GS Counseling Topic Checklist and Script

Control Group (non-decision aid) Session Script

Session preparation:
You need:
- Study id of participant
- Login code and password of participant
- Participant’s phone number
- Confirmation of appointment time
- Study sheet
- Writing utensils
- Copy of study visual aids
- Recording device

Participant needs:
- Copy of slide show (emailed).
- Enough time to complete the session (one to two hours)

Notes on session and using this guide: The goal of this session is for participant’s to select which incidental findings (using a the modified berg model) they would like to receive. The results they are selecting are hypothetical, so the participants are not actually being offered genomic sequencing or incidental findings.

The core of this session is education. Genomic sequencing, incidental findings, the category choices and risk and benefits should be explained to the level that the participant has enough information to make an informed choice. As a counselor for the control group you represent what would be considered the standard of care. Therefore, you should use your professional experience and training on counseling patients about genomic sequencing and incidental findings to guide your session with participants. That is to say, you should approach this session as you normally would in the clinical setting.

However, because this is research it is important to note that there are a couple of elements that are different from your typical clinical session that you will need to incorporate into your session with the patient. First, we are using a modified berg model to categorize the incidental findings and guide the participants’ selection. In many clinical setting, if incidental findings are offered, patients only receive information about those findings that are considered medically actionable. However, our study model gives patients the opportunity to select incidental findings beyond those that are medically actionable. It is important for counselors on this study to be comfortable counseling participants using our study model and offering patient’s the opportunity to learn about incidental findings beyond those that are medically actionable. Secondly, because participants’ selection of incidental finding is hypothetical it is important that counselors make it very clear to the participants that they will not actually be receiving
any genomic sequencing or incidental findings. At the same time, because participants are not making an actual decision, the counselor needs to make sure that participants take their decision seriously by asking participants to select incidental findings, as best they can, as if they were actually faced with this choice.

Below we have outlined a variety of topics of be discussed with participants and have provided some scripts that cover the basics of what should be discussed with participants. We have also laid them out in what is hoped to be a logical manner. This is meant to be as resource to your session and not meant to restrict or limit how you approach your session. Depending on the participant or your style there are sections you will not discuss or there may be topics you discuss that are not included here. This is ok and intended part of the study. The only section that you will need to be sure to include in your session is the study model of categories of incidental findings. If you do not explain this model to participants they will not have the information they need to select which findings they would like to receive. Further, because the goal of this study is the selection of which incidental findings they would like to receive, you need to be sure to end the session with the participants selecting which incidental findings they would like to receive.

**Session preparation:** Before session prep tape recorder, fill out study sheet with participant ID and note time that study begins. Have an email copy of the visual aids ready incase the participant needs new ones sent to them. When the conversation begins turn on tape recorder. Confirm with participant that it is ok to turn on tape recorder. If they are not ok with recording mark this on your study sheet. Make a note of session start time on the data collection sheet.

**Introduction /Study Context**

Thank you for taking the time to speak with me today. I am calling you today because you have agreed to participate in our study.

Today we will be talking about genomic sequencing and incidental findings. After our discussion we will ask you to select which incidental findings you would like to receive. It is important to remember that this decision is hypothetical; we will not be doing any genetic testing and will not be returning any actual results. For the purposes of this study we would like you to imagine or pretend that you are about to receive genomic sequencing for a specific medical condition and are being offered the option of also receiving incidental findings along with the results related to the specific medical condition. Today’s discussion is the type of conversation we would typically have with a patient when they are faced with option of selecting which incidental findings they would like to receive (if any).

If you have questions at any time please ask. We will also save some time at the end for any questions.
**Background Information on Genetics** *(can presented in any order and or as needed in your discussion)*

**Cell, Gene, Variation**
Our bodies are made up of millions of cells which contain our genetic information. There are thousands of different genes which carry the instructions that tell our cells how to grow and develop. Most of our genes come in pairs. One copy of each gene pair comes from our mother and one copy from our father. A change in a gene, called a variation, prevents a gene from working properly and can cause disease.

