Master 4.3 Answer Key

Max's Case: Thyroid Cancer, Men II, and Genetic Testing

Question	Answer
1. Who had thyroid cancer, and when were they diagnosed with it?	*James, Harriet, and Nick all had thyroid cancer; all were diagnosed with it in their teens, 20s, or 30s.*
2. Who died of thyroid cancer?	*James, Harriet, and Nick died of thyroid cancer.*
3. Of those who had thyroid cancer, who is known to have had MEN II?	*At this point, no one (even those who had thyroid cancer) is known to have had MEN II.*
4. Who died of reasons not related to thyroid cancer?	*Susie, when she was 32 years old.*
5. Who has elevated levels of thyroxine, which could be a warning sign of future thyroid cancer?	*Diane.*
6. If someone had MEN II, what would his or her genotype be?	*The MEN II gene is dominant. The genotype could be homozygous dominant (TT) or heterozygous (Tt). Since the dominant allele is rare, assume that a person with MEN II is heterozygous.*
7. If someone did *not* have MEN II (even if he or she did have thyroid cancer), what would his or her genotype be?	*Homozygous recessive (tt).*

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Master 4.6 Answer Key

Thyroid Cancer, Men II, and Genetic Testing: Checking for Understanding

1. What is MEN II? Although many kinds of cancer are linked with MEN II, 100 percent of people with the gene for MEN II will get cancer of what organ?

   MEN II is multiple endocrine neoplasia 2. People with this disease almost always develop a certain type of thyroid cancer and may also develop other kinds, such as adrenal gland, brain, and bone cancer.

2. The Alzheimer's disease genetic test doesn't predict Alzheimer's disease with certainty; a person who tests positive for *E4* has only a 13-to-57-percent lifetime risk of Alzheimer's disease. If a person tests positive for the mutation that causes MEN II, what is the chance that the person will get thyroid cancer?

   100 percent.

3. There is no followup medical procedure that will prevent onset of Alzheimer's disease. What followup medical options are there for a person who has tested positive for the mutation that causes MEN II?

   The thyroid can be removed before any sign of cancer. Therefore, the person will never get thyroid cancer. Because the person doesn't have a thyroid gland anymore, they need to take a daily medication.

4. As noted, this type of thyroid cancer is caused by an autosomal dominant mutation. What does this mean? (What does *autosomal* mean? What does *dominant* mean?)

   An autosomal gene is a gene that is not on the X or Y chromosome. If one inherits the dominant version of the gene from one or both biological parents, he or she will develop the disease.

5. Other than the predictive value of the test and the options for followup medical care, what is another difference between Alzheimer's disease and the type of thyroid cancer associated with MEN II?

   The most typical type of Alzheimer's arises at older ages (age 65 or older); the type of thyroid cancer associated with MEN II arises by a person's 30s. Alzheimer's involves brain degeneration; MEN II leads to an aggressive cancer if left untreated.

6. If Max were to test positive for the mutation, would he know anything more about anyone else in his family? Explain, and be as specific as possible.

   If Max tests positive, that means that others in his family could also have inherited the same mutation. For example, his aunt and uncle could both have inherited this mutation, along with his cousins. This means that others in the family may want to follow up with their own genetic tests for the MEN II mutation.

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Master 4.7 Answer Key

What Impact Would Max's Newly Discovered Mutation Have on Him and Others?

Name	Age	1. If Max had the mutation, what is the chance that the person below also inherited the mutation? 2. What is the chance that the person would develop thyroid cancer?
Max	*15*	1. 100% 2. 100%
Pierre	*39*	*No additional info; married into family; assume he's homozygous recesive* (tt).
Sally	*9*	1. *50% chance of being heterozygous* (Tt)*;* *50% chance of being homozygous recessive* (tt). 2. *50%*
Diane	*31*	1. *50% chance of being heterozygous* (Tt)*;* *50% chance of being homozygous recessive* (tt). 2. *50%*
Lindsey	*5*	1. *25% chance of being heterozygous* (Tt)*;* *75% chance of being homozygous recessive* (tt). 2. *25%*
Eula	*80*	1. *50% chance of being heterozygous* (Tt)*;* *50% chance of being homozygous recessive* (tt). 2. *50%, but she is 80 years old and free of thyroid cancer, so she must be homozygous recessive* (tt).

