



Analyzing Pedigrees

OVERVIEW

In this activity, students interpret several pedigrees of autosomal dominant and recessive conditions and consider the benefits and limitations of genetic testing. Students answer multiple-choice questions about these pedigrees and explain their reasoning. For some questions, the goal is not to get the “right” answer but rather to discuss how pedigrees can be used to make decisions about one’s health.

Students can answer questions as a class, in small groups, or individually. You can share the pedigree images via the “Student Handout” or “Slide Deck” presentation.

The educator document contains multiple resources for implementing this case study with students, including the following (select links to go directly to each section in the document):

- [background](#) on pedigree guidelines
- [teaching tips](#) and suggested [procedure](#) for implementing the activity
- [assessment guidance](#) for the questions in the “Student Handout”

A separate “Additional Background” document provides more information about pedigree symbols and other notations. You may choose to share all or parts of the document with your students.

Additional information can be found on [this resource’s webpage](#), including suggested audience, estimated time, and curriculum connections.

KEY CONCEPTS

- Pedigrees can reveal patterns of inheritance of different health conditions.
- Pedigrees can be used to identify individuals who carry genetic variants associated with a health condition and/or may develop that condition.

STUDENT LEARNING TARGETS

- Interpret data in pedigrees of monogenic autosomal traits.
- Apply the information in a pedigree to predict health outcomes and make decisions about genetic testing.
- Consider the potential benefits and limitations of genetic testing for inherited diseases.

PRIOR KNOWLEDGE

Students should already have some familiarity with:

- interpreting pedigrees
- calculating probabilities of offspring phenotypes from a mating
- the function of genes and impact of genetic variations on phenotype
- autosomal dominant and recessive inheritance patterns

Students should know the meaning of these terms:

- gene, variant
- autosomal, dominant, recessive
- heterozygous, homozygous

MATERIALS

- copies of the “Student Handout” or the “Slide Deck”
- (optional) copies of the “Additional Background” handout

BACKGROUND

This activity uses the 2022 guidelines for reading pedigrees from the National Society of Genetic Counselors (NSGC) ([Bennett et al. 2022](#)). Additional information from these guidelines is provided in the “**Additional Background**” document in the “Materials” box of [this resource’s webpage](#).

The 2022 NSGC guidelines may not be the same as what is in textbooks. Remind students that the basic science (e.g., fundamental concepts of genetic inheritance) has not changed. However, how scientists refer to individuals, families, and different genetic conditions has changed in keeping with societal norms.

For example, previous guidelines indicated that pedigree symbols represented assigned sex at birth. According to the NSGC guidelines, pedigree symbols represent an individual’s gender identity. The NSGC’s rationale for updating the guidelines in this way is that “individuals served through genetic counseling have ownership of their health data and medical narratives.”

- An individual’s **gender identity** is their internal sense of self and how they fit into the world from the perspective of **gender**: the social constructions of roles and behaviors for men, women, and gender-diverse individuals.
- An individual’s gender identity may or may not align with their **assigned sex at birth**, which is based on physical attributes (e.g., the appearance of genitalia and/or sometimes chromosome complement).
- Because pedigrees are a tool to trace genetic inheritance, it may be important to know an individual’s sex assigned at birth and/or an individual’s allosomes (i.e., X and Y chromosomes), especially when examining X-linked inheritance. If that information is known, it is typically included along with the pedigree symbols.

TEACHING TIPS

- Any activities that involve discussion about potentially lethal genetic conditions can be stressful for some students. Consider letting the class know ahead of time about this activity or check in with individual students.
 - A simple example conversation starter could be “We’re learning about genetic conditions tomorrow, and I know this might be difficult for you because your mom recently passed away. Is there anything I can do to support you in my class?”
- It is important to remind students that a pedigree chart is not a family tree but rather a tool for examining how genetic information is passed down from one generation to the next. Many pedigrees include only genetic relatives. At the same time, avoid overgeneralizing about families, which may inadvertently exclude some students.
 - For example, you may want to recognize that there are all kinds of family structures (e.g., adoption, blended families, surrogacy, sperm donors, egg donors, same-gender parents, transgender parents, foster care), which may not be represented in a pedigree.
- When you notice students’ misconceptions, affirm the students’ willingness to participate and share ideas. If students overgeneralize about individuals or families, encourage them to reformulate their claims to be more inclusive of all people.
- Part 3 of this activity includes a transgender individual. If you decide to present this scenario to your class, consider also sharing guidelines for discussion ahead of the activity and ask students to agree to use respectful and inclusive language.
- Question 12, the final question in this activity, asks students to reflect on what they have learned by doing this activity. Students’ answers will provide valuable insights into areas that may require further instruction or discussion.
 - If you have conducted this activity as a discussion, this may be the only question that you ask students to submit. You can also assign this question as homework.
 - You may revise the question to ask students to provide more than one example of something that has changed in their thinking or knowledge.

