R01 CA154517
Disclosing Genomic Incidental Findings in a Cancer Biobank:
An ELSI Experiment

PIs: Barbara A. Koenig, Gloria M. Petersen, Susan M. Wolf

Collected Interview Guides

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Disclosing Genomic Incidental Findings in a Cancer Biobank: An ELSI Experiment

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Interview Discussion Guide for Probands in support of Aim 1a: To assess *a priori* preferences of pancreatic cancer probands and their family members about receiving genomic results that carry health and/or reproductive risks, using in-depth qualitative interviews.

[Opening Statements]

I'd like to start by thanking you for your willingness to participate in this interview, and in the Pancreas Research Registry. It is truly appreciated. I will record our conversation with your permission. Is that OK? Also, just to remind you that your comments will be kept strictly confidential. We will be very careful with everything you tell us.

TURN ON RECORDER/CHECK EQUIPMENT

Have you been able to read or look over the materials that we sent ahead of time**?** *Suggest that they may wish to have the materials we provided available during the interview, but this is not required.*

If interviewee has read the materials, May I ask how much of that information was new to you? For example, had you heard of the three genetic conditions mentioned?

Before we begin, I would like to review and clarify a few things about **the aims** of the project, **my role** in it, and the nature of **this interview**.

First, the aims of the project: While doing research on the cause of pancreatic cancer, Mayo Clinic researchers have discovered some patients who carry mutations in other genes that increase one's risk for having other diseases. This was information we did not expect. During this interview we will call them "unexpected results." Up to now, unexpected genetic research results generally were NOT returned to research participants or to their family members. This standard practice— "a no results" policy—is followed in the Mayo clinic and nearly all research institutes today.

In the future, it is likely that when people participate in research, gene mutations may be found. In fact, it is likely that everyone will carry mutations for several "genetic" diseases, like cystic fibrosis. Unexpected results will become the "new normal" in genetic research.

There is a lot of debate about whether a "no results" policy should change, and if so, how? Answering these questions and developing new policies better adapted to the new situation are the aims of this research.

Clearly, research participants and their family members are most affected by research policies. For this reason we want to learn from you—about your opinions and ideas. We are trying to understand what patients and family members want and need, so you are the expert. We are aware that the issues are very complicated. I will ask for your thoughts on some difficult questions, but don't worry, you are not expected to have all the answers! This is not a test! There are no right answers. We seek your guidance. That is the goal of this interview.

Now, my role: I am part of a team carrying out this research. My role on the project is as an interviewer. I'm not a physician or an expert on pancreas disease, so I may not be able to answer technical questions. Rather, my job is to listen, and to learn from you. Let me also say again that

we DO NOT know anything about your genetic results or genetic risk; that was also explained in the materials we sent by mail.

Now, the interview: The interview should take around 45 minutes; some people have spoken to us for an hour. The amount of time you give us is up to you. Please feel free not to answer a question if you do not want to, or to stop at any time. Or to continue the call later. Feel free to interrupt or ask questions at any point and I'll do my best to answer them.

SO**,** after all that, and before we get started, **do you have any questions about what I just went over or the interview process?**

If not, let's begin!

[(1) Opening: Obtaining the informant's "story" and information about the "family"]

1.1. Could you tell me the story of your experience with pancreatic cancer, starting at any point you think is important.

1.2. Who, in your family, knows about your diagnosis of pancreatic cancer?

Probes: Who did you tell? Not tell? Why?

1.3. I will be asking you a lot of questions about your family and family members. Who would you say "family" refers to for you?

Probes: Who are your blood relatives?

Interviewer may want to draw a family tree with names to help keep track.

1.4. What motivated your participation in the Mayo Clinic pancreas research registry?

[(2) Concern about familial cancer risk]

2.1. Have you ever worried that any of your family members may develop pancreatic cancer?

Probes: *If yes*, can you tell me a little about that? How worried, for how long? Worried for whom?

If the interviewee has not mentioned it already. Have you ever wondered if pancreatic cancer ran in your family?

Have you or your family members ever acted on that worry—for example, have you read about the disease? Asked your physicians or friends about it? Have you ever thought about having genetic testing?

2.2. *If the interviewee has not mentioned it already*. Have you or anyone in your family ever had a genetic test? *Of any kind.*

> *If yes, probe for how communication within the family was handled. Who was tested? For what disease? With what results? Did family members share results with each other? Who did or did not want to know?*

[(3) Unexpected research results/incidental findings]

Now I would like to turn to unexpected research results and what to do about them, the focus of our project. As you may remember from the materials we sent you, when conducting genetic testing for genes related to pancreatic cancer, researchers discovered that some patients with pancreatic cancer have mutations in 1 of 3 genes that are linked to an elevated risk for other diseases. Specifically these diseases are breast cancer, melanoma—a serious kind of skin cancer, and cystic fibrosis—a severe chronic lung disease in children and young adults which can lead to early death.

For example, a mutation in the BRCA2 gene makes a woman more likely to have breast or ovarian cancer, and men more likely to develop prostate or breast cancer. A mutation also raises the risk of pancreatic cancer by a small amount, but that is not the focus of our project. Let's say that in the course of looking for the causes of pancreatic cancer, the researchers unexpectedly find a mutation in a research participant's BRCA2 gene. This would mean that the patient's blood relatives—including children and brothers and sisters—could also have a mutation in the BRCA2 gene. A copy of a gene mutation from just one parent is enough to increase cancer risk.

3.1. What do you think the researchers should do with the information if they find someone has this gene mutation?

> Probes: Do you think researchers should offer it to the person who participated in their study? Before you answer, let me tell you what I mean by offered. I mean that the person who participated in the study could say yes or no to actually hearing their results. So, do you think the participant should have the results offered to him/her?
>
> What about to the research participant's family? Should those who might carry the mutation be offered results?