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Master 4.8 Answer Key

Thyroid Cancer and Genetic Testing: Harms and Benefits

Complete the chart below by applying relevant scientific facts about genetic testing and followup medical care for this type of thyroid cancer.

Type of Harm or Benefit	Harms	Benefits
Physical	• *If Max tested positive and received preventative surgery, he would need to recover from the surgery. This would likely be a very temporary harm. However, there is always a small chance of more major complications from surgery.* • *There are many types of thyroid cancer, and Max is being tested for the mutation that causes just one type. If he tests negative, he might falsely interpret this to mean that he has zero lifetime risk of thyroid cancer and might not be as careful about getting thyroid checkups and screenings, which could save his life were he to develop thyroid cancer.*	• *If Max tested positive, he could have followup surgery that would eliminate his chance of thyroid cancer.* • *Even if Max didn't have the preventive surgery, a positive test result would lead to more screenings and the cancer would be detected earlier.*
Psychological (Emotional)	• *If Max tested positive, he might be upset at first, especially if the testing happens against his will.* • *Max might feel angry about inheriting this mutation.* • *Max might feel guilty about not inheriting this mutation, knowing that others in his family may have inherited it.*	• *If Max tested negative, he would feel relieved and would benefit emotionally.* • *If Max tested positive, he would be able to take concrete medical action, and by taking this kind of control over his own life, he might experience an emotional benefit.*
Social	• *If Max tested positive and got the followup surgery, he would have a thin scar that might be embarrassing.* • *If Max tested positive, others might stigmatize him for having a mutation that will lead to cancer.*	• *Max's friends and family members would greatly benefit from Max's staying alive, in terms of social and family relationships.*
Economic	• *The test is expensive and puts a financial drain on whoever pays for it.*	• *Preventive surgery would probably cost less than cancer medications and treatments (which would probably include surgery).* • *Max would probably miss less school or work if he had the preventive surgery rather than cancer treatment later on.*

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Who Should Decide Whether Max Gets Tested?

(Day 3, Activity 7)

Who Should Decide Whether Max Gets Tested? -

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Remind students that "Who should decide?" and "Should Max get tested?" are two different questions. For example, even though a student thinks that it's a good idea for Max to get tested and that student knows that Max is against having the test, he or she could still be in favor of Max being the decision maker.

Students overwhelmingly think it's obvious that **Max** should decide: respect for Max demands that Max decide for himself.

↓

Teacher can follow up with questions such as:

- What if Max were only five years old?
- Why is it morally permissible for a parent to decide on behalf of a 5-year-old but not a 15-year-old?

↓

Students answer that a 15-year-old is more rational than a 5-year-old.

↓

Teacher can follow up with questions such as:

- Is Max's rational capacity fully developed?
- How do you know that it is developed enough to make a completely autonomous decision about a high-stakes genetic test?

Students overwhelmingly think it's obvious that **Max's dad** should decide.

Students comment that Max is still a minor, so his father should decide.

↓

Teacher can follow up with a question such as, Is what is legal always ethical?

Students comment that the decision is too high-stakes for Max.

↓

Teacher can respond with followup questions such as:

- Don't teenagers make other high-stakes decisions, such as driving and playing high-risk sports? Is there a difference between letting Max make up his own mind about playing a high-risk sport and having a genetic test?
- What if Max were 18? The decision would still be high-stakes. Should Max's dad still decide?

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Additionally, the teacher can pose other hypothetical scenarios for the class to consider, including these:

- Who should get to decide whether Max should have the genetic test if the genetic test were not 100-percent predictive of a future disease or condition? What if a positive result indicated only a 70-percent chance of thyroid cancer developing?
- Who should get to decide if the medication had very prolonged and negative side effects?
- Who should get to decide if the age of onset were in the patient's 50s, 60s, or 70s?
- Who should get to decide if no followup medical care were available for a positive test result?

Teachers should also make sure that students keep the core ethical question—Who should decide?—at the forefront of the discussion. This discussion is *not* about whether Max should have the test or whether it would be best for Max to have the test.

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Who Should Have Access to the Results?

(Day 3, Activity 8)

Who Should Have Access to the Results? -

↓

Make sure that students understand what Max's positive test result means for others in the family.

