand human conduct; human health; to create, assess, and improve interventions; and ultimately, in the context of medical research, to improve the ability of health systems to understand and to meet the needs of the populations that they serve. In contrast, clinical care is the social enterprise of bringing to bear current knowledge, expertise, and interventions to address the health needs of individual patients."

London, A.J., Professor of Philosophy, Carnegie Mellon University, Director, Center for Ethics and Policy, Carnegie Mellon University. (2013). Incidental Findings in Research. Presentation to the Bioethics Commission, April 30. Retrieved from http://bioethics.gov/node/1617.

Research – Legal Considerations

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- No federal law, federal regulation, or state law directly addresses the return of incidental or secondary findings.
- The Common Rule requires disclosure about potential benefits and risks of research; incidental and secondary findings should be disclosed if considered a benefit or risk.
- In limited circumstances, HIPAA grants individuals a right to access certain aspects of their medical information upon request.
- CLIA mandates laboratory standards for certain laboratory testing; uncertainty about whether research findings can be returned if not obtained in a CLIA-certified laboratory.

Research – Ethical Considerations

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- ***Respect for Persons***: Through the informed consent process, researchers must provide enough information for participants to make autonomous, informed decisions to participate.
- ***Beneficence***: Researchers must demonstrate concern for the wellbeing of participants; should consider whether the benefits of disclosure outweigh the risks.
- ***Justice and Fairness***: Equitable distribution of benefits and burdens of research.
- ***Intellectual Freedom and Responsibility***: Researchers have the liberty to investigate, but must act responsibly.

Research – Recommendations

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Recommendation 11: During the informed consent process, **researchers should describe the scope of incidental and secondary findings**, the process for managing the findings, and how participants might opt out of receiving findings.

Recommendation 12: Researchers should develop a plan to manage **anticipatable incidental findings** that is reviewed and approved by an IRB.

Recommendation 13: Researchers should develop a process for evaluating and managing **unanticipatable findings** that is approved by an IRB.

Recommendation 14: Researchers who choose to look for **secondary findings** must have a plan approved by an IRB. Researchers have no duty to look for secondary findings.

Bioethics.gov Educational Materials 37

Bioethics.gov Educational Materials 38

Bioethics.gov Educational Materials 39

Primers:

Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts

- IRB Primer: Incidental and Secondary Findings

Primers for Practitioners:

- Clinician Primer: Incidental and Secondary Findings
- Researcher Primer: Incidental and Secondary Findings
- Direct-to-Consumer Provider Primer: Incidental and Secondary Findings

"Conversation Series" for Recipients:

- For Patients: A Guide to Incidental Findings
- For Research Participants: A Guide to Incidental Findings
- For Consumers: A Guide to Incidental Findings

Bioethics.gov Educational Materials 40

IRB Primer: Incidental and Secondary Findings

In December 2013, the Presidential Commission for the Study of Bioethical Issues (Bioethics Commission) released its report, *Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts*. The report outlines the types of findings that can arise from various tests and procedures in a variety of contexts, and makes 17 recommendations for the ethical and professional management of such findings.

This primer was designed to help institutional review boards (IRBs) understand and implement the Bioethics Commission's recommendations regarding how to manage incidental and secondary findings ethically in the research setting. IRB members can use it to improve their understanding of the Bioethics Commission's recommendations and consider how to ensure the ethical management of incidental and secondary findings that could arise in the protocols they review. Please see *Anticipate and Communicate* for further reading on the Bioethics Commission's analysis and recommendations (Executive Summary, pp. 2-20 and Chapter 5, pp. 75-93).

The final page of this primer provides a list of recommended considerations for IRBs and their members as they review researchers' procedures for ethically managing incidental and secondary findings. This primer and the list of considerations are not derived from regulations. Rather, the primer reflects the Bioethics Commission's recommendations regarding the ethical management of incidental and secondary findings. IRBs can use this primer to aid in their ethical decision making.