3.2. Remember, our research team does not have any specific genetic results about you. But hypothetically, imagine that Mayo Clinic researchers did find the BRCA2 mutation when your sample was tested. Would you want this information to be offered to you?

> Probe: Why/Why not?

3.3. If genetic findings were offered, do you think you would in fact want to learn the results?

> Probe: Why/Why not?

3.4. What about to your family? Do you think that researchers should offer your genetic results to your family members?

Probe: *If yes*, to which family members and why? *If no*, why not?

3.5. Who do you think should control whether this information is offered to your family? In other words, who should decide whether or not this information is offered to your family?

3.6. Do you think your answers would be any different for melanoma, that's the serious type of skin cancer, than for breast cancer?

Probe: *If yes*, how?

I now want to raise the example of cystic fibrosis. Let me remind you how the disease is inherited. To have the disease, a child must inherit 2 copies of the cystic fibrosis gene mutation, one mutation from each parent. If both parents have the mutation, there is a 1 in 4 chance that their child will receive 2 copies of the mutation and have cystic fibrosis. The parents will not have cystic fibrosis if they only have one mutation. And children who inherit one mutation also will not have the disease, but they can pass it along to their children.

3.7. Do you think your answers would be any different for cystic fibrosis than for breast cancer?

Probe: *If yes*, how?

3.8. How, if at all, do you think this kind of information might affect your decisions, or your family members' decisions, about having children?

3.9. What about decisions about prenatal testing? Meaning testing a woman who is pregnant?

CHECK EQUIPMENT

[(4) Motivations, Personal and Clinical Utility of Genetic Findings]

Besides these "real life" examples from the Mayo Clinic pancreas registry, it is likely that many other mutations will be identified in the future when people participate in genetic research. For this reason, we would like to get a sense about what kinds of genetic results—if any—you think researchers should offer to research participants, such as yourself, or to participants' family members?

I'll go through a short list that includes some characteristics of tests. Tell me whether a specific characteristic makes you think it should or shouldn't be offered to research participants or their family members.

4.1. What about results where the research is not yet well established, because it is based on a new discovery and is not yet certain?

4.2. As you know, the Food and Drug Administration, the "FDA," reviews new drugs. What if a genetic test had been reviewed and approved by a government agency like the FDA for routine use?

4.3. What about a serious or fatal disease that can be treated, versus one that can't? Does whether it can be treated or not matter?

4.4. What if the condition causes dementia or cognitive decline, like Alzheimer's?

4.5. What if there is nothing one can do to prevent the disease or to detect it early?

4.6. Are there any conditions that you think you yourself might not want to know about?

5) [Scenario: Family Communication and Decisions about Testing]

Imagine the following situation based on our experience. After her diagnosis with pancreas cancer, "Mrs. Jones" agreed to be in the pancreas research registry. Unfortunately, the treatment she received did not cure her disease. After her death, researchers discovered that Mrs. Jones carried a BRCA2 mutation. She has two daughters, ages 20 and 23. The research team knows that each daughter has a 50/50 chance of having inherited the mutation from Mrs. Jones. If they have the mutation, each daughter's chance of getting breast and ovarian cancer goes up significantly.

5.1. In this situation, do you think the researchers should offer the daughters Mrs. Jones' results? Again, remember that I'm talking about an offer. I am assuming that the daughters' can decide for themselves whether they want to learn their mother's genetic results**.**

Probe: Why/Why not?

Mrs. Jones' husband is her "legal next of kin." In some states, the law requires that researchers offer Mrs. Jones' results to him alone. When the researcher did offer Mr. Jones his wife's genetic results, he said "no I don't want to know, and please do not tell my daughters." He said that talking about his wife's cancer is too painful for the family.

5.2. Do you think Mrs. Jones' daughters have a right to information that might affect their health?

Probe: Whose wishes do you think should have priority in a conflict?

Probes: Why?

5.2.1 What about Mrs. Jones' brothers and sisters? They also have a 50/50 chance of carrying the BRCA2 mutation. Do they have a right to information that might affect their health?

Probe: And what about Mrs. Jones' nieces and nephews?

Genetic analysis takes some time, and it is common, like in Mrs. Jones' story, for the results to be discovered when the patient is no longer alive to decide for herself. Imagine that your results become available after your death.

5.3. How do you think this situation should be handled? Do you think the researchers should offer your results to anyone? What about your biological relatives, such as brothers and sisters or children? *Note that this repeats the "Mrs. Jones question" in 5.1 but this time for the interviewee him/herself.*

Probe: *If yes,* to which relatives? *If not mentioned, ask*: What about to cousins or aunts and uncles? *If not,* why not?

5.4. Should results be offered to your biological relatives even if you had not given your prior permission?

5.5. Would you be comfortable with your legal next of kin or representative deciding for you?

Probes: Why/Why not? Who would you be comfortable with, if anyone?

5.6. Have you ever discussed these types of questions within your family?

Probe: *If yes,* can you tell me about that.

[(6) Practical preferences for communication of unexpected findings]

Continuing to imagine the situation in which a Mayo Clinic researcher has discovered information about you that was unexpected: *Interviewer may need to verify our specific use of unexpected results.*

6.1. If you would want to be notified of your genetic results, how do you think you would prefer that Mayo Clinic make contact with you?

Probes: *phone, letter, email, secure internet portal, in person by health professional*

If personal contact is desired, ask: Who do you think should make contact with you or explain the results? *Probes: genetic counselor, researcher, primary doctor, nurse, research or study assistant*

6.2. Do you have any suggestions about exactly what a first message should include?

Probe: For example, "we have found something that might be important to your health or your family's health and we want to talk to you," or "we found that you carry a mutation linked to breast cancer, putting you at 50% risk of passing on a gene mutation."

6.3. With your permission, should Mayo Clinic researchers share information with your primary care physician?

Probes: Why/Why not?

Before or after contacting you?

