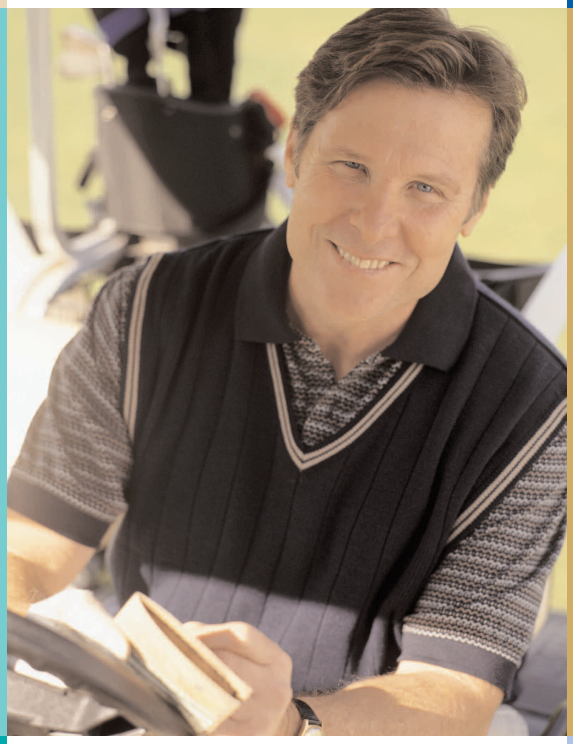
RESULTS *for* LIFE
LAB TESTING: BETTER HEALTH, IMPROVED OUTCOMES



Lab Tests and Personalized Medicine: It's All About You

Genetic tests make diagnosis and treatment as individualized as disease itself.

"Frankly, when I heard 'leukemia,' I thought I was out of luck…in my mind, leukemia meant death."

Patients with cancer, heart disease, HIV, and other conditions are living longer and enjoying better health because of a medical revolution called personalized medicine. At its center are genetic tests that identify the unique genetic profile of individual patients or their disease and allow physicians to tailor treatment to those unique characteristics.

The result is earlier diagnosis and treatment, better prevention, and better-targeted therapy with fewer side-effects. Using the guidance from genetic tests, physicians can prescribe the right drug, at the right time, at the right dose.

The effect of personalized medicine is being felt today, across a range of conditions.

- ✓ A **test for overabundance of the HER2 protein** in breast cancer patients has permitted better-targeting of therapies—and a dramatic improvement in survival rates.
- ✓ A **test that identifies whether a patient is especially sensitive to a drug that prevents blood clots** could eliminate as

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A Virtual Case Study

Back in the Swing

On his way to the golf course, Jeff found out that he had leukemia.

Actually, the doctor had asked him to stop by to go over the results of his recent blood tests. And while Jeff sat there, listening to the doctor tell him about the new genetic tests and treatments for leukemia, Jeff could only think about his best friend in sixth grade, Bobby, who died of leukemia in what seemed a matter of weeks.

"Frankly, when I heard 'leukemia,' I thought I was out of luck," said Jeff. "In my mind, leukemia meant death."

But Jeff learned quickly that things had changed over the past 30 years. While the initial blood tests suggested leukemia, Jeff's doctor also ordered two genetic tests to examine the DNA of the leukemia cells themselves. These tests showed re-arrangement in two chromosomes that created a unique protein which, in turn, produced excessive white blood cells. The disease was called chronic myelogenous leukemia (CML)—very common in the 40-60 age group.

"The doctor said that the genetic tests could identify this out-of-control protein—whatever that is—and that the new type of drugs could switch it off," said Jeff. "That's when I started feeling some hope."

With two girls in private school and a son in college, Jeff had to keep up his busy work schedule, which he was able to do

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many as 17,000 strokes per year and reduce health costs by as much as $1 billion annually.

- ✓ **Tests that read the DNA structure** of the most common form of leukemia in children have helped boost the 10-year survival rate from four percent in the 1960's to more than 80 percent today.
- ✓ **Diagnostic tests that check the genetic code** of an individual's HIV virus and guide physicians in selecting the most appropriate treatment have helped transform HIV from an almost certain death-sentence to a manageable chronic disease.

