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Ethics Rounds: Please test my child for a cancer gene. But don't tell her

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Abstract

A 38 year old woman is diagnosed with Li-Fraumeni syndrome, an autosomal dominant genetic condition that predisposes to a variety of cancers. The woman has an 11-year-old daughter named Karen. The geneticist recommends that the child be tested for the Li-Fraumeni genetic variant. The mother is very concerned about the impact of testing and diagnosis on Karen's psychological well-being. She describes Karen as "highly strung" and as "a worrier." The child has been diagnosed with an anxiety disorder, and is followed by a psychologist for counseling. The child is otherwise well. The mother requests that testing be done without disclosing it to the child by adding the test on to routine blood work done for another reason and the results only revealed if they are positive. Experts in genetics, law, and bioethics discuss whether it is permissible to test the child without her knowledge or assent.

TOC image

A mother requests that her 11-year-old daughter be secretly testing for Li Fraumeni syndrome and only told of the testing if the results are positive.

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Introduction

Genetic testing for autosomal dominant conditions raises many ethical questions. Studies of adults who face decisions about testing for Huntington's disease show that most at-risk adults do not get tested.[1,2] Uptake of testing for genes that pre-dispose to cancer is higher,[3,4] but many adults who are at risk for cancer do not get recommended tests. Some people seem to prefer living with uncertainty over getting test results that may be perceived as depressing. How do we apply these data from adults to children? Professional societies discourage predictive testing for adult onset conditions for which there are no necessary or effective interventions during childhood.[5] That's the easy one (and even that is not so easy. Many parents want such tests. But, at least, one can argue that not testing does no harm, and allows the decision to be deferred until the child has become an adult and can decide for herself.) But what if a genetic test can diagnose a condition that puts the child at risk during childhood, and there is some intervention that can lower the risk. That is the case with Li Fraumeni Syndrome. In such cases, there is a compelling ethical case to be made for testing. It is clearly in the child's best interest. But what happens if the parents do not want such testing, or want testing without telling the child? This month's ethics rounds addresses this situation.

The Case

A 38 year old woman is diagnosed with Li-Fraumeni syndrome, a genetic condition that predisposes to a variety of cancers. Since this condition is transmitted in an autosomal-dominant fashion, the geneticist is discussing testing of family members with her. This includes testing for the woman's siblings, and for her 11 year old daughter, Karen. Karen has a 50% chance of having the same genetic mutation.[1] Li-Fraumeni syndrome carries a cancer risk of 50% by age 30 and 90% by age 60. For age specific cancers, the risk is estimated at 42% for ages 0–16 years, and 38% at ages 17–45 years. There is a significant difference between the genders with Li-Fraumeni syndrome; females have a 100% lifetime risk of cancer while males have a 72% risk.[6] The mother has agreed to screening for herself.

During a conversation with the mother at which the 11 year old Karen is not present, the geneticist recommends that the child be tested for the Li-Fraumeni genetic variant, and shares the above information with the girl's mother. If the test is positive, the geneticist recommends that the child have close surveillance for early cancer diagnosis and management. The recommended screening would follow a protocol that appears to decrease mortality and improve outcomes according to two studies:[78] abdomen and pelvis ultrasound every 3–4 months, urinalysis every 3–4 months, blood testing every 4 months, annual brain MRI, and annual rapid total body MRI. In addition, from age 18, a breast cancer screening program will be offered.

The mother is very concerned about the impact of testing and diagnosis on Karen's psychological well-being. She describes Karen as "highly strung" and as "a worrier." When Karen had a chest X-ray done a year ago for an unrelated matter, Karen apparently ruminated about what is wrong with her. Even though the X-ray was normal, the child kept worrying about illness and the X-ray findings for weeks afterward. The child has been

diagnosed with an anxiety disorder, and is followed by a psychologist for counseling. The child is otherwise well. Despite the geneticist's assurance that information will be shared in an age-appropriate manner, and psychological support will be provided, the mother remains uncertain.