Frequently Asked Questions

1. What are incidental and secondary findings?

Bioethics Commission Classification of Individualized Results of Medical Tests

TYPE OF RESULT DISCOVERED	DESCRIPTION	EXAMPLE
Primary Finding	Practitioner aims to discover A, and result is relevant to A	In a child with unknown vaccine history, a test done to determine a child's immunity status before the chickenpox vaccine is administered
Incidental Finding: *Anticipatable*	Practitioner aims to discover A, but learns B, a result known to be associated with the test or procedure at the time it takes place	Discovering misattributed paternity when assessing a living kidney donor and potential recipient who believe they are biologically related
Incidental Finding: *Unanticipatable*	Practitioner aims to discover A, but learns C, a result not known to be associated with the test or procedure at the time it takes place	When a DTC genetic testing company identifies a health risk based on a newly discovered genetic association not knowable at the time a previous sample was submitted
Secondary Finding	Practitioner aims to discover A, and also actively seeks D per expert recommendation	ACMG recommends that laboratories conducting large-scale genetic sequencing for any purpose should actively look for variants underlying 24 phenotypic traits

Source: Presidential Commission for the Study of Bioethical Issues (PCSBI). (2013, December). *Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts.* Washington, DC: PCSBI, p. 27. Note: DTC = direct-to-consumer, ACMG = American College of Medical Genetics and Genomics.

Case Study: You are overseeing a genome wide association study (GWAS). The purpose of the research is to discover new associations between genetic mutations and heart disease. The researchers begin analyzing data. After conducting genetic tests on 1,000 participants, they come to you for advice. They have discovered the BRCA1 mutation, which increases the risk for hereditary breast cancer, in 5 of their participants. They want to know what they should do.

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Review

Question 5: What kind of finding is this?

a) Primary

b) Secondary

c) Anticipatable incidental

d) Unanticipatable incidental

Frequently Asked Questions

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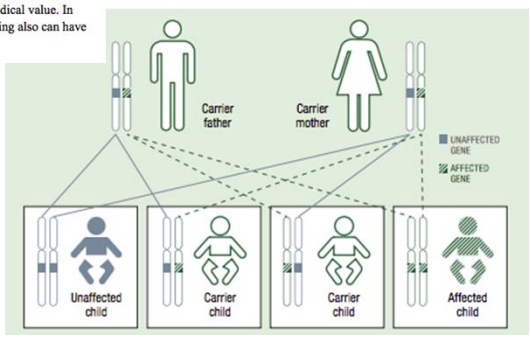
2. What are some of the tests or procedures that could give rise to incidental and secondary findings?

- **Large-Scale Genetic Sequencing:** Genetic sequencing is the analysis and ordering of the billions of base pairs—the As, Ts, Cs, and Gs—that make up the human genome. Large-scale genetic sequencing techniques include whole genome sequencing, whole exome sequencing, and other next-generation genomic analyses. Because of the large number of base pairs sequenced and potentially analyzed, large-scale genetic sequencing has the potential to yield large numbers of incidental and secondary findings. While some variants discovered during large-scale genetic sequencing reveal clinically relevant information, much of the data produced are of unknown or uncertain medical value. In addition, incidental and secondary findings that arise in genetic sequencing also can have implications for biologically-linked family members.



Frequently Asked Questions

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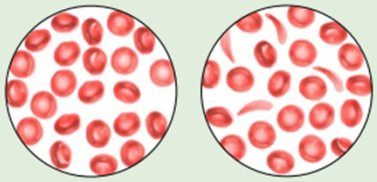
2. What are some of the tests or procedures that could give rise to incidental and secondary findings?

- **Testing of Biological Specimens:** Analysis of biological specimens such as blood, urine, or bodily tissues can be a source of incidental or secondary findings. Incidental and secondary findings arising from blood and tissue testing could definitively indicate a health issue of concern, or could require a series of additional diagnostic tests to determine the health implications, if any, of the result. For example, a researcher might order a metabolic panel to assess kidney function, but the laboratory results might reveal an incidental finding of liver dysfunction.



