

It's So Complicated!
Genomic Research & Disclosure of
Incidental Findings

Dramatic Vignettes from a Series of ELSI Plays

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****The characters in this play are fictitious and the excerpts quoted are based on composites of actual consent forms. Several academic clinical research geneticists provided advice to authenticate the conversations and diagnoses. The referenced community, names and designated disorders are modifiable.****

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NOTE: This vignette is meant to follow our initial ELSI play, “It’s Not That Simple!: Genomic Research & The Informed Consent Process” (GIM online Feb 2012). If time does not permit, we have provided, below, excerpts from “Not Simple!” to introduce the audience to the characters and better frame the dilemmas that are further developed in “It’s So Complicated!” which begins on page 5.

EXCERPTS FROM “IT’S NOT THAT SIMPLE!” (to precede “So Complicated” if not previously seen):

NARRATOR: As the play commences, we find Bobby, Amy, Sam, and Ellen Friedman in the Pediatric Genetic Clinic with Dr. Hardy. Bobby is a nineteen-year-old with an autosomal recessive genetic disorder. His degenerative symptoms manifested several years ago, and are of a similar nature to those beginning to affect his sister, Amy, age sixteen. Sam, their nine-year-old sibling, does not have the heritable condition. They reside with Ellen, their mom, who is an elementary school teacher. Their dad, Howie, lives in another town with his second wife and young son.

DR. HARDY: The reason I gathered you all here today is that I have some good news. We now have a better chance to understand what’s causing your disorder -- and you can be part of a new study. That includes you too Sam.

MOM: We’ll do anything you say Dr. Hardy...as long as it’s safe.

DR HARDY: There’s little danger...just requires a simple blood draw. It’s for a new type of analysis, called genome sequencing. Doctors at several institutions are collaborating to further our understanding of genetic disease...and are especially interested in studying disorders with an adolescent-onset that are known to have increased prevalence in the Ashkenazi population. We will be looking at several groups, including

healthy siblings. Hopefully we'll also be able to learn more about Bobby and Amy's specific heritable defect to help them.....

I have consent forms here; Take them home and read them before signing.

MOM: After all these years with so few answers -- finally, there's some really powerful genetic technology.

BOBBY: Why do you think this is going to be so different and solve our problem?

AMY: Because Dr. Hardy's consent form says so right here:

"We will use new techniques to read all of the genetic information in your cells that might cause a health problem if it contained a mistake."

See, Dr. Hardy's new test will find our genetic mistakes.

SAM: You mean YOUR genetic mistakes.

NARRATOR: After reading through the first five pages of the informed consent form and discussing concerns with each other....

MOM: You know...I have another worry. This says we might get told what's wrong even if we don't want to know. Look,

"You will be given a choice to learn or not to learn the results of your genome sequencing....The only exception to opting out is if we find a result that has urgent importance to your health. We plan to share this type of result with you."

BOBBY: The doctors don't say anywhere in all these pages just how urgent or bad it has to be before they tell us bad news!how will they decide what's really important enough to tell us?

MOM: Why isn't there a checklist for us to say exactly which diseases we want to be told or which we really don't want to be told about?

BOBBY: But what if Amy wants to know everything and you don't, and it turns out both you guys have something like the BRCA gene you hear about so much? And what about Sam?

SAM: Don't worry about me. I'm the healthy kid in the family.

AMY: Of course I'd want to know everything---We'd all want to know.

MOM: I would not want any of us to know if something bad is going to happen way into the future, like Alzheimer's, or breast cancer. Why would we want to know ahead of time and worry?

AMY: The consent form also said something about our relatives learning results.

MOM: My relatives? ...I'll just keep it a secret.

BOBBY: A secret? You're terrible at keeping secrets Mom.

AMY: Mom...Just sign the paper and keep it simple please.

MOM: It's Not That Simple!

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NARRATOR: Several months pass and now we find Dr. Hardy speaking on the phone with Jennifer Smith, the genetic counselor, while in a Pediatric Genetics consultation office moments before the Friedman family arrives.

DR. HARDY: *(speaking into cell)* Okay, so we agree with the IRB about what I should tell them. This is not going to be easy...for any of us. *(puts down phone)*

(Door knocks -- The Friedman family enters Dr. Hardy's office -- Mom first, then Bobby and Amy together, with Sam trailing.)

MOM: Hi Dr. Hardy. We're so anxious to hear what you have to say that may help Bobby and Amy.

AMY: What do Bobby and I have?