But the real hope is for the future—and not just the distant future—with very promising genetic and molecular tests in development that could lead to earlier diagnosis and more effective treatment for lung, ovarian, prostate, and other cancers, as well as heart disease, and other chronic diseases.

Back in the Swing CONTINUED FROM PAGE 1

with the course of treatment his doctor chose. That was once-a-day medication, along with frequent testing to monitor progress. When, after six months, the tests showed that the cancer-causing protein was still more active than the doctor preferred, he increased Jeff's dosage—and continued close tabs on progress with regular genetic tests.

Within a year, the doctor called Jeff and asked him to stop by again when he had a moment. "The leukemia is in total remission," said the doctor, to Jeff's great relief. But the doctor added that Jeff wasn't that unusual. With the combination of genetic tests that identify the problem protein and the medication that targets it, 90 percent of patients with CML respond favorably, and many experience complete remission.

When Jeff left the doctor's office, he decided to play a round of golf to celebrate. "When I walked out of there, I kept thinking about my sixth-grade buddy, Bobby," said Jeff. "And about how fast life changes."

Neither Jeff nor Bobby are real people, but the facts and information presented here depict accurately the role of lab tests in leukemia and the circumstances faced by many patients.

Genetic tests facilitate personalized medicine at various stages of diagnosis and treatment. By identifying a patient's genetic profile, genetic tests help...

Predict	Screen	Diagnose	Select treatment	Manage
Determine if a currently asymptomatic person will develop a specific disease in the future	Test a larger population to identify individuals likely to be at high risk for a specific disease	Determine if the individual actually has a specific disease	Select treatment most appropriate for a person with a specific disease	Monitor progress and adjust treatment

Personalized Medicine: A New Approach to Staying Well

"Today, we are witnessing a revolution in the understanding of health and disease, spurred on by the sequencing of the human genome and the subsequent creation of a map of human genetic variation. And, like most historic movements, this revolution has been given a name: personalized medicine."

Francis S. Collins, Director of the National Human Genome Research Institute, National Institutes of Health, in the *Boston Globe*, July 17, 2005

Personalized Medicine is Not Just About Tomorrow's Possibilities, it is Changing Treatment Today...

Condition	Problem	Personalized Medicine Approach	Result
Selecting the specific medication that will best treat the disease...			
Breast cancer	Overabundance of HER2 protein on the surface of breast cancer tumors prompts excessive cell growth	Genetic test measures HER2, identifying patients who will benefit from a drug that inhibits its growth	Significant improvement in survival rate. Reduces cancer spread by 50%
HIV	Viral genetic variations make the HIV virus resistant to some anti-retroviral drugs	Tests determine the genetic makeup and rapid mutation of an individual's virus and pinpoint most effective drug	Dramatic improvement in quality, length of life. Patients can now live for decades
Cardiovascular disease	Genetic variations in the ability to metabolize warfarin, a common blood-thinning drug, often lead to clotting or bleeding	Genetic tests identify the variation	Allows more precise and individualized dosing. Broad use could reduce strokes by 17,000, costs by $1 billion annually
Colon cancer	Due to a gene variation, patients experience life-threatening side-effects from certain colon cancer drugs	Genetic test identifies the variation	Allows physicians to choose other drugs to address cancer
Predicting the risk of disease before symptoms occur, allowing earlier treatment...			
Breast cancer, ovarian cancer	Variations in the BRCA1 and BRCA2 genes increase risks for breast and ovarian cancer	Genetic test identifies the variation	Allows preventive measures, such as closer monitoring and preventive surgery
Colon cancer (Lynch syndrome)	A gene mutation in one of several genes increases the risk for hereditary colon cancer	Genetic tests identify the variation	Allows early and regular screening to enable early detection and treatment
Blood clotting	Individuals with a variation in the Factor V gene and other genes have five times greater risk of developing blood clots	Genetic test can identify unique variation that increases risk	Allows preventive strategies and medication to manage clotting
Heart disease	Gene variations increase susceptibility to heart disease and heart attack	Gene tests identify the gene variation	Lets physicians increase the dosage of statin drugs, thus significantly reducing risk of heart attack and coronary heart disease
Melanoma	Gene variation leads to up to 40% of hereditary melanoma cases	Test identifies increased susceptibility to melanoma	Allows preventive steps such as surgery on suspicious lesions, less exposure to sun
Emphysema	Gene variation increases likelihood of liver disease in patients with emphysema	Genetic test identifies the variation	Allows diagnosis without biopsy; early identification also enables preventive actions