1. Does it mean that others in the family have also inherited the mutation? (No)
2. Would a negative test result from Max mean that others in the family are free of the mutation? (No)

Students overwhelmingly think it's obvious that Max's father **should** share the information. Students think that everyone should know because "they are part of the family."

↓

Teacher reminds students that family members can only learn this information by getting themselves tested. Max's results will not tell them anything definitive about themselves.

↓

Teacher asks whether the father could share information that Max has had a genetic test and that there has been concern of a particular inherited mutation in the family. Then, each affected family member could decide about getting genetically tested.

↓

Students overwhelmingly think it's obvious that Max's father **should not** share the information.

↓

Teacher asks students to brainstorm scenarios in which a person has an obligation to share information with others. For example, these scenarios could include

1. diagnosis of a very contagious disease and
2. patient tells therapist that he or she intends to kill or hurt someone.

↓

Teacher asks whether there is a difference between scenarios above vs. sharing results of Max's test. If so, what are the differences? If not, why are they similar?

↓

Students can compare the following phrasings: Which is preferable and why?

1. "Max has had a genetic test for an inherited mutation related to thyroid cancer. He asked me not to share his test results, but you can get yourself tested if you choose, and I can give you more information about the test itself."
2. "Max has had a genetic test for an inherited mutation related to thyroid cancer. Since his results may have a bearing on your own health, I can tell you the results if you want to know."
3. "Max has tested positive for a mutation related to thyroid cancer. This means you have a ____ percent chance of also having inherited the mutation.

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Supplementary Information on Alzheimer's Disease and MEN II*

Disease Characteristics	Alzheimer's Disease	MEN II
Brief overview	Different types of Alzheimer's disease exist. This module focuses on the more typical kind of Alzheimer's disease, which arises past the age of 65. Early-onset Alzheimer's disease, on the other hand, can arise in a person's 30s. Alzheimer's disease affects memory, problem-solving ability, and even personality. Eventually, it is fatal.	This inherited disorder almost always leads to a type of thyroid cancer called medullary thyroid carcinoma. MEN II is defined by the overactivity of the thyroid, adrenal, and parathyroid glands. Tumors can appear in any of these glands, but they do not necessarily appear at the same time. If the cancer spreads, it may spread to places such as bones and the brain.
Prevalence (total number of current cases) in the United States	Over 5 million people.	Approximately 10,000 people.
Symptoms	Problems with memory, thinking, and concentration that extend beyond the normal aging process.	Severe headache, rapid heart rate, sweating, irritability, loss of weight, high blood pressure, and enlarged lymph nodes.
Brief description of mutation from biochemical perspective	The version of the *ApoE* gene (on chromosome 19) inherited from each parent plays a role in the development of the more typical (not early-onset) form of Alzheimer's. The gene comes in three versions: *E2*, *E3*, and *E4*. The *E4* version elevates a person's chance of getting Alzheimer's, whereas the *E2* version may actually lessen the chance. The *E3* version does not seem to affect a person's chance of getting Alzheimer's.	Mutation in a proto-oncogene named *RET* (on chromosome 10), which leads to unregulated cell growth.
Predictive ability of genetic test	Partial: positive test result means 13–57% lifetime chance of getting Alzheimer's.	Full: positive test result means nearly 100% chance of thyroid cancer.
Medical Response to a Positive Test Result	There is no medical action to prevent Alzheimer's disease. However, the disease does seem to have an association with diseased arteries and type 2 diabetes. Therefore, eating well and promoting good cardiovascular health may serve to lessen one's chance of getting Alzheimer's disease.	Preventive removal of the thyroid gland (often by age 10) and thyroid hormones then taken orally. This followup medical treatment eliminates the chance of thyroid cancer.
Age of Onset	Age 65 or later.	Teens, 20s, 30s.

*MEN II, multiple endocrine neoplasia type 2.

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Supplementary Information on HNPCC*

"Microsatellite instability" (also known as MSI) is very often associated with HNPCC. Microsatellites are stretches of the genome with repetitive sequences such as "AAAAA" or "CGCGCGCG." These stretches are especially prone to developing errors, when a mismatch-repair gene is mutated. (However, 15 to 20 percent of sporadic, or noninherited, colon cancers also display MSI.) Because MSI is associated with 90 percent of colon cancers caused by HNPCC, the presence of MSI usually means the person has HNPCC.