DR HARDY: Well Amy, as for Bobby and your disorder, unfortunately nothing conclusive was uncovered -- so we need to wait until we gain further knowledge about how some of these genes relate to neurological functioning. Right now there is more we don't know than do---but the field is rapidly evolving.

BOBBY: I told you this high-tech test would be a waste of time. Now how much longer?

SAM: Couldn't you have just told Mom that over the phone rather than make me miss swim practice at school?

DR HARDY: Not exactly Sam. While we didn't get the answers we were hoping for regarding Bobby and Amy's disease, we learned several things that I must discuss with some of you Some potentially significant findings unrelated to what we were looking for.

AMY: Huh? How can you find something if you weren't looking for it?

DR HARDY: Remember the consent document explained that we were sequencing all of the protein coding genes that can cause disease. Next-generation sequencing uncovers a lot of information, not like the earlier genetic tests you've had that just targeted very specific genes. Because your Mom and Bobby are adults, I'll give them their results privately.

BOBBY: See Amy -- I'm an adult! And your not!!

MOM: What do you mean learn my results---I'm not sick!....am I ? I don't have breast cancer, do I? (*panicked*)

SAM: Nothing can happen to Mom --- we all need her. I can't take care of Bobby and Amy.

DR HARDY: First off, everyone needs to stay calm. I understand your fears, however please try to calm down a bit while I talk to your Mom.

AMY: Calm?!! That may be easy for you to say, but now you're telling us we should be worried about Mom, not just me and Bobby.

DR HARDY: Why don't we proceed so they'll be plenty of time for each of you folks to meet with Jennifer should you wish. Let me have a moment to speak with your Mom first.

(Others Exit – move over to farther side)

MOM: Just remember that I don't want to know if I'm getting breast cancer or if other bad things like Alzheimer's are going to happen when I get old...or my kids get old.

DR HARDY: We don't typically report those kinds of findings from a research protocol investigating another disorder.

MOM: Whew! I was so nervous about coming here today to find out how you can help Bobby and Amy that I couldn't remember where I parked my car yesterday. Spent so much time looking for it, and then I was so frazzled that I forgot to pick up Sam from her swim practice.

DR HARDY: I know you mentioned last visit that you thought the stress of dealing with Bobby's and Amy's illness was making you forgetful about a lot of things at work and at home.

MOM: That's for sure. Do you think I need an antidepressant like the one on TV?

DR HARDY: I'd like to recommend...that you see a neurologist...and have some neuroimaging done.....and have a bit of the genomic test redone by a CLIA lab.

MOM: What does my nervousness have to do with my gene test – everyone knows it's because of Bobby and Amy's condition? Who's Dr. Clia, and why does this Dr. Clia neurologist have to redo my test?

DR HARDY: Sorry for the confusion; this is complicated and Jennifer can explain more. There were certain findings from your particular genomic analysis that hints at the possibility...and only a possibility... of a susceptibilityto something...and we want to check it out more clearly. CLIA is not a doctor; rather a specially certified lab that helps determine if our research results were accurate.

MOM: You don't trust your lab to know if your research is bogus? And what does that have to do with my forgetting to pick up Sam from swim practice??
You're not implying that I'm going to go senile when I am 80 year old.....I told you I don't want to know that stuff.

DR HARDY: There are several possibilities that the neurologist will explore....and re-testing at a CLIA lab may help shed light as well.

MOM: Well Alzheimer's is for old people. I'll worry about that when I get old; now I need to think about my kids. Having some pills to relax me about that isn't such a bad idea Dr. Hardy. Thanks for suggesting that.

(Mom leaves)

DR HARDY: *(out loud, to self):* Assuming the CLIA test result confirms my finding, at least it will be the neurologist having to tell her she very likely has EARLY-onset AD. Now I have to brace myself for more.....*(calls out)* Bobby, can I speak with you next please.

MOM: Oh my Gosh---what are you going to tell us now?

DR HARDY: Please let me speak to Bobby alone for a moment. *(Bobby goes with Dr. Hardy)* Bobby, it's your choice as an adult if you want your mom here or not.

BOBBY: This sounds serious....Tell me first.... I thought you said Amy and me had “INCONCLUSIVE” genes?

DR HARDY: Sorry for any confusion Bobby. I was referring to the disease we were investigating. We found some....extra....concerns.....and had the results repeated by a different lab – a CLIA lab – to confirm their validity.

BOBBY: Give it to me straight doc!!