Condition	Problem	Personalized Medicine Approach	Result
Diagnosing the disease more precisely, leading to more effective treatment...			
Childhood leukemia	Various genetic subtypes of the most common form of childhood leukemia make "one-size-fits-all" treatment ineffective	Gene tests identify subtypes. Enables physicians to choose drugs and treatment protocols that are geared to the specific genetic subtype	Today's cure-rate for children exceeds 80% vs. 4% in the 1960's
Adult leukemia	Chromosomal changes create an abnormal protein that increases white blood cells	A genetic test detects the abnormal protein, which can then be treated with a genomics-based drug that slows its growth	Better response rates, less toxicity, complete remission in many patients. Five-year survival rate increased from 69% in 2001 to 89% today
Cervical cancer	Certain high-risk strains of the Human Papilloma Virus (HPV), which causes cervical cancer, are difficult to identify	Genetic test identifies the high-risk strains of the HPV	Allows earlier decisions about treatment and frequency of follow-up monitoring
Managing the disease more effectively with better information...			
Breast cancer	The traditional treatment following surgery for early stage breast cancer is chemotherapy, but it may provide little or no additional benefit to many women	Gene tests measure the specific genetic activity in the tumor itself. This information can be used to quantify the likelihood of cancer recurrence—and the likely need for chemotherapy	Provides more information for physicians and patients to decide whether the benefits of chemotherapy outweigh the side-effects and cost
Cancer	Chemotherapy is often prescribed once cancer has progressed beyond the early, localized stage—yet cancer patients do not respond to chemotherapy 70% of the time	Functional genetic tests can identify with extremely high accuracy those drugs to which the patient's cancer is resistant	Helps in prescribing the most effective treatment, sparing patients unneeded toxicity and saving valuable treatment time
Hereditary hemochromatosis	Hereditary gene variation causes the body to absorb excess iron, leading to liver failure, heart failure, and diabetes	Gene test identifies the variant	Replaces liver biopsy as the first-line confirmatory test for most patients; alerts family members to need for monitoring, preventive therapy
Metabolizing medications	Gene variations can mean an individual absorbs drugs too slowly or too quickly—leading to "too little" or "too much" of the drug	A molecular test detects the group of enzymes that influence metabolism of about half of all drugs	Allows physicians to make more precise, individualized dosing decisions
Screening to determine if the disease is present...			
Sexually transmitted diseases, hepatitis	Older testing methods, including culturing the bacteria or virus, could take days for results	Genetic tests identify these conditions in hours, rather than days	Enables rapid intervention and treatment
Staph infections	A rapidly-morphing group of bacteria—called Methicillin-Resistant Staphylococcus Aureus—is resistant to drugs	A genetic test can identify this form of staph infection rapidly	Helps detect and stop costly, dangerous infections that patients acquire in the hospital

Better Care from Personalized Medicine Comes in Many Different Forms...

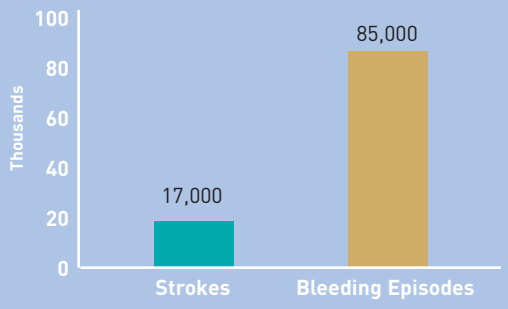
Fewer complications in treating cardiovascular disease

A genetic test that identifies whether a patient is especially sensitive to warfarin—a frequently prescribed drug that prevents blood clots—is saving lives and reducing drug complications. That's because the test identifies the genetic differences among patients in how their bodies process the medication. This allows physicians to be more precise in prescribing a dosage that is most appropriate for each individual. As a result, patients are less likely to suffer from underdoses, which can cause strokes, or from overdoses, which can lead to serious bleeding episodes.