PROCEDURE

General

In this activity, students examine and answer questions about different pedigrees. The goal is not for students to get the “right” answers but to show how they are applying their knowledge to different scenarios.

Students can answer questions:

- individually, by answering polls and/or writing their answers in the “Student Handout”
- by discussing in small groups and then sharing out to the whole class
- by discussing as a whole class
- a combination of these options

Depending on how you choose to conduct the activity, you can do one or both of the following:

- Give students the “Student Handout” to complete or follow along. The handout contains all the instructions and background that students need for the activity.
- Present the information using the “Slide Deck,” which has the same illustrations as the “Student Handout.” The slides do not have all of the background information in the handout. So if you use the slides but not the handout, encourage students to take notes on the key details about each health condition.

You may go through all the pedigrees and questions or choose the ones that are most appropriate for your class.

Pre-Activity

Before presenting the pedigrees, you may want to ask students to list some limitations of pedigrees. You may prod their thinking with the following questions:

- Can you think of examples in which people may not know their genetic relatives?
- Can you think of examples in which people may not know their family’s medical history?
- Can you think of reasons that people may or may not provide accurate medical information to health professionals or family members?

The discussion may touch on the fact that pedigrees rely on information that individuals provide, which may or may not be accurate. In some cases, genetic counselors may combine individuals’ narratives with medical and genetic tests to get more complete information.

Part 3

For Part 3 of the activity, additional information that may be helpful to discuss with students includes the following:

- If students are not familiar with the term “cisgender,” let them know that it refers to an individual whose gender identity matches their assigned sex at birth. The term “transgender” refers to an individual whose gender identity is different from their assigned sex at birth.
- Given the prevalence of breast cancer, it is likely that students will know someone close to them who has or had breast cancer. Consider letting students know ahead of time that breast cancer is discussed in this activity. However, most cases of breast cancer are *not* associated with the *BRCA1* variant, which is a rare variant.
- Both the *SCA1* variant from Part 2 and the *BRCA1* variant from Part 3 are dominant variants, but there are some differences in how they influence an individual’s phenotype.
 - The *SCA1* variant has near complete expression (“penetrance”), so having one copy of the *SCA1* variant usually results in having SCA1. The *BRCA1* variant has a more variable effect on the chance of disease — having one copy of the *BRCA1* variant increases the chance of developing breast cancer by 55%–72% for cisgender women, but the actual chance depends on many factors.
 - Individuals with the *SCA1* variant typically develop SCA1 regardless of their assigned sex at birth. In contrast, the *BRCA1* variant significantly increases the chances of developing breast cancer for individuals assigned female sex at birth.

Once students have had a chance to examine Pedigree 4, you may want to ask them if they have any questions. Potential questions or points of discussion include the following:

- This pedigree includes a transgender man, who is represented by a square labeled AFAB. The square is the symbol for a man, and AFAB means assigned female sex at birth.
 - It may be helpful to point out to students the difference between **gender identity**, a person's internal sense of self and how they fit into the world from the perspective of gender, and **assigned sex at birth**, which is based on physical attributes (e.g., the appearance of genitalia). The distinction may be important to note in a pedigree if you are examining the inheritance of a condition that has different outcomes among the sexes.
- The last generation of this pedigree shows a monozygotic (identical) twin pair. You may want to explain the difference between monozygotic and dizygotic twins to students. If students are not familiar with the pedigree symbol for twins, you may also want to clarify or show it to them earlier.

ASSESSMENT GUIDANCE

The sample answers include more detail than would be provided by most students. They are meant to give you additional information that you may want to discuss with students.

PART 1: Practice Interpreting Pedigrees

1. Which of the following can be inferred about Individual 4 in the second generation (Individual II-4)?
 - a. Individual II-4 is a woman.
 - b. [ANSWER] Individual II-4 has two known biological children.**
 - c. Individual II-4 has one deceased biological sibling who was unaffected.
 - d. Individual II-4 is unaffected.

Explain your reasoning for the answer you selected:

Individual II-4 is an affected man and was in a relationship with someone who is now dead. He does not have any dead biological siblings and has two biological children shown.

2. Individual II-3 had a child (Individual III-5) using a sperm donor. Which of the following can be inferred about Individual III-5?
 - a. She is not genetically related to other individuals in Generation III.
 - b. [ANSWER] She has inherited 50% of her DNA from Individual II-3.**
 - c. She has not inherited any DNA from Individual II-3.
 - d. She is affected with the health condition of interest.

