

Ethical, Legal, and Social Implications (ELSI) Of Genetic Information

A resident asks...

Why would a primary care doctor want to know about the ethical, legal and social implications (ELSI) of genetic information?

Key Points:

Genetic information, like other medical information:

- has the power to help or harm patients and must be considered in making patient care decisions.
- is complex, and communication of risks and uncertainties must be attended to thoughtfully and critically.
- will arise in your practice. It is helpful to think through how you will respond in the face of inevitable questions, some of them involving difficult judgments.

In addition, genetic information, unlike much of medicine:

- provides information about family members and relatives. Disclosure of family information can often be helpful to family members but also can lead to breaches of confidentiality that must be considered and addressed proactively.

Learning Objectives for the Ethical, Legal, and Social Implications (ELSI) Module

Participants will be able to:

- Recognize that ELSI issues are integrated into, not separate from, all medical care.
- Know that family members are affected by genetic testing and screening decisions.
- Understand how disease labels can help some patients and cause psychological harm for others.
- Know that while ELSI issues are highlighted in genetic cases, similar issues are present throughout medicine. Physicians can draw on their expertise in primary care practice in addressing genetics issues and, conversely, bring an awareness to primary care that is heightened by working with genetic cases.

CASE #1

Mrs. M seeks advice about getting BRCA1 gene test. She is 45 years old and generally healthy. Her mother, Mrs. G, was diagnosed with ovarian cancer last year. As part of a research study, the mother was found to carry a BRCA1 mutation conferring increased risk for breast and ovarian cancer. The mother's sister (the patient's maternal aunt) died of breast cancer at age 48 and in retrospect is assumed to have had the same BRCA1 mutation.

The patient's sister has now undergone testing and found that she also carries the BRCA1 mutation; she is considering prophylactic oophorectomy and mastectomy, and she has urged her sister to be tested. Mrs. M is uneasy about being tested. She wonders if there is an alternative.

The resident is not sure what to say. After discussing the case with you, the resident goes back in the room and asks the patient more about her concerns re: testing. Mrs. M states that she thinks a positive test result will make her think about cancer all the time. She is also worried about losing her health insurance. Mrs. M states that she is healthy, has mammograms annually and performs breast self-exams regularly. She had a hysterectomy last year for dysfunctional uterine bleeding. Her surgery was performed about a month after her mother's diagnosis and, because of the diagnosis and the patient's age, her ovaries were removed as well. She is a little shocked that her sister's doctor suggested prophylactic mastectomy and that her sister is considering it. She states that she is not interested in a prophylactic mastectomy.

Question for Discussion:

1. What are the pros and cons of testing for Mrs. M?

CASE # 1 - Discussion

1. What are the pros and cons of testing for Mrs. M?

The pros and cons of testing are strongly influenced by Mrs. M's preferences and expectations. For this reason, it is important for the resident to explore with Mrs. M her thinking about the testing. This discussion also helps to identify additional information the patient may need to make a decision about testing. It is important that the resident creates an atmosphere in which the patient can honestly assess her reasoning and associated emotions. It is also important the resident not convey that there is a **right** decision for this question.

There are two potential benefits of testing. If the test is negative in the face of her mother's positive test (a 50% chance), Mrs. M may have the relief of knowing she has not inherited the high cancer risk present in her family. If the test is positive, Mrs. M might benefit from more aggressive prevention strategies. She has clearly rejected prophylactic mastectomy but might consider tamoxifen or other yet to be identified interventions (see the **Breast Cancer Module** for more discussion of her prevention options). For example, she might be a candidate for research trials such as a current multi-center study on MRI screening for high risk women. The patient might benefit from more information about such possibilities (including the information that they could be pursued without testing). As to harms, Mrs. M has already articulated a major harm of testing: she perceives that a positive test result would lead to breast cancer worry. While the 50% chance of a negative test might offer relief, she still may not choose to be tested, given her concern about a positive test result. Mrs. M's concern also speaks to the issue of labeling.