One study concluded that widespread use of the tests would allow the U.S. to...

- Avoid 17,000 strokes annually
- Avoid 85,000 serious bleeding episodes annually
- Save up to $1 billion annually

Broad use of a genetic test in prescribing blood-thinning drug could avoid...



Source: AEI-Brookings Joint Center for Regulatory Studies, 2006

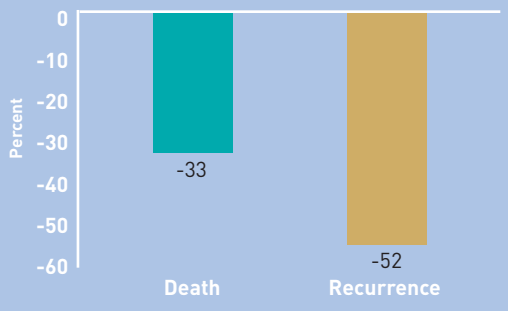
More effective treatment for breast cancer

A genetic test can now tell women with breast cancer whether their tumor bears an overabundance of what is called HER2, a protein which promotes excessive growth of cancer cells. For these women—who usually do not benefit from standard treatments—physicians can prescribe a gene-based drug that will bind to the protein and deactivate it. As a result, these women can avoid excessive treatments that have little effect and benefit from the treatment that fits the exact genetic nature of their illness.

This form of cancer has been one of the most deadly. But studies show that this targeted approach...

- Reduces risk of death by 33 percent
- Reduces risk of recurrence by 52 percent

Genetic tests and therapy lead to dramatic reductions in risk of death and recurrence...

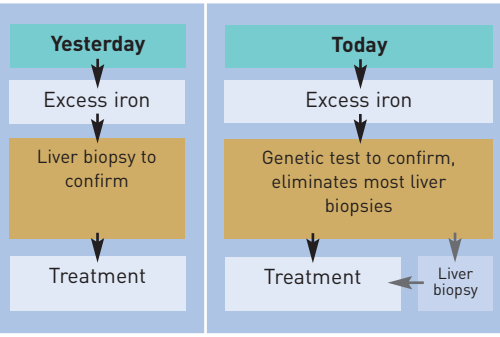


Sources: *New England Journal of Medicine*, 2005; *BMC Cancer*, 2007

Less invasive diagnosis for hereditary hemochromatosis

A genetic test can identify individuals with a gene variation that allows the body to absorb too much iron—a problem that can lead to liver failure, heart failure, and diabetes. In the past, when physicians suspected the disease in a patient, the only option to confirm the diagnosis was a liver biopsy, an invasive and painful procedure.

Today, the genetic test is used instead of liver biopsy as a first-line confirmation, thereby eliminating the need for liver biopsy in most cases. Because the disease is hereditary, the test can also be used with family members to permit preventive treatment—and to reduce their need for liver biopsy as well.



Sources: *New England Journal of Medicine*, 2004; *Annals of Internal Medicine*, 2003

How are They Regulated?

Consumers should look for genetic tests that have been developed under a system of federal or state regulation or oversight by accrediting bodies. Likewise, they should be wary of tests or treatments that have no independent overview. Here is a snapshot of the regulatory environment for genetic tests.

Federal	**Food and Drug Administration**	• Reviews genetic testing medical devices before they go to market • Regulates manufacturing methods • Conducts surveillance of medical devices after they are marketed • Regulates product labeling • Requires independent validation of device performance
	Centers for Medicare and Medicaid Services	Requires all clinical laboratories that perform genetic tests to meet quality standards to ensure accuracy, reliability, and timeliness of tests.
State		Regulation varies by state, with some states maintaining oversight of tests and laboratories. State rules affect when to test, which test to use, whom should be tested, and what actions should be taken following test results.
Accrediting bodies		Independent accrediting organizations accredit labs, develop standards and guidelines, advance best practices and proficiency tests, and promote education to improve care.

Sources: U.S. Department of Health and Human Services, "Personalized Health Care: Opportunities, Pathways, Resources," 2007; "U.S. System of Oversight of Genetic Testing," Report of SACGHS, 2008; "Clinical Laboratory Improvement Amendments," Brochure 2008

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