The mother eventually requests that testing be done without disclosing it to Karen. She says this can be done either through adding the test on to routine blood work for another reason at some point in future, or through inventing a reason why Karen needs routine blood work. If the test is negative, Karen can then be spared all the stress of having to discuss the diagnosis and the reason for the test. If the test is positive, the test and result can be disclosed, and she will then consent to a screening program. If the testing cannot be done in this way, and has to be disclosed, she will refuse testing to "protect her child's childhood" and psychological well-being.

The geneticist asks for an ethics consult to help her direct her response. Should the child be tested without the child's knowledge as the mother asks? If this cannot be done, what should she do if the mother refuses testing for the child?

Johan Bester, PhD, comments

This patient is 11 years old. In such patients the general framework for decision-making is that parents have the authority to make decisions on behalf of their children, guided by the best interest standard.

Since children of this age have the cognitive ability to understand some information and participate somewhat in treatment discussions we often use a framework of seeking patient assent, while seeking permission from the parents. Respecting the personhood of the 11-year-old requires involving her in discussions and providing information to the extent that is appropriate given her level of development.

The first ethical question, then, is whether it is ever permissible to test a child secretly for a genetic condition that would, if she has it, lead to a recommendation that she undergo screening tests in the future.

There are a number of considerations to weigh.

1. The integrity of trusting relationships is an important value. One should carefully think about the effect withholding of information may have on this child's future relationships with healthcare professionals, her parents, and on her future decision-making.
2. It is not clear that the familial diagnosis and test can indefinitely be hidden from the child. Given that the mother and various family members may need to be screened in future, it seems likely that questions around Li-Fraumeni will arise in this family.
3. Transparency is an important value for healthcare professionals. Related to this is the idea of respecting patients as persons, an important and central value in healthcare ethics.

4. The question of psychological harm around genetic testing for rare cancer syndromes is important. One study has examined the rates of adverse psychological impact in patients undergoing genetic testing for Li-Fraumeni; 23% reported clinically relevant psychological distress prior to testing.[9] Insufficient social support was associated with higher risk of psychological distress. Gaining certainty about the diagnosis provided a psychological benefit and decreased distress. A positive result did not generally lead to adverse psychological complications. The presence of some pre-test distress does warrant the provision of psychological support.

How should these considerations, which would nudge one towards disclosure, be balanced against the mother's fear that the child will be harmed by knowledge that she was being tested? Although protecting the child from harm is an important ethical consideration, secret genetic testing creates more ethical problems than it solves. Secretive testing compromises the values of transparency and respect for persons, undermines trust, and potentially compromises important clinical and personal relationships of the child. Furthermore, there is the likelihood of the child finding out about the familial diagnosis through other means. This would expose the child to the very psychological harms that the mother is seeking to prevent through non-disclosure.

A better approach would be to offer the child information and psychological support in an age-appropriate manner. This may involve working with the child's psychologist to deal with the child's possible distress as well as laying the groundwork for ongoing psychological support in the event of a positive diagnosis.

A second question would arise if, after disclosure, the child refuses testing. Could she be tested without her assent based on the mother's legal authority to make health care decisions for her child? Healthcare professionals should weigh the harms and benefits and come to a medical judgment of whether the interests of the child are being compromised to an unacceptable level by not being tested.

There is ongoing discussion in the literature as to whether the benefits of testing and screening program outweigh the risks.[10] Two studies have shown some benefit to screening through early diagnosis of cancers and improved long-term survival.[11,12] Though screening is intensive, many participants express a positive attitude towards the screening program.[10] This may possibly be due to an increased feeling of control over the situation, as well as the network of supportive relationships within the surveillance system.[10]

Testing and subsequent screening can also cause harms. Harms may include psychological distress and potential unnecessary testing. There is some pre-test psychological distress among those who require genetic testing genetic cancer syndromes, but this distress is generally eased by the testing process itself.[9] A 2012 systematic review finds that surveillance for most hereditary cancers is associated with normal levels of psychological distress, but those who had high risk of developing numerous tumors (such as Li-Fraumeni sufferers) have a variable degree of higher risk for psychological distress.[10] The bottom line is that that social and psychological support should be offered to these patients.[10]

In sum, it appears that the benefits of testing outweigh risks, especially if appropriate psychological support is provided. Ultimately, testing is in this child's best interest. If the mother authorizes testing, then it should be done even without the child's assent. Transparency and honesty would therefore require that the child not be given the impression that she can refuse testing during information sharing or the seeking of assent.