Unaffected blood sample

Blood sample of a carrier of one copy of sickle cell gene (asymptomatic)

INCIDENTAL FINDING OF SICKLE CELL TRAIT

Frequently Asked Questions

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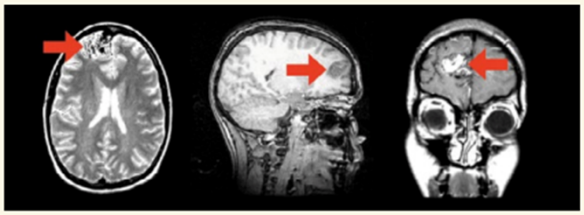
2. What are some of the tests or procedures that could give rise to incidental and secondary findings?

- **Imaging:** Medical imaging includes magnetic resonance imaging (MRI), computed tomography (CT) scans, X-rays, neuroimaging, and ultrasounds, among others. The images produced provide visualization of an entire field of study and can give rise to incidental and secondary findings in areas outside the area of diagnostic interest. For example, scans of the abdomen and pelvis can include images of the kidneys, liver, adrenal glands, and pancreas, only one of which might be the organ of interest to researchers.



As indicated in the image above, researchers incidentally discovered an arteriovenous malformation in Sarah Hilgenberg's brain on a scan during a memory research study.

Frequently Asked Questions

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3. Why should researchers inform research participants about the possibility of incidental and secondary findings?

Researchers should communicate the fundamental aspects of their research—including the possibility of discovering incidental or secondary findings and the plan for their disclosure or management—so that participants can make fully informed decisions about whether to enroll. IRBs should review informed consent materials to ensure that researchers have included information about incidental and secondary findings and the plan for management of these findings.

Frequently Asked Questions

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3. Why should researchers inform research participants about the possibility of incidental and secondary findings?

Researchers can ascertain at the outset what participants prefer to know—and not know—about incidental or secondary findings. For example, a participant might prefer to know about only those findings that are clinically significant, actionable, and lifesaving. Acting in accordance with participants' expressed preferences about whether to receive incidental and secondary findings, to the extent possible, helps researchers to respect participants' autonomy. If practical or logistical constraints prevent a researcher from searching for, interpreting, or disclosing incidental findings, the researcher can propose a plan that incidental and secondary findings will not be returned. Disclosing a plan for managing incidental findings, and allowing for nonparticipation if a prospective participant chooses, appropriately respects an individual's ability to make autonomous and informed decisions about whether to participate in research.

Frequently Asked Questions

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4. What are some of the arguments in favor of returning—or not returning—incidental and/or secondary findings?

Researchers and IRBs should carefully consider both the potential benefits and risks of disclosure of incidental and secondary findings. Disclosing certain incidental findings might lead participants to obtain lifesaving medical interventions, or help participants make informed medical decisions. However, disclosure also could lead to needless further testing, additional incidental findings, costs, and anxiety and distress, potentially with no corresponding medical benefit. Researchers should evaluate whether the prospective benefits of an action outweigh the risks.

Researchers also should consider carefully whether to allocate time and resources to seeking secondary findings, or to interpreting, assessing, and disclosing incidental findings, especially when these decisions might benefit individuals in the research study but stall broader societal benefits of the research activity. Researchers do not have an ethical duty to seek secondary findings. However, researchers must determine how their incidental findings management policy will affect participants as individuals, and how it will affect their ability to create generalizable knowledge. The following table of ethical principles and their application to incidental and secondary findings can help researchers reconcile these considerations.