**Inheritance, penetrance, expressivity:**
Genetic conditions are inherited in different ways. For some genes, having one working copy is sufficient to keep our cells growing and developing properly. In other words, if one copy of the gene doesn't work properly, we are not going to develop disease. For other genes, we need to have two working copies not to develop disease. In other words, we will develop disease even if we have one working copy of the gene because the copy that does not work interferes with normal functioning of the other copy. It is also important to know that even when two members of the same family have the same genetic change in the same gene, they might not develop the same symptoms, and they might not develop symptoms at similar ages.

**Genomic Sequencing** *(Important to review as this is the basis of why we are discussing the offer of incidental findings. This text uses a book metaphor but you are welcome to use any metaphor that you are comfortable with).*

What is “genomic sequencing”? Well first, we need to understand what the “genome” is.......The “genome” is the collection of all of a person’s genes.

We have approximately 25,000 genes, and in general each gene has a single job or role in the cell. Our genes are found on these large structures called chromosomes. We have 23 pairs of chromosomes, so we have about 1000 or more genes on each chromosome. We can imagine that our entire complement of DNA is a bookshelf, our chromosomes are the books and then the genes would be the sentences in the books. Our books would actually look more like a children’s book than an adult book, in the sense that children’s books have one or two sentences per page and lots of space in between them. In our DNA, our genes are spaced out and there is a lot of DNA in between the gene. This space in between may have a job, we do not know what it does. We will not be testing the DNA in-between the genes, although someday we may learn how to do this.

When we say testing we mean that we will be sequencing the genes, which is like reading the sentences, and we will be looking for variations, in the genes. Using the book metaphor, a variation is like a spelling mistake.
However there are a few possible results when we find a spelling difference, as we don’t always know if a difference in DNA sequence is a mistake or if it is just normal variation. All people have differences in their DNA, most of which are normal. A good example of this is the word colour, it can be spelt with a “U” or without a “U”. Now we know that it is fine to spell it either way so we don’t consider it a mistake. However our DNA is not in English, so for each difference we always have to ask if they are similar to the “U” in colour and are they just normal variations or are they a spelling mistake and do they cause disease.

**Positive result**
Sequencing has identified a mutation that is known to cause disease. It has been seen in patients with similar symptoms.

**Negative Result**
The sequencing has not identified any variations that are related to disease. This does not rule out a genetic condition. If the patient who was tested has a condition, a negative result simply means that we could not identify the cause of the condition with this technology. Testing may improve in the future and new options may be available.

**Possibly associated**
A variant was identified and it is unclear if this causes disease. This may be for multiple reasons including but not limited to:
- The condition is recessive and only one variation was found
- The patient’s symptoms are not the usual symptoms caused by such a variation.
- The Variation has not been well documented in people with the same condition

**Secondary/Incidental Findings**
This is when a variation has been identified which is known to cause disease however it is not related to the reason for testing.

**Concept of Categories**
Just to re-iterate, if you participate in the study, we will not perform clinical testing on your sample for variants associated with thousands of different disease risks but are asking that you imagine a scenario in which this type of testing is being performed. The type of incidental results that would be reported depend on your decisions as to what type of results you would like to learn. Let’s review the different kinds of genomic test results you can hypothetically choose to receive. There are too many possible results to discuss each one. However, all of the possible test results can be sorted into 5 general categories. These categories are organized by whether they have any medical interventions, and what type of information they give you.

Note that each category is a complete package. You can choose to receive all the results in a given category, or none of the results in that category. You cannot pick and choose results within one category.
**Category 1, medically actionable high**

Positive results in category 1 mean you have a high risk for certain diseases. However medical interventions are available, which doctors generally agree can reduce risk. Examples are screening tests or preventive medications. The interventions do not take away all the risk.

*Example: Long QT Syndrome – multiple genes*

Another example is Long QT syndrome, this syndrome is associated with an irregular heartbeat, called arrhythmia. Long QT Syndrome can cause fainting, heart attacks and even death, at any age. Medication can reduce the risk of the heart attacks.

**Pharmocogenetics**

There may also be results in Category 1 that can help predict your body’s response to certain medications. If you ever need to take those medications in the future, your doctor may wish to alter the dose, or give you a different medication altogether. For example, genomic testing could show that codeine could cause more nausea and dizziness than other people, or might not be an effective painkiller for you. With this information, your doctor may suggest a different painkiller.

For all the remaining categories presented here, there are no medical interventions, agreed upon by doctors, to reduce the risk of getting the disease.