DR HARDY: The genome analysis shows that you carry the BRCA mutation....that doesn't necessarily mean you'll get breast cancer, it only indicates a susceptibility....the possibility for getting a disease. Indeed, your risk is quite low, only about 6% lifetime risk for breast cancer. But since it's much higher than the average male, we felt we should share it with you so you can be monitored now that we know to look.

BOBBY: I think you confused my results with Amy's or Mom's---that's a girl's disease.

DR HARDY: While prevalent in females, it also occurs in males.

BOBBY: Do Amy and Sam have breast cancer too? And Mom?

DR HARDY: First off, please let me be clear that I am not saying you have breast cancer. Only that you carry the genetic mutation associated with the possibility for developing the disease. We call that higher risk; not definitely getting the disease

BOBBY: This is so embarrassing. Do I need to tell my friends?

DR HARDY: Of course you don't need to tell your friends. This is private information that you don't need to share with anyone. Why don't you see Jennifer while I speak with your Mom about something else.

BOBBY: *(stumbles out dazed – then blurts out when passing Mom in hallway)* I have breast cancer!

DR HARDY: Please remember you don't have breast cancer now and might never even get it. It's only a potential future possibility.... a slight future possibility.
(brings Mom into office)

MOM: Oh my, is this some nightmare? We came here for you to tell us results that can help my kids' disease, and now you're telling Bobby he'll die from breast cancer instead?

DR HARDY: I did not say that Bobby had breast cancer, or would die from it. Just that the sequencing showed a small increased risk. Jennifer can explain further after we are done here.....but first I need to discuss something else with you....about Sam.

MOM: Please don't tell me you discovered that she has Amy and Bobby's bad gene.

DR HARDY: No, absolutely not, please rest assured...

MOM: *(cut Dr. Hardy off)* Thank heavens she's OK...she's my healthy one.

DR HARDY: Sam definitely does not carry that genetic defect.....however...

MOM: Oh my, you're going to tell me she has the breast cancer gene too.

DR HARDY: I'm not referring to those disorders...and given Sam's age, most geneticists would not report research results that may possibly have health implications much later in life.

MOM: So she is OK then.

DR HARDY: We are concerned....about something else that we found in the genomic testing...related to her heart.

MOM: You must be mistaken. Sam doesn't have a murmur. And she's a really good athlete. She runs and swims like a fish, has since she was little. Has been on our Y's swim team and hopes to be on the High School team one day.

DR HARDY: There's a condition called Long QT syndrome that is associated with rhythm disturbances in the heart, and potentially can be very serious and lead to passing out or sudden death. I advise kids to avoid competitive sports. Unfortunately competitive swimming can be particularly dangerous because passing out in the water can result in drowning.....at this point in time we can't perfectly predict when or which patients with the genetic predisposition to Long QT syndrome will have an arrhythmia associated with sudden cardiac arrest. So I need to share the seriousness of this with Sam and tell her we very strongly recommend that competitive athletics be forsaken.

MOM: Oh no, you can't tell her anything is wrong. Remember you just said doctors don't tell kids Sam's age. And anyway, remember you told me these tests aren't certain!

DR HARDY: You are correct that for kids we do not report disease susceptibility that may affect them later in life. This however has immediate implications. There is the potential for sudden death without treatment and an excellent outcome with treatment -- including taking a medication to protect the heart. And we've already

confirmed this result in a CLIA lab – they validated our findings. Because of the severe ramifications for some kids – and we don't know who -- I must inform her so she'll give up competitive sports... especially competitive swimming.

MOM: No... that would devastate her...let's wait till High School then I can just say I have to go to work earlier so can't take her to 6 AM swim practice.

DR HARDY: She should be closely followed by a cardiologist, who may also consider an implantable defibrillator. We really need to bring Sam into this discussion now—

(Dr. Hardy gives Mom tissues, touches her shoulder, and gets Sam)

SAM: Why does my Mom look so sad?

DR HARDY: Sam, your mom is concerned because we found something in your test -- called Long QT syndrome -- that has been linked to very serious heart problems in some young people -- though not everyone. Problem is, we aren't fully sure who will be the kid whose heart suddenly stops.....Because it can be most dangerous when doing competitive sports, I must advise you to immediately stop competitive swimming. There are so many wonderful activities you can do...art, music...

SAM: *(sobbing)* But you're telling me I can't do what I do best....

MOM: *(sobbing)* I can't believe this is happening....Sam was my healthy kid this morning....

DR HARDY: *(reflective)* I am so sorry.....*It's So Complicated!*