Explain your reasoning for the answer you selected:

Individual III-5 inherited half her DNA from Individual II-3 and half from the sperm donor. She is not affected since her symbol is not shaded. She is genetically related to Individual II-3, Individual II-3's biological siblings, and their biological offspring (in Generation III).

This question provides an opportunity to discuss the following with students:

- **One possible limitation of pedigrees is that genetic counselors sometimes don't have information about all biological parents. For example, an individual may have had a child with someone for whom the counselors don't have any medical information. In this case, the counselors did not have medical information on the sperm donor, so they did not include the sperm donor on the pedigree.**
- **Genetic counselors may also choose not to include an individual on a pedigree if they are not genetically related to the other individuals in the pedigree (i.e., if they were related only through marriage). So, it's possible that Individual II-3 has a spouse who was not included in the pedigree because they did not contribute any DNA to their child.**

PART 2: Examining Patterns of Autosomal Inheritance

3. Pedigree 2 most likely shows the inheritance of an autosomal dominant condition because:

- a. Most affected individuals are men.
- b. The family is very large.
- c. **[ANSWER] The condition occurs in every generation.**
- d. Filled symbols always show an autosomal dominant trait.

Explain your reasoning for the answer you selected:

Autosomal dominant traits usually show up in every generation of a large pedigree. None of the other answers are indicative of an autosomal dominant trait.

4. The following figure represents a small section of Pedigree 2. Which of the following does this figure show about the affected individual?
- a. She has several affected biological children.
 - b. **[ANSWER] She had four biological children with three different partners.**
 - c. She had three biological children with two different partners.
 - d. She has three biological siblings who are all unaffected.

Explain your reasoning for the answer you selected:

This individual has lines going from the middle of her symbol to other symbols, which indicate partner relationships. She had two biological children from one relationship and one biological child from each of the other two relationships.

5. If an individual affected with SCA1 has a biological child with an individual without the condition, what are the chances that their child has SCA1?
- a. 0%
 - b. 25%
 - c. **[ANSWER] 50%**
 - d. 100%

Explain your reasoning for the answer you selected:

The most likely answer is c (50%), because almost all individuals with SCA1 are heterozygous, meaning they have one copy of an SCA1-associated variant. This gives them a 50% chance of passing the variant to their child.

Students may also pick d (100%) thinking that the individual affected with SCA1 could be homozygous for the SCA1-associated variant. Remind students that a rare autosomal dominant disease like SCA1 typically will not appear in homozygous form, as individuals with two copies of the associated variant are unlikely to survive to adulthood.

This question also provides an opportunity to clarify that the chance of inheriting a genetic condition is for each pregnancy, regardless of the number of children who were born with or without this condition (e.g., “chance has no memory”). Based on the information provided, each child of these two individuals has a 50% chance of having SCA1.

6. If one of your genetic relatives had SCA1, do you think you would want to get tested for a genetic variant associated with the condition? (There are no right or wrong answers.)
- a. Yes
 - b. No

Explain your reasoning for the answer you selected:

Genetic testing is a highly personal decision, so there is no right or wrong answer or reasoning for this question. Some students may say “Yes” because it could help them make decisions about themselves or family members. Other students may say “No” because genetic testing is not accessible to them or because there is currently no cure for SCA1, so that information would just create stress.

If you have a class discussion on this topic, share some guidelines at the beginning of the discussion to make sure that everyone is respectful of other students' opinions. Let students know that they don't need to share their reasoning for this answer with others. Other topics relevant to this discussion could include the following:

- *The role of genetic counseling is to provide the best possible information to patients so that they can make informed choices. This includes making sure that individuals have sufficient information about the benefits and limitations of testing.*
- *Point out to students that genetic counselors would never "encourage" genetic testing for relatives, as this is a personal choice and will differ between all individuals.*
- *The Genetic Information Nondiscrimination Act (GINA) of 2008 protects against some types of genetic discrimination. For example, it prohibits health insurers from denying coverage based on a genetic predisposition to a disease, and it bans employers from using genetic information for making any employment decisions. However, GINA does not cover life, long-term care, and disability insurance.*

7. Pedigree 3 is typical of autosomal recessive inheritance because:
- Most affected individuals are women.
 - Many people have died, as shown by the crossed-out symbols.
 - Affected individuals inherited DNA from individuals who are also affected.
 - [ANSWER] Affected individuals inherited DNA from individuals who are carriers.**

Explain your reasoning for the answer you selected:

For autosomal recessive traits, the biological parents of affected individuals are almost always unaffected carriers. (For autosomal dominant traits, affected individuals often, but not always, have at least one biological parent who is affected.)