Ethical Principles

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Principle	*Definition*	*Application*
Respect for Persons	This principle recognizes the fundamental human capacity for rational self-determination.	Researchers must communicate the fundamental aspects of their research—including the possibility of discovering incidental or secondary findings and the plan for their disclosure or management—so that participants can make informed decisions about whether to enroll.
Beneficence	This principle calls on professionals to take action to ensure the wellbeing of others. Its corollary, non-maleficence, requires not imposing harm on others.	This principle supports returning findings when disclosure might help forestall or prevent harm. By contrast, disclosing an incidental finding for which no preventive or positive action can be taken has the potential to cause anxiety and distress with no corresponding medical benefit.
Justice and Fairness	This principle requires fair and equitable distribution of the potential benefits and burdens across society.	The principle of justice and fairness calls upon researchers to take into account how policies for returning incidental and secondary findings could benefit or burden some participants or, alternatively, could burden the research enterprise and the ability to create generalizable knowledge.
Intellectual Freedom and Responsibility	This principle protects sustained and dedicated creative intellectual exploration that furthers scientific progress, while requiring that researchers take responsibility for their actions.	This principle supports affording wide latitude to researchers in pursuing their scientific goals and engaging in intellectual exploration for the good of society, while also expecting that researchers uphold and respect the trust placed in them by participants. Ethical conduct of research with human participants includes acknowledgment and planning for incidental and secondary findings.

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Case Study: You are overseeing a genome wide association study (GWAS). The purpose of the research is to discover new associations between genetic mutations and heart disease. The researchers begin analyzing data. After conducting genetic tests on 1,000 participants, they come to you for advice. They have discovered the BRCA1 mutation, which increases the risk for hereditary breast cancer, in 5 of their participants. They want to know what they should do.

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Review

Question 6: When obtaining initial informed consent, the researchers never told the participants that they might notify them of individualized genetic test results. Some researchers feel strongly that the participants need to be notified about this significant, potentially lifesaving information. Which ethical principle(s) are these researchers primarily drawing from?

a) Respect for Persons

b) Beneficence

c) Justice and Fairness

d) Intellectual Freedom and Responsibility

Case Study: You are overseeing a genome wide association study (GWAS). The purpose of the research is to discover new associations between genetic mutations and heart disease. The researchers begin analyzing data. After conducting genetic tests on 1,000 participants, they come to you for advice. They have discovered the BRCA1 mutation, which increases the risk for hereditary breast cancer, in 5 of their participants. They want to know what they should do.

Review

Question 7: Others on the team feel that it will be expensive and time consuming to contact all of these participants and possibly hire a genetic counselor to deliver the news. This will detract from their main research agenda and limit the amount of data they will be able to afford to analyze. Which ethical principle(s) are these researchers primarily drawing from?

a) Respect for Persons

b) Beneficence

c) Justice and Fairness

d) Intellectual Freedom and Responsibility

55

Case Study: You are overseeing a genome wide association study (GWAS). The purpose of the research is to discover new associations between genetic mutations and heart disease. The researchers begin analyzing data. After conducting genetic tests on 1,000 participants, they come to you for advice. They have discovered the BRCA1 mutation, which increases the risk for hereditary breast cancer, in 5 of their participants. They want to know what they should do.

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Review

Question 8: And still others on the team feel that, although they should revisit their policy on returning findings for the future, they should not notify current participants about their results because the participants have never been given the opportunity to express preferences about notification and did not consent to the return of individualized results. Which ethical principles are these researchers primarily drawing from?

a) Respect for Persons

b) Beneficence

c) Justice and Fairness

d) Intellectual Freedom and Responsibility

Frequently Asked Questions

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5. What constitutes an ethically appropriate plan for the management of incidental and secondary findings?

Informed Consent

Researchers should develop a plan for managing the types of findings that might arise, and clearly communicate the plan to participants during the informed consent process—even if the plan is not to disclose any incidental or secondary findings. This allows individuals to choose not to participate in research if they are uncomfortable with a researcher's management plan. When reviewing consent materials, IRBs should evaluate whether the following elements have been considered and included.

- Secondary findings that will be actively sought and returned to participants should be conveyed in the informed consent process, and there should be a specific plan for their return.
- A plan for anticipatable incidental findings (e.g., that researchers will or will not return some or all potential findings) also should be conveyed in the informed consent process, and, to the extent that the findings will be returned, a plan should be described.
- For findings that are unanticipatable, researchers should plan for the types of findings that might arise and plan for return if applicable (e.g., that researchers will return unanticipatable lifesaving findings, but will not return unanticipatable findings of unknown significance).

