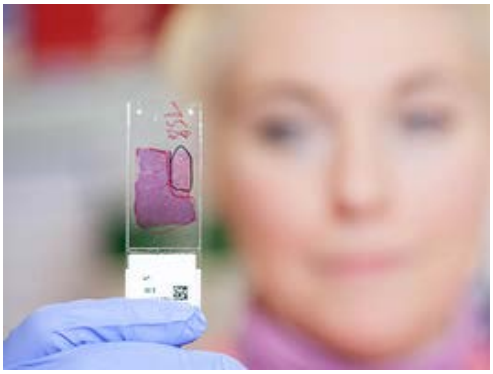
Personalized Healthcare

Molecular testing improves outcomes and reduces healthcare costs by personalizing treatments to each individual patient based on genomic insights.



Patients often react differently to drugs, even apart from factors such as age or weight. An effective treatment for one person may not work for someone else, or may cause adverse reactions. The main cause of this variation is the inherent diversity of our genetic makeup. Understanding individual differences in the human genome can help physicians select and tailor treatments – the right drug at the right time for the right patient. This is the foundation of Personalized Healthcare.

Personalized Healthcare draws on pharmacogenomics – the study of how a person's genetic makeup affects the body's response to drugs – to enable development of new therapeutics and to help doctors customize treatments to achieve the best possible results. Instead of a trial-and-error approach, physicians can use each patient's genomic information to choose the most effective medication with the fewest side effects. For example, companion diagnostics are now routinely used to assess potential benefits of targeted therapies in many types of cancer patients.

The key to Personalized Healthcare is the close connection between therapeutics and diagnostics. Personalized Healthcare benefits both the patient and society as a whole, enabling more effective treatments and more efficient use of resources in healthcare systems.

Economic and Social Effects

Billions of dollars are spent each year on prescriptions for drugs and other therapies that turn out to be ineffective or even harmful to particular individuals. In the United States, studies have shown that the most frequently prescribed medications show the desired effect in fewer than 60% of patients.[1]

Examples of drugs' efficacy rates

Drugs for treatment of:	Ineffective in % of patients:
Depression	38%
Asthma	40%
Diabetes	43%
Arthritis	50%
Alzheimer's	70%
Cancer	75%

Source: Brian B. Spear, Margo Heath-Chiozzi, Jeffrey Juff, "Clinical Trends in Molecular Medicine," Volume 7, Issue 5, 1. May 2001, pp. 201-204.

Without significant improvements in the ability to target the right treatment to the most appropriate patients, these adverse effects are likely to intensify and become more frequent in an aging population, with treatment costs rising as a result. The number of complications and deaths associated with medicines has already seen a significant increase since mid-1990.[2] Personalized Healthcare helps overcome these challenges by maximizing the efficacy and safety of therapies. With the market poised for sustainable growth, McKinsey & Co. expects the global volume of companion diagnostics to exceed $8 billion by 2018.[3]

Views on Personalized Healthcare

Personalized Healthcare is already a reality. The genomic knowledge base is constantly growing, and the essential techniques in molecular diagnostics are readily available. The U.S. Food and Drug Administration (FDA) has identified diagnostic biomarkers for about 160[4] existing drugs that target a variety of diseases and has approved more than 20 companion diagnostics.[5] Given the significant benefits of personalized healthcare, this number is expected to grow.

- Oncology: The detection of mutations in genes such as KRAS, EGFR, JAK2 or BRAF helps to predict how patients suffering from various malignancies respond to specific therapies. Many new cancer therapies offer great promise, but they are very costly and only effective in patients who either have or lack a specific gene mutation. In the case of colorectal cancer, where therapy with so-called monoclonal antibodies can cost up to $60,000 per treatment cycle, only patients without mutations (approx. 60% of the patient population) in the KRAS gene are likely to benefit from the targeted medication. Many biomarkers can also help to guide treatments of other cancers such as lung, pancreatic, brain, thyroid, leukemia, etc.
- Tissue typing: In tissue transplants (such as bone marrow), donors are linked to recipients who offer the best genetic match – thus reducing the risk of an adverse immune response.

In addition to medical and economic demands, the growing use of Personalized Healthcare is driven by the economics of pharmaceutical R&D. By understanding and optimizing the risk-benefit profile of drugs for specific types of patients, Personalized Healthcare can improve the development of new therapeutics. The challenges in drug development include:

- Cost of development: On average, developing a new drug costs about $1.2[6] billion and is associated with significant risks. Using molecular tests, pharmaceutical companies can design more efficient clinical trials and increase the likelihood of approval of new drugs.
- Compensation costs: Unexpected adverse side effects also pose high legal risks, even if cause and effect are not proven. For instance, in the case of Merck's painkiller Vioxx, victims were awarded damages of $253 million.
- Loss of value: The withdrawal of Vioxx caused a drop in the manufacturer's share price that exceeded the turnover of the entire diagnostics industry. Such events also damage company reputations.
- Product life cycle: By combining drugs with genetic tests pharmaceutical companies can expand the indications of drugs following initial approval and thus enhance their life cycle.
- Second chance: Many drug candidates fail in a late development stage or during the approval process because their efficacy and safety cannot be proven across large, diverse patient groups. Some of these "fallen angels" can still be approved for treatment of individual patient groups with a specific genetic makeup.
- Pricing: As the efficacy of drugs rise, pharmaceutical companies can change existing price models. Herceptin®, for example, adds more than $5 billion to Roche's sales[7].