CHECK EQUIPMENT

7) [Genetic Privacy and Discrimination]

7.1. Would you have concerns about others finding out that you have a particular mutation?

Probes: *If yes,* who and why? *If not, why not?*

Would you have concerns about family members finding out that you have a particular mutation? If yes, why?

What about your employer?

Your health insurance company?

7.2. Did you know that the Genetic Information Non-discrimination Act (called GINA) prohibits employers and health insurers from using your genetic information against you?

Probe: Does knowing about this law change your concerns?

7.3. Did you know that GINA doesn't cover life insurance, disability and long term care policies?

Probe: What, if any, concerns does this raise?

7.4. How important do you think it is to keep someone's genetic information private after his or her death?

Probe: If important, why? If not important, why not?

7.5. How important is it to keep information private within the family? That means not disclosing one person's genetic results to another.

[(8) Policy considerations]

8.1. Now, given what we have discussed thus far, as a general policy, what do you think researchers should do if they discover a serious genetic finding in a research participant who is

no longer living? Should they offer information to the family? To next-of-kin only? To everyone at the same time? Should researchers be responsible to find and notify all close family members?

8.2. I'm going to review a few of the policy ideas that are being considered: One approach Mayo Clinic could take would be to ask explicitly for permission to share results with family members when a patient first agrees to be in the pancreas registry. Unexpected results could then only be offered to family members if the patient has granted written permission. What do you think of this idea?

Probes: *If they raise no concerns.*

One drawback to this approach is that at the time we ask for a patient's permission to include them in the registry they are often very ill; it is a stressful time, often they have just learned they have cancer. Does that change your view?

Thinking about Mrs. Jones again, this means that if she said no, researchers could not inform her daughters that they might have the BRCA2 mutation.. Is that OK with you?

8.3. Another issue is honoring the wishes of people who do not want to hear ANY bad news about their genes. We could show respect for them by not offering results to any research participants. How important is it to honor the wishes of people who do not want to know?

Probe: Why important or why not important? *If informant is having difficulty, probe with,* Some people just don't want the burden of worry. Should we protect them from that?

8.4. One way around this would be for researchers to communicate only results about the entire pancreas registry, without disclosing any individual's results. For example, researchers could put an article in the Pancreas Research Registry Newsletter or on a website, saying that some families might have mutations in a particular gene. Participants can then call the registry if they want more information, or they can go to their own doctor for testing. Researchers would then NOT contact patients or family members. What do you think of this approach?

8.5. By law, research results must be repeated in a certified clinical lab before being given out. What would you think about having to pay to have your genetic results confirmed in a certified lab? In some cases insurance would cover this, but some insurers may not. It could cost from several hundred to several thousand dollars, depending on the genes involved.

Probe: Do you think Mayo Clinic should offer you the opportunity to be retested at no charge?

[(9) Implications for continued participation in Pancreas Research Registry]

Research teams, like those at Mayo Clinic, must decide whether and when to return unexpected results.

9.1. How would you feel if Mayo Clinic's policy was not to offer unexpected results?

9.2. What if Mayo's policy was always to offer results?

9.3. How might these two alternatives affect your participation in the registry?

Probe: Why?

[(10) Closing]

10.1. I've finished with the questions I wanted to ask. Is there anything else you would like to tell me or think is important that I know?

10.2. I know I have asked you many hard questions about difficult situations. Did the conversation bring up strong feelings or worries? How are you feeling?

Probes if needed: Do you have worries about your own health or your family's?

Well just in case, I want to remind you of the 800 number that you can call if any concerns come up later. The number is 1-800-914-7962. Press #1 for [study coordinator]. It is also in the materials we mailed.

My phone number is XXXXXX and my email is YYYYYY, in case you think of any other things you'd like to tell me. Thank you very much for your participation!

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An ELSI Experiment

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Interview Discussion Guide for Biological Relatives in support of Aim 1a: To assess *a priori* preferences of pancreatic cancer probands and their family members about receiving genomic results that carry health and/or reproductive risks, using in-depth qualitative interviews.

[Opening Statements]

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Have you been able to read or look over the materials that we sent ahead of time**?** *Suggest that they may wish to have the materials we provided available during the interview, but this is not required.*

If interviewee has read the materials, May I ask how much of that information was new to you? For example, had you heard of the three genetic conditions mentioned?

Before we begin, I would like to review and clarify a few things about **the aims** of the project, **my role** in it, and the nature of **this interview**.

First, the aims of the project: While doing research on the cause of pancreatic cancer, Mayo Clinic researchers have discovered some patients who carry mutations in other genes that increase one's risk for having other diseases. This was information we did not expect. During this interview we will call them "unexpected results." Up to now, unexpected genetic research results generally were NOT returned to research participants or to their family members. This standard practice— "a no results" policy—is followed in the Mayo clinic and nearly all research institutes today.

In the future, it is likely that when people participate in research, gene mutations may be found. In fact, it is likely that everyone will carry mutations for several "genetic" diseases, like cystic fibrosis. Unexpected results will become the "new normal" in genetic research.

There is a lot of debate about whether a "no results" policy should change, and if so, how? Answering these questions and developing new policies better adapted to the new situation are the aims of this research.

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Now, my role: I am part of a team carrying out this research. My role on the project is as an interviewer. I'm not a physician or an expert on pancreas disease, so I may not be able to answer technical questions. Rather, my job is to listen, and to learn from you. Let me also say again that

we DO NOT know anything about your family's genetic results or genetic risk; that was also explained in the materials we sent by mail.

Now, the interview: The interview should take around 45 minutes; some people have spoken to us for an hour. The amount of time you give us is up to you. Please feel free not to answer a question if you do not want to, or to stop at any time. Or to continue the call later. Feel free to interrupt or ask questions at any point and I'll do my best to answer them.

SO**,** after all that, and before we get started, **do you have any questions about what I just went over or the interview process?**

If not, let's begin!

Note that in this guide the proband is referred to as "[NOP]." (This means "name of proband.") Please use a formal means of address, such as "Mr. Adams" initially, and thereafter defer to what is comfortable for the interviewee. It is also OK to refer to the proband by a family relationship, for example, as "your brother" or "your mother."