Frequently Asked Questions

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5. What constitutes an ethically appropriate plan for the management of incidental and secondary findings?

Expertise

Some incidental findings could fall outside of researchers' expertise. IRBs should verify that researchers are sufficiently familiar with anticipatable incidental findings associated with the tests or procedures used in their research to formulate and communicate a plan for how these findings will be managed. If researchers need additional expertise to manage incidental and secondary findings, an IRB could suggest they add this expertise by, for example:

- adding members to the research team who have sufficient expertise to manage the range of anticipatable incidental findings;
- relying on research ethics consultants or IRBs if there is uncertainty as to the advisability of disclosing a particular finding to a participant; and/or
- seeking qualified clinical or diagnostic experts for consultation when researchers are uncertain whether a finding has clinical or reproductive significance.

IRBs should consider whether they have the resources or expertise to assist researchers when considering difficult cases. In addition, IRBs should provide guidance to inform how researchers might develop and communicate the plan for disclosing and managing findings that are outside the researchers' area of expertise. For example, researchers might wish to disclose genetic incidental findings in the presence of a genetic counselor to assist participants in understanding the finding's significance.

Frequently Asked Questions

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5. What constitutes an ethically appropriate plan for the management of incidental and secondary findings?

Participant Preferences

If researchers plan to inform participants of certain types of incidental or secondary findings, they should decide in advance how to respect the wishes of participants who choose to opt out of receiving these findings. IRBs should review researchers' plan for communicating findings, which should be communicated as part of the informed consent process.

- If researchers have ethical objections to allowing participants to opt out of receiving clinically significant, actionable, and lifesaving findings, they need not enroll such individuals in their research study. Delineating such exclusion criteria for study enrollment will minimize this type of ethically challenging situation once the research protocol is underway.
- If researchers do not object to allowing participants to opt out of receiving incidental findings—and participants are well informed regarding what opting out could mean for their health and wellbeing—researchers may enroll such participants in the research.
- If a researcher discovers a potentially lifesaving unanticipatable incidental finding for a participant who has opted out of receiving incidental findings generally, the investigator should seek advice from an IRB about whether and how to disclose it. IRBs should be prepared to answer researchers' questions about whether to disclose a lifesaving incidental finding to a participant who has opted out.

Frequently Asked Questions

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5. What constitutes an ethically appropriate plan for the management of incidental and secondary findings?

Researcher Responsibilities

Researchers' plans for managing incidental findings also should include a description of the research team's responsibilities following disclosure of such a finding. In some cases, researchers might provide:

- basic educational information about the nature of the finding;
- advice regarding how to seek care from a clinician or specialist;
- guidance about obtaining health insurance to secure treatment; and/or
- a referral to a clinical specialist, if one is required.

Considerations "Checklist"

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Considerations for Ethical Management of Incidental and Secondary Findings

Identifying Incidental and Secondary Findings:

- Researchers should identify any secondary findings they plan to seek actively during their research.
- Researchers should identify any anticipatable incidental findings that might arise during their research.
- Researchers should identify the general types of unanticipatable incidental findings that might arise during their research (e.g., lifesaving, clinically actionable, of unknown significance).

Recognizing and Analyzing Incidental and Secondary Findings:

- Researchers should have a plan for recognizing, analyzing, and handling incidental and secondary findings.
- If anticipatable incidental or secondary findings might require additional expertise to recognize or analyze, researchers should consider adding such expertise to the team (e.g., consulting a professional with the necessary expertise or otherwise having one available for consultation).

Considerations "Checklist"

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Informed Consent for Incidental and Secondary Findings:

- Researchers should inform potential participants of the following:
  - Secondary findings they intend to seek and return.
  - Anticipatable incidental findings that might arise during the research and the plan for returning results.
  - General types of unanticipatable incidental findings that might arise during the research and the plan for management of such findings.
- Researchers should describe the kinds of findings that might be disclosed, the process for disclosing them, and whether and how participants might opt out of receiving certain findings.
- Researchers should indicate in the informed consent process any exclusion criteria for individuals who wish to opt out of receiving clinically significant, actionable, and lifesaving findings.