Labeling can occur in both genetic and non-genetic diagnoses. While being identified as at risk for a disease is not the same as being diagnosed with the disease, the effect of the risk label on an individual's self-perception could be similar. The individual might start thinking of herself as a "genetic time bomb" and wonder when, rather than if, the disease will occur. The individual might view herself as a "mutant," or not "normal." Knowing that she has a genetic predisposition might make her more likely to pursue other risk reduction strategies more actively. Or, it might make her feel that disease is inevitable and that other risk reduction is

worthless. Others (friends, family members, physicians) might also have different expectations of the individual given her risk status. This kind of effect has been seen in patients with elevated cholesterol, who sometimes think of themselves as having heart disease rather than a risk for it. Some studies suggest that when the risk predictor is genetic the condition may be viewed as being more likely and less susceptible to modification.

Anxiety and depression are also potential reactions to labeling, whether genetic or non-genetic. As Mrs. M's concern suggests, one cannot assume that because no disease condition has been diagnosed – only some degree of future risk – there is reduced worry. Another, less obvious, negative psychological reaction is survivor guilt on the part of individuals in a family who test negative for a deleterious mutation and feel guilty, responsible and unsure of how to act in regard to their own good fortune and their relative's misfortune.

Mrs. M has also expressed concern about losing her health insurance. If she receives health insurance through a large group plan based on her or her husband's employer (as most Americans do), she is unlikely to lose her health insurance as the result of a genetic test. However, this concern cannot be routinely dismissed. Genetic information, like other risk information, is potentially of interest to insurers providing individually rated or small group plans. Many states have passed legislation intending to prevent the use of genetic test results, and efforts to create federal legislation are also on-going, reflecting a societal consensus that characterizes such practice as unfair discrimination. (However, few laws prevent insurers' use of family history information in individual rating.) These laws have not yet been tested in the courts, and the potential for health insurance discrimination remains problematic for those having individual or small business health insurance (a minority of the insureds). Genetic information may also be of interest to life and disability insurers; few state laws address the use of genetic information for these insurance products.

In summary, Mrs. M has expressed two important personal arguments against testing: concerns that a positive test result will increase her worry and that it will potentially threaten her health insurance. Equally important, she has already had an oophorectomy and is uninterested in a prophylactic mastectomy. All other available risk reduction strategies – including aggressive

breast cancer screening and consideration of tamoxifen – are available to her without genetic testing.

For women in Mrs. M's situation, testing is an option but not an "indicated" procedure. In Mrs. M's case, she has made it clear that she does not want testing. The most important goal of the counseling discussion is to ensure that she has considered all aspects of the testing opportunity to her satisfaction in making this decision.

CASE #2

A resident presents a 35-year-old man with a 5-year history of intermittent abdominal pain consistent with irritable bowel syndrome. In the course of a full examination, small testes are noted. On questioning, the patient notes low sex-drive. Initial work-up reveals a low testosterone level; further work-up includes a chromosomal study that indicates the patient has a 47,XXY karyotype (Klinefelter's). He has an appointment to discuss his results.

He teaches mathematics in middle school. He lives with his wife and son.

Questions for Discussion:

1. What advice would you give the resident to help in the discussion of the diagnosis with the patient?
2. What are the benefits and burdens of labeling to consider?

CASE # 2 - Discussion

1. *What advice would you give the resident to help in the discussion of the diagnosis with the patient?*

As the resident discusses the diagnosis, he is doing more than informing the patient of a medical condition and the appropriate treatment. All diagnoses carry with them other social, cultural and psychological meanings as filtered through the patient's viewpoint and health model. The resident must simultaneously assess the medical information to be conveyed, the patient's baseline perspective and comprehension of the new information, the psychosocial implications of the diagnosis for the patient, and the support systems the patient has. The visit should attempt to establish or continue a strong patient-doctor relationship, because the patient's understanding is likely to be an ongoing process that cannot be addressed in one visit.

While the diagnosis is new, the patient has had this condition all his life. If the diagnosis feels overwhelming, it may be helpful for the patient to put the diagnosis in that context. Patients often go through different phases of reaction and incorporation of new diagnoses; what is positive to the patient at one stage may become negative at another. Over time, the resident can help the patient gain a perspective on his disease.