[(1) Opening: Obtaining the informant's "story" and information about the "family"]

1.0. I know that [NOP] was/is a participant in the Mayo Clinic Pancreas Research Registry. Are you also a participant?

1.1. Could you tell me the story of your family's experience with pancreatic cancer, starting at any point you think is important.

1.2. Who in your family knows about the pancreatic cancer?

Probes: Is it discussed openly? Is it sometimes not talked about?

1.3. I will be asking you a lot of questions about your family and family members. Who would you say "family" refers to for you?

Probe: Who are your blood relatives?

Interviewer may want to draw a family tree with names to help keep track.

1.4. *If interviewee is also in the registry:* What motivated you to participate in the registry?

What do you think motivated [NOP] to participate in the registry? Did you discuss the registry?

[(2) Concern about familial cancer risk]

2.1. Have you ever worried that you or any of your other family members may develop pancreatic cancer?

Probes: *If yes,* can you tell me a little about that? How worried, for how long? Worried for whom?

If the interviewee has not mentioned it already. Have you ever wondered if pancreatic cancer ran in your family?

Have you or your family members ever acted on that worry—for example, have you read about the disease? Asked your physicians or friends about it? Have you ever thought about having genetic testing? Have you or any relatives had any screening tests for pancreatic cancer?

2.2. *If the interviewee has not mentioned it already.* Have you or anyone in your family ever <u>had</u> a genetic test? *Of any kind.*

If yes, probe for how communication within the family was handled. Who was tested? For what disease? With what results? Did family members share results with each other? Who did or did not want to know?

[(3) Unexpected research results/incidental findings]

Now I would like to turn to <u>unexpected</u> <u>research results</u> and what to do about them, the focus of our project. As you may remember from the materials we sent you, when conducting genetic testing for genes related to pancreatic cancer, researchers discovered that some patients with pancreatic cancer have mutations in 1 of 3 genes that are linked to an elevated risk for <u>other</u> diseases. Specifically these diseases are breast cancer, melanoma—a serious kind of skin cancer, and cystic fibrosis—a severe chronic lung disease in children and young adults which can lead to early death.

For example, a mutation in the BRCA2 gene makes a woman more likely to have breast or ovarian cancer, and men more likely to develop prostate or breast cancer. A mutation also raises the risk of pancreatic cancer by a small amount, but that is not the focus of our project. Let's say that in the course of looking for the causes of pancreatic cancer, the researchers unexpectedly find a mutation in a research participant's BRCA2 gene. This would mean that the patient's blood relatives—including children and brothers and sisters—could also have a mutation in the BRCA2 gene. A copy of a gene mutation from just one parent is enough to increase cancer risk.

3.1. What do you think the researchers should do with the information if they find someone has this gene mutation?

Probes: Do you think researchers should offer it to the person who participated in their study? Before you answer, let me tell you what I mean by <u>offered</u>. I mean that the person

who participated in the study could say yes or no to actually hearing their results. So, do you think results should be offered to the research participant?

What about to the research participant's family? Should those who might carry the mutation be offered results?

3.2. Remember, our research team does not have any specific genetic results about [NOP] or your family. But hypothetically, imagine that Mayo Clinic researchers did find the BRCA2 mutation when [NOP's] sample was tested. Would you want [NOP's] information to be offered to you?

Probe: Why/Why not?

3.3. If genetic findings were offered, do you think you would in fact want to hear [NOP's] results?

Probe: *If no,* Why not?

3.4. *If yes to wanting [NOP's] test results offered:* If [NOP's] results show that he/she carries/carried the BRCA2 mutation, would you wish to be tested yourself?

Probe: Why/Why not?

3.5. Who do you think should control whether this information is offered to family members of [NOP]? In other words, who should decide whether or not [NOP's] information is offered to your family?

3.6. Do you think your answers would be any different for melanoma, that's the serious type of skin cancer, than for breast cancer?

Probe: *If yes,* how?

I now want to raise the example of cystic fibrosis. Let me remind you how the disease is inherited. In contrast to BRCA2 or melanoma, To have this disease, a child must inherit 2 copies of the cystic fibrosis gene mutation, one mutation from each parent. If both parents have the mutation, there is a 1 in 4 chance that their child will receive 2 copies of the mutation and have cystic fibrosis. The parents will not have cystic fibrosis if they only have one mutation. And children who inherit one mutation also will not have the disease, but they can pass it along to their children.

3.7. Do you think your answers would be any different for cystic fibrosis than for breast cancer?

Probe: *If yes,* how?

3.8. How, if at all, do you think this kind of information might affect your decisions, or your family members' decisions, about having children?

3.9. What about decisions about prenatal testing? Meaning testing a woman who is pregnant?

CHECK EQUIPMENT

[(4) Motivations, Personal and Clinical Utility of Genetic Findings]

Besides these "real life" examples from the Mayo Clinic pancreas registry, it is likely that many other mutations will be identified in the future when people participate in genetic research. For this reason, we would like to get a sense about what kinds of genetic results—if any—you think researchers should offer to research participants' family members, such as yourself.

I'll go through a short list that includes some characteristics of tests. Tell me whether a specific characteristic makes you think it should or shouldn't be offered to research participants or their family members.

4.1. What about results where the research is not yet well established, because it is based on a new discovery and is not yet certain?

4.2. As you know, the Food and Drug Administration, the "FDA," reviews new drugs. What if a genetic test had been reviewed and approved by a government agency like the FDA for routine use?

4.3. What about a serious or fatal disease that can be treated, versus one that can't? Does whether it can be treated or not matter?