There are three options here that are not necessarily mutually exclusive: 1) Test the child secretly, and only tell her if she is positive for the genetic syndrome; 2) Test the child with full disclosure if the mother gives permission, even if the child does not assent; 3) Defer testing or discussion until the child is eighteen and can legally make decisions for herself. Option 1 is not ethically supportable due to reasons explored above. Option 2 appears to be the best option, given the various complex ethical values at stake. But it depends upon the mother's willingness. Option 3 resolves some of the ethical difficulties, in that it allows the child to consent over her own treatment once she becomes of age. The problem with this option is that childhood cancers that may be diagnosed and treated prior to the child's coming of age will be missed, probably compromising important interests of the child. A fourth option, if the mother refuses disclosure or testing, would be to seek a court order. But it seems likely that, with sensitive communication, that draconian solution could be avoided.

I conclude: testing is in the child's best interest, and should be done. Disclosure should accompany testing, as non-disclosure is ethically problematic. Careful communication can probably avoid the necessity of seeking a legal remedy to ensure that the right thing is done.

Maya Sabatello, LLB, PhD, comments

Parents are legally entrusted to give or refuse to give consent for their child's genetic testing. Nevertheless, clinicians, scholars, and policy makers recommend that older children and adolescents be involved in making decisions relating to their healthcare.[13] Such an approach is believed to strengthen the clinician/pediatric-patient relationship and improve children's compliance with their treatment plan. It also recognizes the child as a moral agent and acknowledges children's growing maturity and cognitive abilities for medical decision-making before age 18. With regard to children ages 7–14 years like Karen, the American Academy of Pediatrics' (AAP) stated policy is that the presumption of decision-making incapacity is rebuttable and that assent tailored to the individual child should be sought, unless the intervention is medically essential.[13]

The geneticist's starting point that Karen—an 11 year-old—should be told about (but not necessarily be asked to assent to) genetic testing is consistent with ethical and policy guidelines if the testing is medically necessary. Here, the test is undeniably medically appropriate. An LFS-positive test means that Karen would be at high-risk for childhood specific cancers. If she is positive, and then follows the proposed screening plan for these cancers, her risk of dying will decrease. Her mother is committed to sharing results with Karen, if they are positive. This would make screening possible. However, Karen's individualized risk and, importantly, the level of genetic risk that translates into a medically necessary intervention—an inherently subjective decision—must first be determined. If the mother (and other relatives) did not have LFS-related cancer during childhood, Karen's risk of developing cancer during her childhood, even if she is LFS-positive, would likely be

lower than it is for the general pediatric LFS-population. In that case, testing is unlikely to qualify as medically necessary. Karen's assent should thus be sought or the testing should be postponed until Karen can decide for herself.

Conversely, if the family history indicates early onset of LFS-related cancer, Karen's risk may be significantly higher than it is for her LFS-positive peers. In this case, testing could qualify as medically necessary. Karen's assent will thus not be required, although in most circumstances, she should be told that she is being tested.[13]

In this case, however, her mother claims that the mere knowledge that she is being tested could be harmful for Karen, and she refuses testing unless it is done without Karen's knowledge. If the mother's assessment of Karen's vulnerability is correct, then the balancing of projected harms and benefits could allow for Karen's testing without her knowledge. First, the benefits of testing Karen as early as possible outweigh the harm of the initial non-disclosure, as requested by the mother. Accepting the mother's request is further less intrusive to parental autonomy and less costly than overriding her decision by a legal intervention—a time-consuming process that may fail and is likely to create tensions that risk the family's future care. Second, there are risks of informing Karen about testing. As the mother conveys, Karen has a history of exaggerated worry over a simple medical procedure of chest X-ray despite the normal results. Karen's anxiety disorder may further deteriorate once she learns about testing that may disclose a high risk and life-altering genetic mutation such as LFS. Why risk triggering her anxiety—which can take weeks or months to recover—when there is 50% chance that it would turn out to be a false alarm?