For many patients, the idea of a genetic diagnosis often has powerful associations with inferiority. Patients may feel shame or guilt upon hearing a genetic diagnosis, and self-stigmatization can occur. This concern is often raised in the context of genetics, but may be of equal concern when a non-genetic diagnosis is made – e.g. cancer, diabetes or HIV. In this case, a patient with the diagnosis of Klinefelter's might wonder if he is "not truly a man." On the other hand, providing a diagnosis for previously mysterious signs and symptoms can be very reassuring. Some diagnoses, including Klinefelter's, can indicate the need for specific treatment (in this case, testosterone), or make a patient eligible for certain services and support groups.

2. *What are the benefits and burdens of labeling to consider?*

For this patient, the diagnosis of Klinefelter’s syndrome came as a relief. His diminished sex-drive had caused tension in his marriage. The diagnosis provided a basis for treatment with testosterone, which led to improved sex drive and sense of well-being. The diagnosis also led to a social issue with important and sensitive implications. The fact that 95% of people with Klinefelter’s are infertile raises doubt about the paternity of his child. However, raising the question of his likely infertility could be painful and disruptive. Further it would be difficult to disprove that he is his son’s biological father, short of a formal paternity analysis – a procedure not likely to be in the family’s best interests. While it is appropriate for him to know that most men with Klinefelter’s syndrome are infertile, further exploration of the topic should perhaps follow the patient’s initiative. Like many other conversations between patient and physician, this discussion will benefit from sensitivity and established trust.

Genetic labeling often involves both benefits and burdens (see **Table 1**). The balance between these is often highly subjective.

Table 1
Benefits and Burdens of Disease Labeling

Benefit	Burden
Understanding	Stigmatization
Specific management or prevention options	Discrimination
Access to services	Helplessness

CASE # 3

A 35-year-old man is diagnosed with medullary carcinoma of the thyroid and undergoes a successful resection. He has no family history of thyroid cancer, pheochromocytoma or other endocrine abnormalities. He is an only child; his father died at age 32 in an automobile accident, and his mother is in good health at age 67. Given the early age at which his cancer occurred, he is tested for mutations in the RET gene and found to have a mutation associated with Multiple Endocrine Neoplasia Type 2 (MEN2). He is counseled about autosomal dominant inheritance and the risk to future children. He asks whether a child already born would be at risk, because he has a 10-year-old son, with whom he has not been in contact for many years.

Based on the counseling he receives, he calls the mother of his child to let her know of their son's 50% risk to inherit the RET mutation and the recommendation that the child be tested. She tells him she doesn't ever want to hear from him again and hangs up. He notes that they parted under bad circumstances (he was drinking heavily) and asks his primary care provider to contact her to explain the need for follow-up for his son. The resident wants to know how to proceed.

Questions for Discussion:

1. Is testing of the patient's son recommended?
2. If so, what role should the resident play in helping this patient get the information to the child's mother?

CASE # 3 - Discussion

1. Is testing of the patient's son recommended?

The American Society of Human Genetics -American College of Medical Genetics

(ASHG/ACMG) recommends against testing children unless there are medical indications:

“If the medical or psychosocial benefits of a genetic test will not accrue until adulthood, as in the case of carrier status or adult-onset diseases, genetic testing generally should be deferred. . . The stigmatization and deleterious effects on self-image are great and should only be risked when medical benefit is possible. Although sympathetic to the considerable difficulties inherent in living with uncertainty about the health status of the child, the Task Force does not feel that these warrant foreclosing the child’s right to make an independent decision in regard to testing in adulthood.”

However, childhood testing is recommended if a genetic test is associated with high penetrance, the disease may occur during childhood, and there is an intervention to prevent the disease that must occur during childhood.

This statement of principle is at the center of the ethical issues raised by this case. The stringent criteria for testing in childhood are met in this case. Medullary carcinoma of the thyroid can occur in early childhood in MEN2, and prophylactic thyroidectomy is usually recommended by age 5. Uncontrolled clinical studies support this approach (see **GeneClinics** summary: <http://www.geneclinics.org>). For families who are unwilling to consent to prophylactic thyroidectomy, periodic screening (for evidence of C-cell hyperplasia) is an alternate approach. Thus, specific preventive actions are available to monitor a child carrying an MEN2 mutation.