Most commonly, the mutated gene is either *MLH1* or *MSH2*, both of which are part of chromosome 2. Both the MLH1 and MSH2 proteins are responsible for DNA repair. The mutations leading to HNPCC are autosomal dominant mutations and include insertions, nonsense mutations, and mutations at splicing sites. The normal MLH1 protein contains 746 amino acids, coded for by 19 exons. When the corresponding gene is mutated, an abnormal MLH1 protein is formed, and it is more difficult for the cell to properly correct DNA damage. However, on its own, this abnormal protein isn't enough to cause cancer; other mutations must also arise over the person's lifetime. Therefore, these other mutations are somatic. If these somatic mutations occur in a person's colon cells, for example, the person will get colon cancer. If these somatic mutations occur in a person's ovary, ovarian cancer would instead develop. Thus, each of these cancers (when associated with the *MLH1* or *MLH2* mutation) displays a polygenic inheritance pattern.

Cancer Risks in the General Population Compared with Individuals with HNPCC

Cancer	General Population Risk	HNPCC Risk	HNPCC Mean Age of Onset
Colon	5.5%	80%	44 years
Endometrium	2.7%	20–60%	46 years
Stomach	less than 1%	11–19%	56 years
Ovary	1.6%	9–12%	42.5 years
Urinary tract	less than 1%	4–5%	approximately 55 years
Brain, central nervous system	less than 1%	1–3%	approximately 50 years

Source: *http://www.genetests.org/*. Copyright University of Washington and Children's Health System, Seattle. Reprinted with permission.

* Hereditary nonpolyposis colorectal cancer.

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Comparison of Alzheimer's Disease, MEN II, and HNPCC*

Disease Characteristics	Alzheimer's Disease	MEN II	HNPCC
Part of body (most) affected	Brain	Thyroid gland	Large intestine, colon
Examples of other parts of the body that could also be affected	—	Adrenal glands, parathyroid glands, bones, brain	Stomach, uterus, ovaries
Cancer?	No	Yes	Yes
Age of onset	65 or older	Teens, 20s, 30s	Mid 40s, on average; onset before age 20 is very rare.
Positive test result indicates what lifetime percentage chance of disease?	13–57%	Nearly 100%	80% by age 75
Medical followup available?	No medical intervention is known to lower one's chance of developing Alzheimer's disease. General wellness should be stressed, as it should be for any patient.	Yes, full removal of thyroid followed by daily medication. This eliminates any chance of thyroid cancer.	Yes, more regular colonoscopies (usually beginning at age 20 to 25) in hopes of early detection of any colon irregularities. Also, dietary changes and medication might be recommended. Surgery is also possible (to remove colon, ovaries, etc.), but frequent screenings are thought to offer the same medical benefit in terms of lifespan.
Mutation inheritable by future generations?	Yes	Yes	Yes
Mutation type	Autosomal, incomplete dominance	Autosomal, dominant	Autosomal, dominant

*MEN II, multiple endocrine neoplasia type 2; HNPCC, hereditary nonpolyposis colorectal cancer.

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Evaluative Criteria for the Final Assessment

Who should decide?

Level of Achievement	General Characteristics of Response	Actual Student Response	Analysis of Response
Exemplary	Student provides **three reasons** and clearly understands how to **apply both the ethical considerations and the relevant scientific facts**; student elaborates and shows **original thinking**; student goes beyond class discussions.	*"Camilla should get to decide whether she gets tested because she has the greatest understanding of how the results will psychologically affect her, and she will have to deal most directly with the results of the test. Also, not taking the test now does not preclude her chances of taking the test in the future so she can wait until she feels emotionally prepared. The parent may exert influence over her decision, but because [Camilla] will have to make the medical decisions in the future, she should be able to make this decision now."* *"Camilla should be the one to decide whether she will take this test.... She could get regular colonoscopies [even if she didn't take] the test. This will help catch the cancer if she is predisposed, but keeps her from taking the test...."* (Note that this response could be exemplary or proficient, depending upon the nature of the class discussions. If this response essentially rephrases a class discussion, then it would be proficient. If, however, it extends reasonably far beyond class discussions, it would be exemplary.)	**Ethical Considerations** *minimizing harms and maximizing benefits* Delaying testing could simultaneously • pave the way for minimizing emotional harm and • maximize physical benefit. **Scientific Facts** • Regular colonoscopies are most critical in terms of diagnosis. • Colonoscopies can occur in absence of genetic tests.
Proficient	Student provides **three reasons** and clearly understands how to **apply both the ethical considerations and the relevant scientific facts**; although the explanation is organized and logical, it **repeats much of what was already discussed in class**.	See sample response above. If this response essentially rephrases a class discussion, it would be proficient.	**Same as analysis above**