Still, the medical team should probe into the mother's anxiety-related concerns. Although parents often know their child better than anyone, studies indicate that parents commonly under-estimate their child's maturity to make medical decisions,[14] and that they view their own management of their child's genetic data as a parental right and duty.[15] Moreover, it is possible that the mother's own anxiety is projected onto her child. In studies of families with history of breast cancer or deleterious mutations of the BRCA gene, daughters age 10–19 showed more cancer-specific distress if their mothers had high levels of anxiety. Such anxiety can be relieved by better communication, not by keeping secrets.[16,17] The medical team should thus discuss with the mother options for evaluating Karen's mental state either in-person, by a pediatrician-mental health professional, or through a consultation with Karen's primary pediatrician and treating psychologist, without her presence. Such a consultation might alleviate the mother's concerns and persuade her to rethink her preferred approach to testing Karen. Alternatively, it might confirm her concerns, which would then justify waiving Karen's knowledge prior to testing on the basis of the risks of triggering anxiety.

How should the testing be done without Karen's knowledge? The mother suggests "adding the test on to routine blood work for another reason" or "inventing a reason why Karen needs routine blood work." Although both options would achieve the medical goal of genetic testing, the latter should be rejected. LFS requires life-long surveillance and treatment, and if Karen is LFS-positive, establishing a trust-based relationship with the treating team will be key for her continuing care. Deception—which Karen will realize had

occurred once told about the results—will likely undermine this trust and be counter-productive for her medical care. Conversely, “looping” the testing with other routine blood work, assuming it is done soon, preserves the trust and accomplishes the medical goal. It also follows current practice. Children undergoing lab testing are not normally provided with a list of conditions they are being screened for but only explained in general terms that the procedure is needed to better inform the doctor about their health. There is no overwhelming moral reason why Karen needs to be told more details of her LFS-screening than she would about tests for iron deficiency or cholesterol levels.

Regardless, an intervention to support the family’s genomic communication is urgently needed. We don’t know whether Karen has already had any LFS conversations, experienced familial cancer-related distress, or if she knows about preventative interventions. However, both mother and Karen would benefit from genetic education and increased psychosocial supports to better understand the implications of familial LFS mutation and to care for themselves—as a family and as individuals—including, as necessary, by following the screening regime and adopting health practices known to reduce risk for cancer, e.g., exercise and healthy eating. (Indeed, Karen should be told also about LFS-negative results: once her mother develops LFS-related cancers, Karen’s anxiety could be triggered if she believes she inherited it.) Thus, child-appropriate and tailored discussions should take place *regardless* of Karen’s LFS-status. Those could take place before or after she is tested, whether she is told about the testing ahead of time or not. Such discussions are the best way to protect Karen’s wellbeing.

Clara D.M. van Karnebeek, MD PhD comments

In my profession as a pediatrician and geneticist, the Ottawa Declaration of the World Medical Association concerning child health is central to my view on making decisions for children; this declaration stipulates in its general principles that “the best interests of the child shall be the primary consideration in the provision of health care”.[1] At the same time the notion of the best interest of the child, guided by the principles of harm avoidance and doing good,[2] raises the question of the criteria used to assess this best interest.

Kopelman[18] has noted that in the absence of an objective determination of what is in the best interest of the child, the parental position, provided that it does not clearly place the child in danger, should be considered, as parents act *a priori* to ensure the well-being of their children.[19]

Against this background, the issues in this case become clear. One must ask whether there is an objective way to determine what is in the best interest of the child. Will this child, who is clearly at risk, benefit from pre-symptomatic screening for Li-Fraumeni syndrome? Five years ago,[20] the answer was likely different than today: In 2016, Savage et al published an 11-year follow-up prospective observational study in which they reported that pre-symptomatic screening for cancer in individuals with molecularly confirmed Li-Fraumeni syndrome led to higher survival rates. The difference (88·8% vs 59·6%; p=0·0132) was striking.[21] So far, no other studies have confirmed this benefit.