**Category 2 – Common Disease, low risk**

Category 2 gives you information about slightly higher or lower risks for common diseases. You could learn you have certain genomic risk factors for diseases that are already common. Examples of these diseases, are diabetes, melanoma, colon cancer, and coronary artery disease. We all have a risk of developing these conditions, regardless of genetics. These results would indicate your risk may be little bit higher, or a little bit lower than other people. While there are many intervention available to help people lower their general risks to getting these diseases, there are not medical interventions to reduce their genetic risk.

*(note to counselors - patients can get confused by this category and our label of no medical interventions, since they have been told that disease such as diabetes can be prevented. Be sure to explain multifactor diseases, the role genetics play in these cases and lack of interventions to impact the genetic part of their risk.)*

**Category 3 (includes variants conferring moderate to high risks for Mendelian diseases)**

You could develop these conditions in the future , or you may have them right now and not realize it. (e.g., inherited blindness or deafness, etc.). Another example is muscular dystrophy, which can cause gradual muscle weakness, loss of feeling and loss of ability to move. The severity of the condition can vary and while there may be some medical interventions to treat symptoms, there are no medical interventions available to reduce the risk of getting these diseases.
**Category 4 include early—onset neurological conditions**

(e.g., early—onset Alzheimer’s, Parkinson’s disease, etc.)

Category 4 contains risks for serious brain diseases that could happen at an early age. These could affect your memory, ability to move, ability to think, and your personality. They generally become worse as time goes forward, and there is no known prevention or cure. Examples of these are “early onset familial Alzheimer disease” which can happen between ages 20 and 60. Early-onset Parkinson disease can happen between ages 20 and 40. Perhaps you know someone who’s had Alzheimers or Parkinsons, and if so, you may have an idea of what these diseases involve.

These conditions can have significant emotional impact on patients and families especially when the risk is known before a diagnosis occurs. Possible causes of distress can include knowing you will get a debilitating disease, considering no known prevention exists. Questions can arise in regards to searching for a treatment and optimizing years before disease onset. However additional causes of distress can include conveying the information to family members and their potential to have the disease and reproductive risks for those who still plan to have children. There are no medical interventions available to reduce the risk of getting these diseases.

**Category 5 - carrier results**

*(Can review AR inheritance again or introduce it here for the first time.)*

(e.g., cystic fibrosis, sickle cell disease)

You might remember that we spoke about the way diseases were inherited earlier. You know that we have two copies of all our genes, one copy we inherit from our mother, the other copy from our father. For some genetic conditions, such as cystic fibrosis for example, as long as one copy of the gene is working properly, i.e. does not have a mistake in it, we will not develop cystic fibrosis. If a person has a mistake in both copies of the gene however, he/she will develop CF. So, if a person has one working copy of the gene and one copy that is not working, they will not develop CF, but they are a “carrier” of CF. A carrier could pass on the copy of the gene with a mistake to their offspring and if the child inherits another copy with a mistake form the other parent, that child will have CF.

As we’ll discuss later, positive results from all of the categories can affect your children. In category 5, though, these results affect only your children (and not yourself).

For example, you could find out you are a carrier of a disease that causes intellectual disability, difficulty walking or moving, cystic fibrosis (which causes difficulty breathing and infertility in men) or sickle cell anemia (which causes pain, infections and organ damage). You won’t have these diseases, but you could have a child with mental retardation, problems walking, cystic fibrosis, or sickle cell anemia. Some of these diseases are treatable, once they are diagnosed. For example, children with phenylketonuria should avoid certain foods to help prevent seizures and intellectual disability, but there is no cure. We will revisit risks to children later.

Everyone is a carrier of around 10 different conditions. However many conditions are not well understood, and therefore we cannot properly identify all mutations that make someone a carrier. Therefore, although we expect to find carrier results for everyone, we are unlikely to identify all conditions that you may carry.
Randomized Controlled Trial of a Decision aid Decision Aid for Incidental Genomic Findings

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Hospitals routinely test newborns for some of these diseases. There is treatment for some of them, but no way to prevent them.