Continued

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Level of Achievement	General Characteristics of Response	Actual Student Response	Analysis of Response
Developing	Student provides **one or two reasons** or is **unable to fully apply both the ethical considerations and the relevant scientific facts.**	*"By getting her tested, [her mother] can give her a longer life by giving her better access to colonoscopies and medication. It has been proven that when colon cancer is detected in its early stages, … 90 percent of patients will live at least five years after diagnosis…."*	**Ethical Considerations** *minimizing harms and maximizing benefits* Attention to physical benefits but not to potential harms. (To fully examine this consideration, the student would need to weigh out more harms and benefits than just physical benefit.) **Scientific Facts** • Early detection predicts greater longevity.
Unacceptable	Student provides **one or two reasons** but is **unable to apply the ethical considerations and the relevant scientific facts.**	*"[Camilla's] family should decide… because they are responsible for [Camilla] and they want to make sure that [she is not going] to get the cancer."* Or *"It is important for Camilla to have the test so that her parents can test themselves and their other children."*	Student provides a reason (parental responsibility) but applies **no** ethical considerations and has the scientific facts wrong. (Student seems to think that the test results can prevent or cure the cancer.) Student doesn't understand that family members can get tested independently of Camilla and that her results—whether positive or negative—offer no definitive information.

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If Camilla were to have the genetic test, who else (if anyone) should learn the results (other than Camilla, her doctor, and her mother)?

Level of Achievement	General Characteristics of Response	Actual Student Response*	Analysis of Response
Exemplary	Student provides **two reasons** and clearly understands how to **apply both the ethical considerations and the relevant scientific facts**; student elaborates, and shows **original thinking**; student goes beyond class discussions.	*"If Camilla were to take the test, she should not have to tell her family. It is her medical result, and she should be able to keep [it] confidential. Secondly, the other members of the family already knew they were at risk, because Felicia had colon cancer. The other family members could take the test as well. They could then tell the results to whichever family members they want. Not only would this solution allow Camilla to keep her confidentiality, but the results would also be much more helpful to the person taking the test than just knowing Camilla's results. Because it is her information, Camilla should control her course of action, and what is happening. "[Finally,] unlike something like HIV, the gene is not transmissible or except to her offspring...."* *"Camilla's mother should share information about the HNPCC test availability with the family while keeping Camilla's personal genetic testing results confidential. The testing does pave the way for significant medical intervention and benefit, so it would be a good idea to make sure that all family members know about the availability of the test. Each family member could then make up their own mind for testing. Camilla's results don't definitively predict other family members' results, anyway. Even if Camilla is negative, her sisters could still have the mutation."*	**Ethical Consideration** • *Confidentiality* • *Minimizing harms, maximizing benefits* **Scientific Facts** • Mendelian genetics and specific inheritance patterns apply to this situation. • Infectious and inherited diseases are significantly different. • The nature of the genetic test

Continued

*Note that this response could be exemplary or proficient, depending upon the nature of the class discussions. If it extends reasonably far beyond class discussions, it would be exemplary.