4.4. What if the condition causes dementia or cognitive decline, like Alzheimer's?

4.5. What if there is nothing one can do to prevent the disease or to detect it early?

4.6. Are there any conditions that you think you yourself might not want to know about?

5) [Scenario: Family Communication and Decisions about Testing]

Imagine the following situation based on our experience. After her diagnosis with pancreas cancer, "Mrs. Jones" agreed to be in the pancreas research registry. Unfortunately, the treatment she received did not cure her disease. After her death, researchers discovered that Mrs. Jones carried a BRCA2 mutation. She has two daughters, ages 20 and 23. The research team knows that each daughter has a 50/50 chance of having inherited the mutation from Mrs. Jones. If they have the mutation, each daughter's chance of getting breast and ovarian cancer goes up significantly.

5.1. In this situation, do you think the researchers should offer the daughters Mrs. Jones' results? Again, remember that I'm talking about an offer. I am assuming that the daughters' can decide for themselves whether they want to learn their mother's genetic results**.**

Probe: Why/Why not?

Mrs. Jones' husband is her "legal next of kin." In some states, the law requires that researchers offer Mrs. Jones' results to him alone. When the researcher did offer Mr. Jones his wife's genetic results, he said "no I don't want to know, and please do not tell my daughters." He said that talking about his wife's cancer is too painful for the family.

5.2. Do you think Mrs. Jones' daughters have a right to information that might affect their health?

Probes: Whose wishes do you think should have priority in a conflict?

Why?

5.2.1 What about Mrs. Jones' brothers and sisters? They also have a 50/50 chance of carrying the BRCA2 mutation? Do they have a right to information that might affect their health?

Probe: And what about Mrs. Jones' nieces and nephews?

Genetic analysis takes some time, and it is common, like in Mrs. Jones' story, for the results to be discovered when the patient is no longer alive to decide for him/herself. Imagine that [NOP's] results become available after his/her death.

5.3. How do you think this situation should be handled? To whom, if anyone, do you think the researchers should offer [NOP's] results?

5.4. Should results be offered to you directly, even if [NOP] had not given his/her prior permission?

Probe: If it was your genetic result, would you want it shared with others in the family?

5.5. Do you think [NOP's] legal next of kin or representative should be able to decide who is offered results? *This might be [NOP's] spouse; use specific examples from family tree if helpful.*

Probes: Why/Why not? *If not,* who do you think would be best, if anyone?

5.6. Have you ever discussed these types of questions within your family?

Probe: *If yes,* can you tell me about that.

Could the situation that occurred in Mrs. Jones' case happen in your family?

[(6) Practical preferences for communication of unexpected findings]

Continuing to imagine the situation in which a Mayo Clinic researcher has discovered information about [NOP] that was "unexpected": *Interviewer may need to verify our specific use of unexpected results.*

6.1. If you would want to be notified of [NOP's] genetic results, how do you think you would prefer that Mayo Clinic make contact with you?

Probes: *phone, letter, email, secure internet portal, in person by health professional*

If personal contact is desired, ask: Who do you think should make contact with you or explain the results? *Probes: genetic counselor, researcher, primary doctor, nurse, research or study assistant*

6.2. Do you have any suggestions about exactly what a first message should include?

Probe: For example, "we have found something that might be important to your health or your family's health and we want to talk to you," or "we found that [NOP] carries a mutation linked to breast cancer, putting you at a 50% risk of having the same gene mutation."

6.3.0. Do you think Mayo Clinic should offer you the opportunity to get a test for [NOP's] gene mutation yourself?

Probes: Why/Why not?

6.3.1. Or, would you prefer that Mayo Clinic researchers share the information about [NOP's] genetic results with your primary care physician? Then your doctor could follow up directly.

Probes: Why/Why not?

CHECK EQUIPMENT

7) [Genetic Privacy and Discrimination]

7.1. Would you have concerns about others finding out that you, or someone in your family, has a particular mutation?

Probes: *If yes,* who and why? *If not,* why *not?*

If disclosure within the family is not mentioned: Would you have concerns about family members' finding out that you have a particular mutation? Why/Why not?

What about your employer?

Your health insurance company?

7.2. Did you know that the Genetic Information Non-discrimination Act (called GINA) prohibits employers and health insurers from using your genetic information against you?

Probe: Does knowing about this law change your concerns?

7.3. Did you know that GINA doesn't cover life insurance, disability and long term care policies?

Probe: What, if any, concerns does this raise?

7.4. How important do you think it is to keep someone's genetic information private after his or her death?

Probe: If important, why? If not important, why not?

7.5. How important is it to keep information private within the family? That means not disclosing one person's genetic results to another.

[(8) Policy considerations]

8.1. Now, given what we have discussed thus far, as a general policy, what do you think researchers should do if they discover a serious genetic finding in a research participant who is no longer living? Should they offer information to the family? To the next-of-kin only? To everyone at the same time? Should researchers be responsible to find and notify all close family members?

8.2. I'm going to review a few of the policy ideas that are being considered: One approach Mayo Clinic could take would be to ask explicitly for permission to share results with family members when a patient first agrees to be in the pancreas registry. Unexpected results could then only be offered to family members if the patient has granted written permission. What do you think of this idea?

Probes: *If they raise no concerns.*

One drawback to this approach is that at the time we ask for a patient's permission to include them in the registry they are often very ill; it is a stressful time, often they have just learned they have cancer. Does that change your view?

Thinking about Mrs. Jones again, this means that if a patient said no, researchers could not inform her daughters that they might have the BRCA2 mutation. And in your family's situation, researchers could not inform you. What do you think about that?

8.3. Another issue is honoring the wishes of people who do not want to hear ANY bad news about their genes. We could show respect for them by not offering results to any research participants? How important is it to honor the wishes of people who do not want to know?

Probe: Why important or why not important? *If informant is having difficulty, probe with,* Some people just don't want the burden of worry. Should we protect them from that?

8.4. Another idea would be for researchers to communicate only results about the entire pancreas registry, without disclosing any individual's results. For example, researchers could put an article in the Pancreas Research Registry Newsletter or on a website, saying that some families might have mutations in a particular gene. Participants can then call the registry if they want more information, or they can go to their own doctor for testing. Researchers would then NOT contact patients or family members. What do you think of this approach?