The decision for testing remains a dilemma however, because there is significant unpredictability in symptomatology among children with a molecular diagnosis. This likely reflects variable penetrance and expressivity. Furthermore, we lack of a cure for many of the cancers which an individual with Fraumeni syndrome may go on to develop.[22] This challenging situation is reflected in the relatively low adult uptake of pre-symptomatic testing for this condition.

The current ethical question is however not whether pre-symptomatic minor testing should be offered to the family. It is whether or not to honor mom's request to perform the testing in secret, i.e. without her daughter knowing. The mother's intention is good. She wants to protect her "highly strung" daughter's childhood. It is understandable that mom does not want her daughter to worry even more. But perhaps her 11-daughter has picked up more than mom realizes and is actually aware of -and fretting about- her own risk for cancer given mom's diagnosis of Li-Fraumeni syndrome. This situation may well be the reason that the daughter was so anxious about the X-ray. In this sense, the daughter's unperturbed experience of 'childhood' may not actually exist anymore. Explaining this to mom and reiterating that straightforwardness, i.e. informed consent with age-appropriate counseling, is likely the better option on the short and long-term, may be useful. Such an approach will respect the child's autonomy and will instill further trust in mother.

For females with Li-Fraumeni, there is a 100% lifetime risk of developing cancer. If the daughter tests positive, this knowledge will be a huge burden, especially at such a young age. Unfortunately, her Mother cannot prevent the anxieties her daughter might experience if she were diagnosed with Li-Fraumeni syndrome.

But what if she tests negative? If Li Fraumeni syndrome is ruled out, it would be a great relief for the mother. Can and should mother withhold the knowledge of testing from her daughter? After all chances are 50/50 that things will work out for the best. A secretly done negative test will relieve the mother and not upset the daughter.

We could play out another scenario. Suppose the pediatrician refuses to order secret testing. Suppose, then, that the mother then decides not to have her daughter tested. What should the clinical geneticist do then? My answer would be to keep the door open to mom and to offer her a second opinion, an interaction with another geneticist. In these situations, multiple consultations may be useful. The mother's wishes may evolve over time as the child grows older, mom's own medical situation changes, and science yields novel insights and diagnostic and therapeutic possibilities, such as with personalized onco-genomics.[23]

Clear-cut solutions to such ethical conundrums seldomly exist, and certainly our opinions and considerations are never static. The principle of "do no harm" remains unchanged as a guiding light for ethical decision-making. Ongoing research on the factors that influence decisions making with regard to genetic testing of minors may help. We don't always know the right answers. But, with research, we might be able to improve our ethical sensitivities and come up with better decisions more often.

John D. Lantos comments

In some ways, genetic testing is just like any other testing. We decide whether a test will give results that might change management and, if so, then we generally order to the test. Through newborn screening programs, we test all newborns for a variety of conditions. In routine well-baby care, we do other tests on a routine basis, tests ranging from periodic measurements of height, weight, and blood pressure to tests looking for anemia or developmental delays. With the advent of genomic testing, and, in particular, exome sequencing, we can now test children for thousands of conditions. But genetic test results are unique. They usually reveal a propensity for disease, rather than disease itself. Furthermore, in many cases, we don't know how precise they are. Sometimes, they indicate an increased risk for developing a disease, but that risk might be very slight. Thus, the process of deciding which tests ought to be done, which results returned to parents (or teens), and which follow-up screening tests should be done is quite complex and individualistic.

In this case, the doctors and parents both agreed that the test should be done. They disagreed about whether the patient should be told that the test was being done. It would be best for the patient to be told. But it would be tragic if the testing wasn't done at all. Seeking a court order seems like a draconian overreaction in this case. I would try as hard as I could to convince the mother that disclosure and transparency are the best policy here. But if I could not, and the choices were to not do the test, to do it without disclosure, or to seek a court order for testing, I would do the test without disclosure. My justification: With any of these choices, there will be bad psychological sequelae. But I'm not sure which would be worse. So I'd defer to the mother's judgment, after I'd informed her of my recommendations and reasons.

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Abbreviations

LFS Li Fraumani Syndrome

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