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Evaluative Criteria for the Final Assessment
CONTINUED

Level of Achievement	General Characteristics of Response	Actual Student Response	Analysis of Response
Proficient	Student provides **two reasons** and clearly understands how to **apply both the ethical considerations and the relevant scientific facts**; although the explanation is organized and logical, it **repeats much of what was already discussed in class**.	See sample response above. If this response essentially rephrases a class discussion, it would be proficient.	**Same as analysis above**
Developing	Student provides **one reason**, or is **unable to fully apply both the ethical considerations and the relevant scientific facts**.	*"The only other people that should learn the results of Camilla's genetic test are the ones [who themselves could have the mutation]. Both of Camilla's sisters, Erlinda and Ella, could have inherited the [mutation], meaning that they, too, are at risk of being diagnosed with or developing colon cancer in the future. As the mutation is autosomal and dominant, if it is present only once in either or both of her sisters, they will also have a [high chance of] colon cancer and will need to know this before making any decisions [regarding followup care]. Her paternal grandfather, Ronald, [could] also be affected [as he] could still feasibly develop colon cancer, even though he is past the average age of 44. Felicia should not learn the results because she specifically asked not to be informed."*	**Ethical Considerations** *confidentiality and physical benefit of followup medical care* **Scientific Facts** • Colon cancer typically arises in someone's mid 40s, and Mendelian genetics applies to this situation. • However, the student doesn't make it clear that Camilla's result won't give any definitive information regarding the sisters. (Student has successfully applied some of the scientific facts [age of colon cancer onset, for example], but doesn't make it clear that Camilla's result won't give any definitive information regarding the sisters.) To bring this response to the next level, the student could write something such as, *"Learning that a close relative has an inherited mutation is different from learning that an inherited form of colon cancer may run in the family. Therefore, it's important that the sisters learn of Camilla's test result, especially if she turns out to be positive. This will more likely encourage them to take the test themselves, and receive early followup care if necessary."*
Unacceptable	Student provides one reason with very little or no application of the ethical considerations and the relevant scientific facts.	*"Nobody [else] should get to see the result. If people are in constant fear that others will learn their medical information, they will be disinclined to ever get tested."*	**Ethical Consideration** *beginning of confidentiality* **Scientific Facts** none

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Extension (Optional)

Should Employers Have Access to Genetic Test Results?

Estimated Time: 45 minutes

If you have another class period to devote to this work, you might want to explore this ethical question: Should employers be able to require and gain access to genetic testing results that could affect a person's ability to do his or her job? Master 4.11: About Retinitis Pigmentosa will guide you and your students through an exploration of a degenerative eye condition. This case focuses on the following question:

Should airline companies be able to screen prospective pilots for associated genetic mutations?

Procedure

1. **Give each student a copy of Master 4.11.**
2. **Read the scenario aloud and pose the following ethical question: Should an airline company be able to require perspective employees to have a genetic test for retinitis pigmentosa?**
3. **Remind students that the next step is to consider all relevant information. A great deal of information is available in Master 4.11.**
4. **Ask students, "Who or what will be affected by the decision?"**
5. **Ask students to identify the relevant ethical considerations.**
   Students will likely identify ethical considerations such as minimizing harms and maximizing benefits, fairness, and respect for persons.
6. **Now that students have identified the ethical considerations, help them elaborate on their initial ideas by asking questions such as these:**

   a. **What are the associated harms and benefits for airline companies that require retinitis pigmentosa genetic screening for perspective employees?**
   Students will likely bring up economic benefits as part of this discussion.

   b. **What are the associated harms and benefits for prospective employees who receive retinitis pigmentosa genetic screening from airline companies?**
   Students may bring up
   - economic harms if these employees are not hired as a result of a positive test,
   - emotional harms if the prospective employee must now explain to family and friends why he or she was not hired, and
   - economic or emotional benefit if the prospective pilot can now choose a different career that he or she can do for a longer period of time.

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c. **How do the harms and benefits compare? Which outweighs the other? Why?**

d. **Should a company be able to require this kind of information from prospective employees? Why or why not?**

   Note: By bringing up coercion, you can connect this to the ethical consideration of respect for persons.

e. **If airlines refuse to hire someone with retinitis pigmentosa, is this unfair discrimination? Why or why not?**

   Note: This links back to the ethical consideration of fairness.

f. **Compare and contrast the current case with the following:**

   Should an airline company be able to require prospective employees to have a routine vision test (including peripheral vision)? If prospective employees do not pass this test, the company plans to not hire them. Additionally, the company will conduct annual vision tests of all employees. Failure to pass means that the person's contract will not be renewed.

   Note: In this case, the motivation is more about safety than economic benefit for the airline company.

g. **Should an airline company be able to require prospective employees to have a drug test for a substance such as marijuana? If the test comes back positive, the company plans not to hire or train the prospective pilot.**

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