2. *If so, what role should the resident play in helping this patient get the information to the child's mother?*

This question raises the physician's duty to disclose information to a family member. The American Society of Human Genetics has published a position statement on this issue (Knoppers et al. 1998). This document suggests that disclosure should be permissible under exceptional circumstances when:

- attempts to encourage disclosure on the part of the patient have failed
- harm is highly likely, serious, imminent and foreseeable
- at-risk relatives are identifiable
- disease is preventable, or medically accepted standards for treatment or screening are available
- the harm from failing to disclose outweighs the harm from disclosure

(see Knoppers et al. 1998 for detailed discussion of these issues).

When genetic risk is identified, genetic professionals typically encourage family members to share information with others who may benefit from testing. In the case of MEN2, risk to children is usually discussed as part of the initial counseling (as occurred in this case) and follow-up testing is arranged as part of care for the family as a whole. Here, because of the estrangement between the parents, the father cannot participate in ensuring his son's care. However, he has given the provider permission to contact his son's mother to ensure care for his son. This point is important, because current privacy regulations require a patient's explicit permission before medical information is shared. In this circumstance, it is permissible for the provider to contact the mother directly.

Privacy regulations underscore the provider's obligation to maintain the confidentiality of medical information. However, if the information represents a significant, imminent and remediable threat to another's person's health, the provider may need to consider whether s/he has a duty to contact the person at risk (or in the case of a minor, as here, the minor's guardian or legal representative), in the absence of explicit permission. This is similar to cases in which a patient makes a serious threat to injure another identifiable person, in which the provider is

obligated to inform the person at risk (see discussion in Knoppers et al. 1998). Most cases of genetic risk provide less clear-cut evidence of imminent risk. Finding the correct balance between the obligation to disclose and the obligation to maintain patient confidentiality may be difficult, and it may be appropriate to seek legal counsel if this conflict arises.

CASE #4:

A resident presents a 42-year-old woman who has come for an annual exam. The resident has performed routine health maintenance, including a pelvic examination with Pap test and a clinician breast exam; a dT booster has been ordered. The patient is a non-smoker, drinks minimal alcohol, and has no known family history of breast, colorectal or ovarian cancer. Her father has heart disease at age 70 and she reports no other family history of concern. She notes that her brother is an alcoholic. Her exam is normal.

The resident is troubled because she has received a phone call from the patient's brother prior to the visit, asking her to work the patient up for Charcot-Marie-Tooth disease (CMT). The brother states that he is worried about his sister because he has seen her stumble many times and thinks she has the disease, which also affects him and their father. He has tried to talk with his sister about it and she has refused to discuss it. He does not want the resident to mention that he has called. He also asks that the resident inform him of the patient's status so that he can take whatever measures are necessary to ensure that she is protected from complications of her neurological disease.

The resident has reviewed information about CMT disease on the **GeneClinics** website. She understands that this is an autosomal dominant disorder resulting in peripheral neuropathy. Thus, the brother's history (if reliable) would indicate that the patient has a 50% risk to inherit the condition. In the absence of physical findings, and with conflicting history from the patient and her brother, the resident is unsure how to proceed.

Question for Discussion:

1. What ELSI concerns are raised by this situation?

CASE #4 - Discussion

1. What ethical concerns are raised by this situation?

The patient is apparently unaware of her father's and brother's diagnosis. The history from the brother may be unreliable, but CMT would be an unusual diagnosis to provide in a fabricated medical history.

Physicians are obligated to respect the confidentiality of medical information. However, in this case, the resident has obtained information with potential consequences for her patient from an outside source. The provider of the information (the patient's brother) has requested that his call not be disclosed; but his call is not protected by medical confidentiality. As a result, whether or not to disclose the call is a matter of physician discretion. Among the issues the resident should consider are: preserving family relations, whether or not knowing about the call will foster or hinder trust from her patient, and whether the source of the information is especially germane to the case. Will it help or hurt the patient's care or the doctor-patient relationship to disclose the call? On the one hand, disclosing the call could provide the basis for a discussion of CMT and family members who are reported to be affected. This discussion could be helpful in assessing the patient's knowledge and attitudes toward her potential risk. It might also provide further insights about the patient's family. On the other hand, the patient might react with anger to the information that her brother called, and her brother can be expected to feel anger if his call is revealed. At minimum, the information provided by the brother's call should be evaluated for its contribution to the patient's care and well-being.

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