

## Pharmacogenetic testing for patients being treated with anticoagulants

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Draft key questions: comment and response

*January 26, 2018*

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**Pharmacogenetic Testing for Patients Being  
Treated with Anticoagulants**

**Draft Key Questions  
Comment and Response**

**Provided by:**

**Center for Evidence-based Policy  
Oregon Health & Science University**



*January 26, 2018*



## Responses to public comment on draft key questions

*The Center for Evidence-based Policy is an independent vendor contracted to produce evidence assessment reports for the Washington Health Technology Assessment (HTA) program. For transparency, all comments received during the public comment periods are included in this response document. Comments related to program decisions, process, or other matters not pertaining to the evidence report are acknowledged through inclusion only.*

*Draft key question document comments received:*

- Henry Mead

Specific responses pertaining to comments are shown in Table 1.

**Table 1. Responses to comments on Draft key questions for Pharmacogenetic testing for patients being treated with anticoagulants**

Comments		Response
<b>Commenter: Henry Mead</b>		
	<b>Specific comments:</b>	
<b>Key Question 1</b>	<p>There are three forms of genetic testing: diagnostic, carrier, and predictive testing. Diagnostic testing involves identifying current disease states. This includes prenatal and newborn screening—the most common forms of genetic testing. Carrier testing determines whether an individual carries a certain genetic trait. Each person’s genetic traits are comprised of two chromosomes: one inherited from his/her mother and one from his/her father. If a genetic disorder is dominant, the disease characteristics will be expressed when a person has one abnormal chromosome. If a genetic disorder is recessive, the disease characteristics are present when the individual has two abnormal chromosomes. If the disorder is X-linked, the disease characteristics will be present in males. The third type of genetic testing, predictive testing, is used to determine whether a person has a genetic mutation that will lead to a late onset disorder. Implicit in the effectiveness question is the reliability and validity of the tests being considered. Without adequate population based evidence any or all of these genetic tests may lead to high rates of false positive or false negative results which may have important implications for clinical utility and for patient treatment decisions.</p>	<p>Thank you for your comments.</p> <p>This information is useful background, but is not specific to the scope of this topic.</p>
<b>Key Question 2</b>	<p>Genetic discrimination has moral and ethical implications. The notion that genetic testing is different from testing for other disorders is termed “genetic exceptionalism.” Genetic information is private and is directly related to an individual’s identity. Not only is confidentiality an issue for health care, insurance coverage, and employment, but information from a genetic test can affect an entire family. If the disorder is either genetically dominant or carried by an individual, that person’s parents, children, brothers, sisters, and even extended family may also be affected. Furthermore, a person may make life altering decisions based on the results of a genetic test. Disclosure of genetic test results can be critical in all aspects of an individual’s life.</p> <p>Once a genetic disorder is discovered, the question then arises as to who should counsel the patient and/or family, and how the patient and/or family should be counselled. Additionally, what is the responsibility for disclosure? A key question then becomes when and by whom should family members be informed of the (predictive) test results. What</p>	<p>Thank you for your comments.</p> <p>This information is useful background for most forms of genetic testing. However, the comments are not specific to the scope of this topic.</p>

Comments		Response
<b>Commenter: Henry Mead</b>		
	<b>Specific comments:</b>	
	are the moral obligations of the patient and the physician? Should someone diagnosed with a genetic disorder or variant that influences risk or pharmacokinetic characteristics inform his/her family they may be at risk?	





## Pharmacogenetic testing for patients being treated with anticoagulants

### Key Questions

#### **1. Effectiveness: What is the clinical utility of genetic testing to inform treatment decisions for patients being treated with anticoagulants?**

There are three forms of genetic testing: diagnostic, carrier, and predictive testing. Diagnostic testing involves identifying current disease states. This includes prenatal and newborn screening—the most common forms of genetic testing. Carrier testing determines whether an individual carries a certain genetic trait. Each person's genetic traits are comprised of two chromosomes: one inherited from his/her mother and one from his/her father. If a genetic disorder is dominant, the disease characteristics will be expressed when a person has one abnormal chromosome. If a genetic disorder is recessive, the disease characteristics are present when the individual has two abnormal chromosomes. If the disorder is X-linked, the disease characteristics will be present in males. The third type of genetic testing, predictive testing, is used to determine whether a person has a genetic mutation that will lead to a late onset disorder. Implicit in the effectiveness question is the reliability and validity of the tests being considered. Without adequate population based evidence any or all of these genetic tests may lead to high rates of false positive or false negative results which may have important implications for clinical utility and for patient treatment decisions.

- a. Do treatment decisions guided by genetic testing result in clinically meaningful improvements in important patient outcomes (e.g., death and stroke) or reductions in adverse events (e.g., bleeding) compared with usual care without genetic testing?
- b. Does genetic testing to inform the selection or dose of medications change the drug or dosage selected by prescribers or patients compared with usual care without genetic testing?

#### **2. Harms: What direct harms are associated with conducting genetic testing when it is used to inform the selection or dosage of oral anticoagulant medication?**

Genetic discrimination has moral and ethical implications. The notion that genetic testing is different from testing for other disorders is termed “genetic exceptionalism”. Genetic information is private and is directly related to an individual's identity. Not only is confidentiality an issue for health care, insurance coverage, and employment, but information from a genetic test can affect an entire family. If the disorder is either genetically dominant or carried by an individual, that person's parents, children, brothers, sisters, and even extended family may also be affected. Furthermore, a person may make life altering decisions based on the results of a genetic test. Disclosure of genetic test results can be critical in all aspects of an individual's life.

Once a genetic disorder is discovered, the question then arises as to who should counsel the patient and/or family, and how the patient and/or family should be counselled. Additionally, what is the responsibility for disclosure? A key question then becomes when and by whom should family members be informed of the (predictive) test results. What are the moral obligations of the patient and the physician? Should someone diagnosed with a genetic disorder or variant that influences risk or pharmacokinetic characteristics inform his/her family they may be at risk?

3. Special populations: Compared with usual care without genetic testing, do important patient outcomes or harms after genetic testing vary by:

a. Patient characteristics (e.g., age, sex, race/ethnicity)?

b. Clinical history (e.g., medical comorbidities, underlying condition requiring anticoagulation, severity of illness, concurrent medication use, whether treatment decision is initial or subsequent)?

4. What are the cost-effectiveness and other economic outcomes of genetic testing used to inform the selection or dosage of oral anticoagulant medication?