8.5. By law, research results must be repeated in a certified clinical lab before being given out. What would you think about having to pay to have [NOP's] genetic results confirmed in a certified lab? In some cases insurance would cover this, but some insurers may not. It could cost from several hundred to several thousand dollars, depending on the genes involved.

[(9) Implications for continued participation in Pancreas Research Registry]

Research teams, like those at Mayo Clinic, must decide whether and when to return unexpected results.

9.1. How would you feel if Mayo Clinic's policy was not to offer unexpected results?

9.2. What if Mayo's policy was always to offer results?

9.3. How might these two alternatives affect your participation in research like the Pancreas Registry? *Customize depending on whether informant is or is not in the registry.*

Probe: Why?

[(10) Closing]

10.1. I've finished with the questions I wanted to ask. Is there anything else you would like to tell me or think is important that I know?

10.2. I know I have asked you many hard questions about difficult situations. Did the conversation bring up strong feelings or worries? How are you feeling?

Probes if needed: Do you have worries about your own health or your family's?

Well just in case, I want to remind you of the 800 number that you can call if any concerns come up later. The number is 1-800-914-7962. Press #1 for [study coordinator]. It is also in the materials we mailed.

My phone number is XXXXXX and my email is YYYYYY, in case you think of any other things you'd like to tell me. Thank you very much for your participation!

R01 CA154517
Disclosing Genomic Incidental Findings in a Cancer Biobank:
An ELSI Experiment

PIs: Barbara A. Koenig, Gloria M. Petersen, Susan M. Wolf

Interview Discussion Guide for Spouses in support of Aim 1a: To assess *a priori* preferences of pancreatic cancer probands and their family members about receiving genomic results that carry health and/or reproductive risks, using in-depth qualitative interviews.

[Opening Statements]

I'd like to start by thanking you for your willingness to participate in this interview. It is truly appreciated. I will record our conversation with your permission. Is that OK? Also, just to remind you that your comments will be kept strictly confidential. We will be very careful with everything you tell us.

TURN ON RECORDER/CHECK EQUIPMENT

Have you been able to read or look over the materials that we sent ahead of time**?** *Suggest that they may wish to have the materials we provided available during the interview, but this is not required.*

If interviewee has read the materials, May I ask how much of that information was new to you? For example, had you heard of the three genetic conditions mentioned?

Before we begin, I would like to review and clarify a few things about **the aims** of the project, **my role** in it, and the nature of **this interview**.

First, the aims of the project: While doing research on the cause of pancreatic cancer, Mayo Clinic researchers have discovered some patients who carry mutations in other genes that increase one's risk for having other diseases. This was information we did not expect. During this interview we will call them "unexpected results." Up to now, unexpected genetic research results generally were NOT returned to research participants or to their family members. This standard practice— "a no results" policy—is followed in the Mayo clinic and nearly all research institutes today.

In the future, it is likely that when people participate in research, gene mutations may be found. In fact, it is likely that everyone will carry mutations for several "genetic" diseases, like cystic fibrosis. Unexpected results will become the "new normal" in genetic research.

There is a lot of debate about whether a "no results" policy should change, and if so, how? Answering these questions and developing new policies better adapted to the new situation are the aims of this research.

Clearly, research participants and their family members, like yourself, are most affected by research policies. For this reason we want to learn from you—about your opinions and ideas. We are trying to understand what patients and family members want and need, so you are the expert. We are aware that the issues are very complicated. I will ask for your thoughts on some difficult questions, but don't worry, you are not expected to have all the answers! This is not a test! There are no right answers. We seek your guidance. That is the goal of this interview.

Now, my role: I am part of a team carrying out this research. My role on the project is as an interviewer. I'm not a physician or an expert on pancreas disease, so I may not be able to answer technical questions. Rather, my job is to listen, and to learn from you. Let me also say again that

we DO NOT know anything about your family's genetic results or genetic risk; that was also explained in the materials we sent by mail.

Now, the interview: The interview should take around 45 minutes; some people have spoken to us for an hour. The amount of time you give us is up to you. Please feel free not to answer a question if you do not want to, or to stop at any time. Or to continue the call later. Feel free to interrupt or ask questions at any point and I'll do my best to answer them.

SO**,** after all that, and before we get started, **do you have any questions about what I just went over or the interview process?**

If not, let's begin!

Note that in this guide the proband is referred to as "[NOP]." (This means "name of proband.") Please use a formal means of address, such as "Mr. Adams" initially, and thereafter defer to what is comfortable for the interviewee. It is also OK to refer to the proband by a family relationship, for example, as "your wife" or "your mother-in-law."

[(1) Opening: Obtaining the informant's "story" and information about the "family"]

1.0. I know that [NOP] was/is a participant in the Mayo Clinic Pancreas Research Registry. Are you also a participant?

1.1. Could you tell me the story of your family's experience with pancreatic cancer, starting at any point you think is important.

1.2. Who in your family knows about the pancreatic cancer?

Probes: Is it discussed openly? Is it sometimes not talked about?

1.3. I will be asking you a lot of questions about your family and family members. Who would you say "family" refers to for you?

Probe: Exactly how are you related to [NOP]?

Interviewer may want to draw a family tree with names to help keep track.

1.4. *If interviewee is also in the registry:* What motivated you to participate in the registry?

What do you think motivated [NOP] to participate in the registry? Did you discuss the registry?

[(2) Concern about familial cancer risk]

2.1. Have you ever worried that your family members may develop pancreatic cancer?

Probes: *If yes*, can you tell me a little about that? How worried, for how long? Worried for whom?

If the interviewee has not mentioned it already. Have you ever wondered if pancreatic cancer ran in [NOP'S] family?