Returning Incidental and Secondary Findings:

- Researchers should have a designated plan for returning incidental and secondary findings to participants. The plan might include the option for participants to opt out of receiving incidental or secondary findings, or might be to return no findings to participants.
- Researchers should respect the wishes of participants who choose to opt out of receiving incidental or secondary findings, but in the event a researcher discovers a potentially lifesaving unanticipatable incidental finding for a participant who has opted out of receiving incidental findings, the investigator should seek advice from an IRB about whether and how to disclose it.

Bioethics.gov Educational Materials

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Primers:

Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts

- IRB Primer: Incidental and Secondary Findings

Primers for Practitioners:

- Clinician Primer: Incidental and Secondary Findings
- Researcher Primer: Incidental and Secondary Findings
- Direct-to-Consumer Provider Primer: Incidental and Secondary Findings

"Conversation Series" for Recipients:

- ~~For Patients: A Guide to Incidental Findings~~
- For Research Participants: A Guide to Incidental Findings
- ~~For Consumers: A Guide to Incidental Findings~~

Participant Primer

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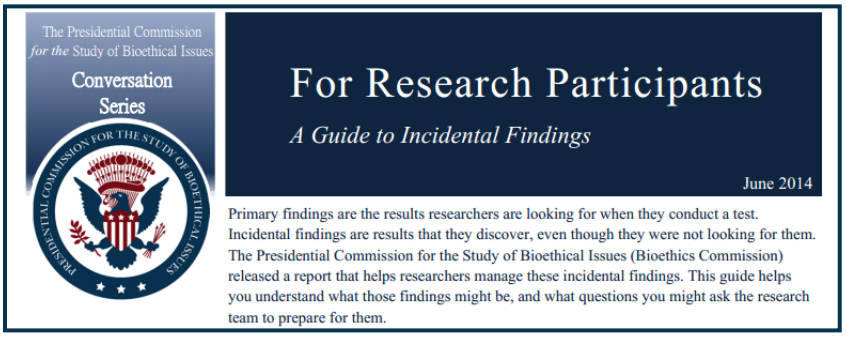

Participant Primer

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What tests might have incidental findings?

Genetic testing:
Researchers might conduct a genetic test for their study. They might discover something in your DNA that they did not expect.

Tests on your blood or urine:
Researchers might do a test on your blood or urine. Usually researchers will order the test for a specific purpose. But the lab might conduct many tests in a bundle. As a result, researchers might discover something they were not looking for.

Imaging:
Researchers might order a medical imaging test, such as an X-ray, MRI, or ultrasound. Imaging sometimes shows things that researchers were not looking for.

What questions should I ask the research team?

What might you find?
Ask a member of the research team to explain the tests they will be conducting, and what results they might discover.

What will you tell me?
Some research studies do not return any results to participants. Ask the researchers if they will tell you about any of the results they discover, and if so, which ones. This will help you understand what you might learn from the tests they are doing.

What will happen next?
Ask the researchers how they will follow up on the results they find. For example, ask if they will help you find a doctor if they discover something that could be important for your health.

What if I don't want to know?
Make sure to tell the researchers if there are any results you don't want to know about. The research team will listen to your preferences, and determine how best to follow them.

Participant Primer

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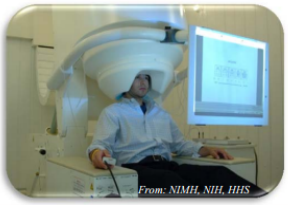
PARTICIPANT EXPERIENCES

Isabelle signed up for a research study in which the researchers scanned her brain. The researchers saw something abnormal in her scan. They told Isabelle to see a doctor, and the doctor recommended surgery to take out a mass. She credits this finding with saving her life.



From: NIMH, NIH, HHS

James took part in the same research study. The researchers scanned his brain. When the researchers reviewed his brain scans, they found nothing out of the ordinary. James was happy to be a part of an interesting research study.

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Thank you!

Questions and comments

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Elisa A. Hurley, PhD
Executive Director

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