**Benefits Risks and Limitations**

**Possible benefits**
The main goal of genome sequencing/testing is to identify a cause for a specific condition in an affected person. For example, a person has breast cancer and we want to find the genetic cause that lead to developing that cancer. Learning about incidental findings could lead to surveillance or early detection that would reduce the risk of certain disease or modify it's course. this information can also be useful to other family members. For example, some people may be motivated to speak to their doctor about starting an exercise routine, quitting smoking, and eating a healthier diet, based on their results. These measures are considered healthy choices for most people, genetics aside.

**Possible Risks**
There could also be risks from genomic testing: Many diseases cannot be prevented or cured, or even treated. Learning results from any of the categories could be emotionally upsetting or frightening, even if you don't anticipate that reaction beforehand. The uncertainty can feel uncomfortable for some. Reactions are personal and hard to predict. If you have one or more disease risks, how would you feel? Would it change anything for you? Is there anything you would do differently? Would you tell your doctors, family members or friends?

All possible results - from all the categories - are hereditary. This means that your family members could share your disease risks. This could include your children, siblings, parents and more distant relatives. You should consider telling them about the study. Your relatives may feel differently about this information than you do. Some people have had their relationships affected because of this. The risk to your relatives for a particular disease will depend on the pattern of inheritance for that disease. However, nobody can predict exactly how or when it may affect them.

With any kind of genetic or genomic testing, there is a theoretical risk of genetic discrimination; this refers to the concern that someone could use this information against you. Often people think of life/disability insurance or insurance outside of your provincial health care and at this time there are no Canadian laws that protect you genomic information from insurance providers. Other risks include false reassurance or false worry, because of the limitations of testing.

**Reproductive Implications**
Diseases in all of the categories have reproductive risks. Any disease risks you carry could be passed on to your children, or your relatives’ children. A disease could be more, or less, severe in a child than it is in you. Remember the example of Waardenburg syndrome from Category 2. In some people, Waardenberg syndrome causes hearing loss. So even if you have Waardenburg syndrome with normal hearing, your child could be born with hearing loss.
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Recall that **Category 5 tests for carrier status**. If you and your partner are both carriers of the same disease, your child could be born with the disease. Hospitals routinely test newborns for some of these diseases. There is treatment for some of them, but no way to prevent them. Genomic test results can be used for reproductive planning. Embryos can be tested and selected before pregnancy to avoid passing along a disease risk to one’s children. If you have questions about inheritance of disease, it may be appropriate for you see a genetic counselor to discuss family planning options. The best time to see a genetic counselor is **before** attempting pregnancy.

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**Limitations**  
There are limitations of Genomic Testing  
First, you will not be tested for all diseases. If you do not receive any positive results, this does not mean you are negative for everything. Although this test analyzes thousands of genes, it only focuses on a tiny fraction of your genome. You could have a variant that is not detected, or not focused on during the analysis. In other words, genomic testing does not rule out risk for any disease. Risk estimates are fuzzy; there are no guarantees. You could have a high risk for a particular disease, but still you never develop it. Or you may be at low genetic risk, but you get the disease anyway. It will not be possible to give you a numerical risk for any specific disease. Scientists’ interpretation of genomic test results will likely change over time, as medical science advances. In some cases you will probably not be contacted with updates as genetic information changes.

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**Questions**  
Now that we have reviewed this information lets take some time to answer any question you may have and find out where you may need more information before making your decision. What question do you have and what would you like more information about?

*(Take as much time as need to answer the participants questions and review any information before mobbing on to the category selection.)*

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**Selecting which categories of incidental findings**  
Ok now that we have discussed genomic sequencing and incidental findings and have an opportunity to answer your questions it is time to select which incidental finding you would like to receive. Please refer to the Category Diagram. Now thinking about everything you have learned today and looking at this diagram, can you tell me which categories of incidental findings you would select?

*(record selection on data collection sheet)*

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**Next steps**  
Thank you for taking the time today. Next we would like you to complete the online follow-up questions. It is important that you answer these questions right after our session today, so please log into the site right after our call is over and complete the questions. This should only take you 10 to 15
min to complete. You should have received an email with a link to the online questions and a user name. If you do not have this info I can provide it to you now. Thank you again for your time.

End of session instructions for Genetic Counsellor: Write down results selections on study sheet. Thank the participant for their time, ask if they have any further questions and end session. Turn off tape recording, note on data collection sheet end time. Fill out study sheet notes. Upload recording and label with study id.