Has anyone in the family ever acted on that worry—for example, have you read about the disease? Asked your physicians or friends about it? Have you ever thought about recommending genetic testing to a relative? Have any relatives had screening tests for pancreatic cancer?

2.2. *If the interviewee has not mentioned it already.* Has anyone in the family ever <u>had</u> a genetic test? *Of any kind.*

If yes, probe for how communication within the family was handled. Who was tested? For what disease? With what results? Did family members share results with each other? Who did or did not want to know?

[(3) Unexpected research results/incidental findings]

Now I would like to turn to <u>unexpected</u> <u>research results</u> and what to do about them, the focus of our project. As you may remember from the materials we sent you, when conducting genetic testing for genes related to pancreatic cancer, researchers discovered that some patients with pancreatic cancer have mutations in 1 of 3 genes that are linked to an elevated risk for <u>other</u> diseases. Specifically these diseases are breast cancer, melanoma—a serious kind of skin cancer, and cystic fibrosis—a severe chronic lung disease in children and young adults which can lead to early death.

For example, a mutation in the BRCA2 gene makes a woman more likely to have breast or ovarian cancer, and men more likely to develop prostate or breast cancer. A mutation also raises the risk of pancreatic cancer by a small amount, but that is not the focus of our project. Let's say that in the course of looking for the causes of pancreatic cancer, the researchers unexpectedly find a mutation in a research participant's BRCA2 gene. This would mean that the patient's blood relatives—including children and brothers and sisters—could also have a mutation in the BRCA2 gene. A copy of a gene mutation from just one parent is enough to increase cancer risk.

3.1. What do you think the researchers should do with the information if they find someone has this gene mutation?

Probes: Do you think researchers should offer it to the person who participated in their study? Before you answer, let me tell you what I mean by <u>offered</u>. I mean that the person

who participated in the study could say yes or no to actually hearing their results. So, do you think results should be offered to the research participant?

What about to the research participant's family? Should those who might carry the mutation be offered results?

3.2. Remember, our research team does not have any specific genetic results about [NOP] or his/her family. But hypothetically, imagine that Mayo Clinic researchers did find the BRCA2 mutation when [NOP's] sample was tested. Would you want [NOP's] information to be offered to you?

Probe: Why/Why not?

3.3. If genetic findings were offered, do you think you would in fact want to hear [NOP's] results?

Probe: *If no,* Why not?

3.4. *If yes to wanting [NOP's] test results offered:* If [NOP's] results show that he/she carries/carried the BRCA2 mutation, would you wish to share that information with other members of your family?

Probe: Why/Why not?

3.5. Who do you think should control whether this information is offered to family members of [NOP]? In other words, who should decide whether or not [NOP's] information is offered to your family?

3.6. Do you think your answers would be any different for melanoma, that's the serious type of skin cancer, than for breast cancer?

Probe: *If yes,* how?

I now want to raise the example of cystic fibrosis. Let me remind you how the disease is inherited. In contrast to BRCA2 or melanoma, To have this disease, a child must inherit 2 copies of the cystic fibrosis gene mutation, one mutation from each parent. If both parents have a mutation, there is a 1 in 4 chance that their child will receive 2 copies of the mutation and have cystic fibrosis. The parents will not have cystic fibrosis if they only have one mutation. And children who inherit one mutation also will not have the disease, but they can pass it along to their children.

3.7. Do you think your answers would be any different for cystic fibrosis than for breast cancer?

Probe: *If yes,* how?

3.8. How, if at all, do you think this kind of information might affect your family members' decisions about having children?

3.9. What about decisions about prenatal testing? Meaning testing a woman who is pregnant?

CHECK EQUIPMENT

[(4) Motivations, Personal and Clinical Utility of Genetic Findings]

Besides these "real life" examples from the Mayo Clinic pancreas registry, it is likely that many other mutations will be identified in the future when people participate in genetic research. For this reason, we would like to get a sense about what kinds of genetic results—if any—you think researchers should offer to research participants' family members, such as yourself.

I'll go through a short list that includes some characteristics of tests. Tell me whether a specific characteristic makes you think it should or shouldn't be offered to research participants or their family members.

4.1. What about results where the research is not yet well established, because it is based on a new discovery and is not yet certain?

4.2. As you know, the Food and Drug Administration, the "FDA," reviews new drugs. What if a genetic test had been reviewed and approved by a government agency like the FDA for routine use?

4.3. What about a serious or fatal disease that can be treated, versus one that can't? Does whether it can be treated or not matter?

4.4. What if the condition causes dementia or cognitive decline, like Alzheimer's?

4.5. What if there is nothing one can do to prevent the disease or to detect it early?

4.6. Are there any conditions that you think you yourself might not want to know about? Or that you might not want to share with family members?

5) [Scenario: Family Communication and Decisions about Testing]

Imagine the following situation based on our experience. After her diagnosis with pancreas cancer, "Mrs. Jones" agreed to be in the pancreas research registry. Unfortunately, the treatment she received did not cure her disease. After her death, researchers discovered that Mrs. Jones carried a BRCA2 mutation. She has two daughters, ages 20 and 23. The research team knows that each daughter has a 50/50 chance of having inherited the mutation from Mrs. Jones. If they have the mutation, each daughter's chance of getting breast and ovarian cancer goes up significantly.

5.1. In this situation, do you think the researchers should offer the daughters Mrs. Jones' results? Again, remember that I'm talking about an offer. I am assuming that the daughters' can decide for themselves whether they want to learn their mother's genetic results**.**

Probe: Why/Why not?

Mrs. Jones' husband is her "legal next of kin." In some states, the law requires that researchers offer Mrs. Jones' results to him alone. When the researcher did offer Mr. Jones his wife's genetic results, he said "no I don't want to know, and please do not tell my daughters." He said that talking about his wife's cancer is too painful for the family.

5.2. Do you think Mrs. Jones' daughters have a right to information that might affect their health?

Probes: Whose wishes do you think should have priority in a conflict?

Why?