While Personalized Healthcare is already a reality, several challenges have to be addressed:

- Regulatory obligations: In some countries it can take up to 15 years to obtain governmental approval for new diagnostics or drugs. This discourages companies from developing new treatments for small population groups. Nevertheless, regulatory bodies such as the FDA are increasingly integrating genetic testing into pharmaceutical product labels. To date, the FDA

has included biomarker information in labels of about 160 drugs. A guideline for the development of companion diagnostics is now also available from the FDA.

- Doctors' behavior: Many physicians lack sufficient knowledge about Personalized Healthcare and therefore continue with traditional treatments.
- Healthcare system: Opposing interests in the healthcare and political systems delay decisions regarding best practice and reimbursement – and thus the introduction of innovations. Often, the lag in reimbursement policies and systems encourages the treatment of diseases rather than their prevention through the early use of diagnostics. However, as healthcare costs in developed nations are predicted to grow to 20% of GDP by 2020, personalized healthcare represents an increasingly attractive way to reduce costs by eliminating ineffective treatments. Take KRAS, for example: Studies[8] show that more than $600 million could be saved annually in the U.S. alone by using companion diagnostics to guide certain colorectal cancer treatments.
- Reimbursement policies: Often, reimbursement levels for new diagnostics are based on technical aspects of the diagnostic method and don't reflect the clinical value of a test. Decision making is too slow and is non-transparent. This hampers necessary investments in the development of novel diagnostic tests. However, there is a shift in thinking to value-based reimbursement of diagnostics among some health payers.
- Biomarker research: Personalized therapies rely upon biomarkers that are indicative for certain physical conditions or processes and allow for the personalization of treatment strategies. Given the enormous complexity and scope of molecular information in the human body, the identification and validation of biomarkers continues to pose significant challenges to biomedical research.

QIAGEN and Personalized Healthcare

With a broad offering of Sample to Insight solutions, QIAGEN is a global leader in Personalized Healthcare. The company's existing portfolio and development pipeline of companion diagnostics and biomarker research assays is unmatched, covering multiple sample types and detection technologies.
QIAGEN is also a pioneer in minimally invasive liquid biopsy methods for companion diagnostics in Europe. Amid the explosion of genomic data from next-generation sequencing, QIAGEN is the industry's leader in bioinformatics to interpret complex biological data and provide actionable insights for clinical decision support.

- With about 15 collaborations and over 30 projects with pharmaceutical companies, QIAGEN is developing and offering more companion diagnostics than any other company. Partnerships include collaborations with Amgen, Array BioPharma, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, Novartis and many others.
- QIAGEN's test portfolio for personalized healthcare applications covers a broad range of biomarkers. The product offering includes regulatory approved assays for oncogenes such as KRAS and EGFR.
- With leading technologies for extraction and processing of nucleic acids from body fluids, QIAGEN is pioneering the development of companion diagnostics based on minimally invasive liquid biopsies. In Europe, QIAGEN markets the first companion diagnostic for a cancer drug based on this technology.-

the *therascreen* EGFR Plasma RGQ PCR Kit paired with IRESSA from AstraZeneca. Together with Tokai Pharmaceuticals, QIAGEN is developing a companion diagnostic for treatment of castration-resistant prostate cancer (CRPC) based on QIAGEN's proprietary AdnaGen technology for the analysis circulating tumor cells (CTCs).

- QIAGEN's bioinformatics solutions allow users to generate valuable molecular insights from highly complex genomic data. QIAGEN Clinical Insight, a clinical decision support system tailored for the needs of clinical labs, was launched in 2015.
- QIAGEN offers a broad range of technology platforms for development of companion diagnostics, including real-time PCR, Pyrosequencing, next-generation sequencing and the multimodal Modaplex platform, which can process multiple sample types and biomarkers in a single test.

[1] Harvard Business Review, October 2007.
[2] WirtschaftsWoche, Oktober 2014, http://www.wiwo.de/technologie/forschung/leiden-auf-rezept-krank-durch-medikamente-seite-all/10831808-all.html
[3] McKinsey & Company, Personalized Medicine – the path forward, March 2013.
[4] FDA, http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm May 2015
[5] FDA, www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm301431.htm, October 2015.
[6] Phrma, www.phrma.org/sites/default/files/159/phrma_industry_profile.pdf, January 2013.
[7] Roche, www.roche.com/irp120201_full.pdf, January 2013.
[8] Genomic Health Website, Economic Validity, www.oncotypedx.com, April 2009.