8. If a carrier has a biological child with an individual with beta thalassemia major, what are the chances the child has beta thalassemia major?
- 0%
 - 25%
 - [ANSWER] 50%**
 - 100%

Explain your reasoning for the answer you selected:

The individual with beta thalassemia major has two copies of the genetic variant associated with the condition. If they have a child with someone who is a heterozygous carrier, there is a 50% chance that the child will have beta thalassemia major (two copies of the variant) and a 50% chance that they will be a carrier (one copy of the variant).

9. If one of your relatives had beta thalassemia major, do you think you would want to get tested for the disease-associated variant? (There are no right or wrong answers.)
- Yes
 - No

Explain your reasoning for the answer you selected:

Students may provide reasoning similar to that in Question 6. Make sure to point out that genetic testing is not accessible to everyone and whether to get tested is a highly personal decision, so there are no right or wrong choices.

As with Question 6, you can ask students to share in a class discussion their reasoning for their answers. In addition, you may ask them whether their answer was different than their answer to Question 6. Topics relevant to this discussion could include:

- Unlike SCA1, for which there is no cure, beta thalassemia major can be managed with medical treatments.
- In the case of an autosomal recessive condition like beta thalassemia major, genetic testing can help identify carriers who don't have any symptoms and may not even know they are carriers.
- In the United States, newborns are tested for certain genetic conditions — generally conditions for which early diagnosis is important for treating or preventing symptoms.
 - Testing requirements depend on the state. You could discuss the conditions for which your state mandates newborn testing.
- Some people may choose to have prenatal testing and preimplantation genetic testing, so that they can have information even before a child is born.

PART 3: Determining Inherited Breast Cancer Risk

The [Part 3 procedure](#) provides more information on implementing this part of the activity, including additional information that may be helpful to discuss with students.

10. A 19-year-old transgender man visited a genetic counselor to find out whether he is more likely to develop breast cancer. This individual is indicated with an arrow in Pedigree 4. Is it possible he would have inherited the *BRCA1* variant associated with breast cancer?
- a. No, because he is a man.
 - b. Yes, because his monozygotic twin has breast cancer.
 - c. No, because his biological parents do not have breast cancer.
 - d. **[ANSWER] Yes, because one of his biological parents has the harmful *BRCA1* variant.**

Explain your reasoning for the answer you selected:

This individual has a 50% chance of inheriting the *BRCA1* variant from one of his biological parents.

His other biological parent was not tested but might also have the *BRCA1* variant. (If so, the chances of the 19-year-old patient inheriting the *BRCA1* variant would be higher than 50%.) The untested parent has a biological sibling with the *BRCA1* variant and thus may also have inherited the variant.

11. To reduce the chance of developing breast cancer, some individuals with the harmful *BRCA1* variant may decide, in consultation with their doctors, to have their breasts and/or ovaries removed before any signs of cancer develop. If you were the individual seeking genetic counseling, would you want to get tested for the *BRCA1* variant? (There are no right or wrong answers.)
- a. Yes
 - b. No

Explain your reasoning for the answer you selected:

As with Questions 6 and 9, this choice is highly personal.

Some students may say that this individual is a man and unlikely to develop breast cancer. This is an opportunity to remind students that the symbols denote gender identity, which may or may not match assigned sex at birth.

- ***The 19-year-old patient is a transgender man. If he has the *BRCA1* variant, both he and his twin sister may have a higher chance of developing breast cancer.***
- ***As discussed in the original paper ([Sacca et al. 2019](#)), this 19-year-old man told genetic counselors that he was planning to have gender-affirming top surgery before graduating from college. If he had the harmful *BRCA1* variant, he wanted surgery to completely remove breast tissue (i.e., bilateral mastectomy) rather than the standard gender-affirming top surgery for men (in which some breast tissue is left behind for cosmetic purposes).***

Some students may have heard that the actor Angelina Jolie decided to have a bilateral mastectomy after she found out that she had the harmful *BRCA1* variant. The treatment options that an individual chooses

to pursue are highly personal choices that may be informed by conversations with their healthcare professionals and loved ones.

12. Reflect on how your thinking has changed by doing this activity. Write your answer by completing the following prompts.

I used to think:

And now I think:

Students' responses will vary and may indicate areas that require further instruction or discussion.

REFERENCES

Pedigree Guidelines

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Pedigree 2

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Pedigree 3

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Pedigree 4

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Part 3

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