5.2.1 What about Mrs. Jones' brothers and sisters? They also have a 50/50 chance of carrying the BRCA2 mutation? Do they have a right to information that might affect their health?

Probe: And what about Mrs. Jones' nieces and nephews?

Genetic analysis takes some time, and it is common, like in Mrs. Jones' story, for the results to be discovered when the patient is no longer alive to decide for him/herself. Imagine that [NOP's] results become available after his/her death.

5.3. How do you think this situation should be handled? To whom, if anyone, do you think the researchers should offer [NOP's] results?

5.4. Should results be offered to family members directly, even if [NOP] had not given his/her prior permission?

Probe: If it was your genetic result, would you want it shared with others in the family?

5.5. As [NOP's] legal next of kin or representative, are you comfortable making decisions about whether results should be offered to other family members?

Probes: Why/Why not? *If not,* who do you think would be best, if anyone?

5.6. Have you ever discussed these types of questions within your family?

Probe: *If yes,* can you tell me about that.

Could the situation that occurred in Mrs. Jones' case happen in your family?

[(6) Practical preferences for communication of unexpected findings]

Continuing to imagine the situation in which a Mayo Clinic researcher has discovered information about [NOP] that was "unexpected": *Interviewer may need to verify our specific use of unexpected results.*

6.1. If you would want to be notified of [NOP's] genetic results, how do you think you would prefer that Mayo Clinic make contact with you?

Probes: *phone, letter, email, secure internet portal, in person by health professional*

If personal contact is desired, ask: Who do you think should make contact with you or explain the results? *Probes: genetic counselor, researcher, primary doctor, nurse, research or study assistant*

6.2. Do you have any suggestions about exactly what a first message should include?

Probe: For example, "we have found something that might be important to your family's health and we want to talk to you," or "we found that [NOP] carries a mutation linked to breast cancer, putting her biological relatives at a 50% risk of having the same gene mutation."

6.3.0. Do you think Mayo Clinic should offer [NOP's] relatives the opportunity to get a test for his/her gene mutation?

Probes: Why/Why not?

6.3.1. Or, would you prefer that Mayo Clinic researchers share the information about [NOP's] genetic results with [specific family member's] primary care physician? Then the doctor could follow up directly.

Probes: Why/Why not?

CHECK EQUIPMENT

7) [Genetic Privacy and Discrimination]

7.1. Would you have concerns about others finding out that someone in your familyhas a particular mutation?

Probes: *If yes,* who and why? *If not, why not?*

If disclosure within the family is not mentioned: Would you have concerns about family members' finding out that [NOP] has/had a particular mutation? Why/Why not?

What about an employer?

A health insurance company?

7.2. Did you know that the Genetic Information Non-discrimination Act (called GINA) prohibits employers and health insurers from using a person's genetic information against him or her?

Probe: Does knowing about this law change your concerns?

7.3. Did you know that GINA doesn't cover life insurance, disability and long term care policies?

Probe: What, if any, concerns does this raise?

7.4. How important do you think it is to keep someone's genetic information private after his or her death?

Probe: If important, why? If not important, why not?

7.5. How important is it to keep information private within the family? That means not disclosing one person's genetic results to another.

[(8) Policy considerations]

8.1. Now, given what we have discussed thus far, as a general policy, what do you think researchers should do if they discover a serious genetic finding in a research participant who is no longer living? Should they offer information to the family? To the next-of-kin only? To everyone at the same time? Should researchers be responsible to find and notify all close family members?

8.2. I'm going to review a few of the policy ideas that are being considered: One approach Mayo Clinic could take would be to ask explicitly for permission to share results with family members when a patient first agrees to be in the pancreas registry. Unexpected results could then only be offered to family members if the patient has granted written permission. What do you think of this idea?

Probes: *If they raise no concerns.*

One drawback to this approach is that at the time we ask for a patient's permission to include them in the registry they are often very ill; it is a stressful time, often they have just learned they have cancer. Does that change your view?

Thinking about Mrs. Jones again, this means that if she said no, researchers could not inform her daughters that they might have the BRCA2 mutation. And in your family's

situation, researchers could not inform [NOP's] blood relatives. What do you think about that?

8.3. Another issue is honoring the wishes of people who do not want to hear ANY bad news about their genes. We could show respect for them by not offering results to any research participants? How important is it to honor the wishes of people who do not want to know?

Probe: Why important or why not important? *If informant is having difficulty, probe with,* Some people just don't want the burden of worry. Should we protect them from that?

8.4. Another idea would be for researchers to communicate only results about the entire pancreas registry, without disclosing any individual's results. For example, researchers could put an article in the Pancreas Research Registry Newsletter or on a website, saying that some families might have mutations in a particular gene. Participants can then call the registry if they want more information, or they can go to their own doctor for testing. Researchers would then NOT contact patients or family members. What do you think of this approach?

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[(9) Implications for continued participation in Pancreas Research Registry]

Research teams, like those at Mayo Clinic, must decide whether and when to return unexpected results.

9.1. How would you feel if Mayo Clinic's policy was not to offer unexpected results?

9.2. What if Mayo's policy was always to offer results?

9.3. How might these two alternatives affect your participation in research like the Pancreas Registry? *"Customize depending on whether informant is or is not in the registry." (Is this later part that is in quotations necessary for next-of-kin? Would they be in the registry?)*

Probe: Why?

[(10) Closing]

10.1. I've finished with the questions I wanted to ask. Is there anything else you would like to tell me or think is important that I know?

10.2. I know I have asked you many hard questions about difficult situations. Did the conversation bring up strong feelings or worries? How are you feeling?

Probes if needed: Do you have worries about your family's health?

Well just in case, I want to remind you of the 800 number that you can call if any concerns come up later. The number is 1-800-914-7962. Press #1 for [study coordinator]. It is also in the materials we mailed.

My phone number is XXXXXX and my email is YYYYYY, in case you think of any other things you'd like to tell me. Thank you very much for your participation!