

Precision
Medicine



Precision Medicine

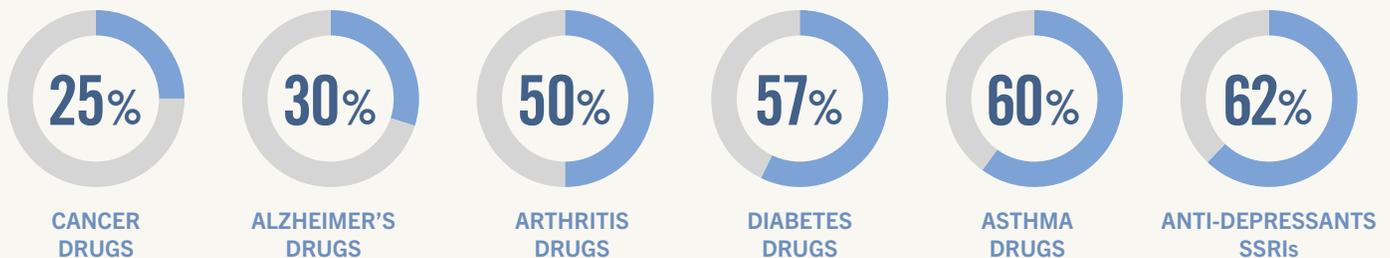
A PROMISING FUTURE FOR
PATIENT OUTCOMES

Precision medicine has the potential to provide a tailored approach to care, for improved patient outcomes and lower costs

The National Institutes of Health defines precision medicine as an “emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person.”¹

This type of personalized medicine—with targeted treatment and prevention plans—has the potential to improve early disease detection and prevent progression, while improving healthcare efficiency, quality, access, and affordability.² The “one-size-fits-all” approach to treatment can be ineffective and expensive.³ By understanding which patients are likely to benefit from a specific treatment intervention, outcomes may often be improved while lowering costs and reducing side effects.²

RESPONSE RATES OF DRUGS IN SELECT THERAPEUTIC AREAS³



Five key areas of precision medicine have been identified as particularly promising.⁴



DIAGNOSIS/ PROGNOSIS

to evaluate certain subtypes of a disease or the distinctive characteristics of a health condition



TREATMENT PREDICTION

to determine whether a patient, infection, or tumor with certain characteristics may respond to a specific treatment



DOSING

to analyze the appropriate amounts or strengths of treatment to give to a certain individual



SAFETY

to anticipate adverse events and reactions in certain subpopulations of patients



MONITORING

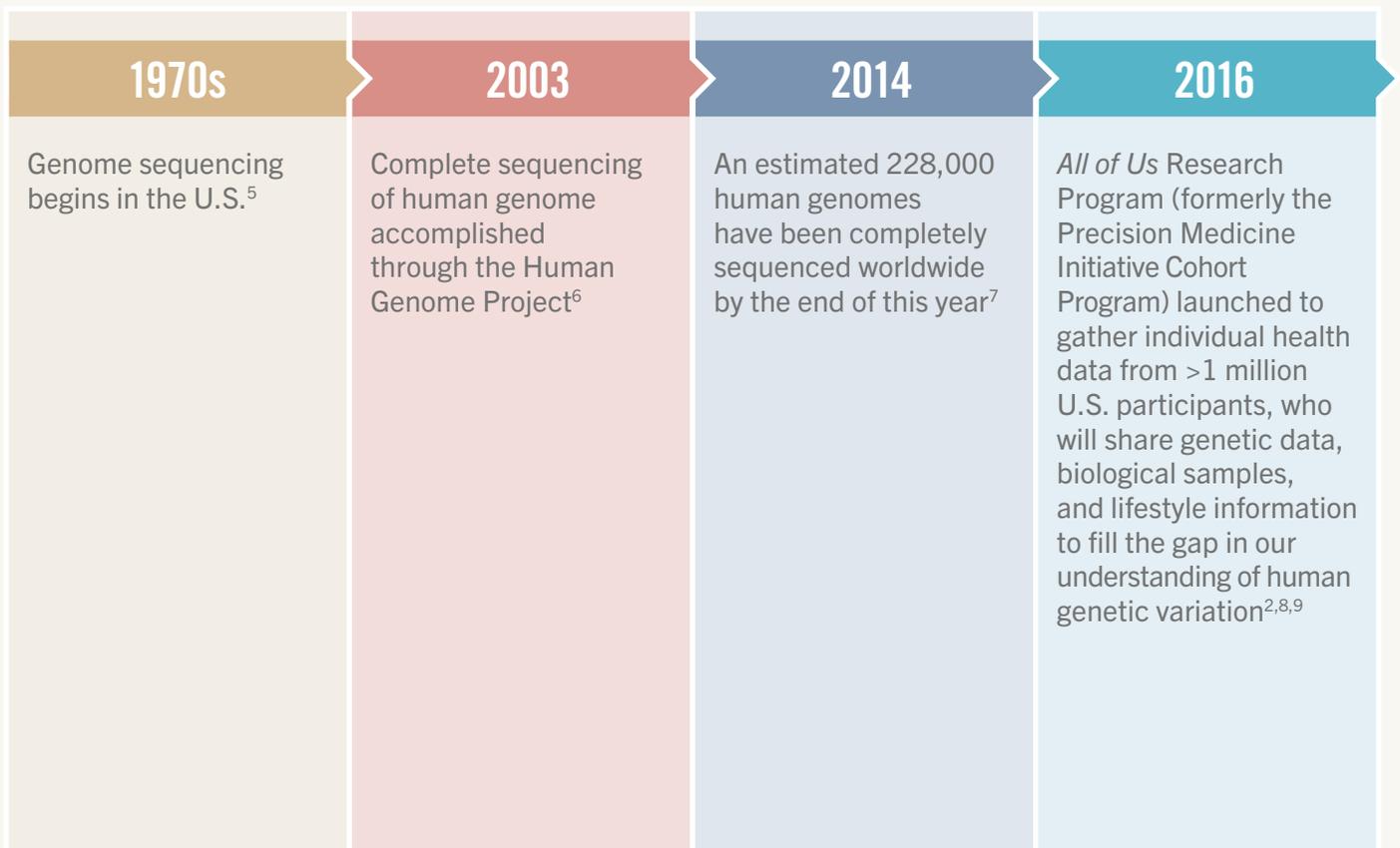
to track and observe a patient's response to treatment, partly to assess if any modifications to treatment may be necessary

Precision medicine allows physicians and researchers to more accurately predict which drugs, treatment, and prevention strategies for a disease may work best in certain subpopulations, avoiding costly trial-and-error methods.^{1,2}

Genome sequencing, the cornerstone of precision medicine, continues to advance

Sequencing of the human genome has greatly accelerated the process of linking specific gene variants with disease, which is likely to expand as sequencing plays a larger role in healthcare and delivery of the appropriate and most efficacious treatments.

TECHNOLOGICAL INNOVATION IS SPEEDING GENOMIC SEQUENCING FORWARD



Clinical diagnostics and biomarkers help identify appropriate treatment options, but challenges remain

Research & development pipelines embrace precision medicine

With the rise of precision medicine, diagnostic and biomarker tests are identifying appropriate treatments and drug therapies for individual patients earlier in the disease course. The focus on precision medicine in product development pipelines is also expanding, indicating a growing commitment to precision medicine in the biopharmaceutical industry.

As of 2016, 132 personalized medicines with specific biomarkers included in product labeling were on the market.²

The FDA has approved 29 companion diagnostic tests that are required for the use of certain cancer treatments. Other complementary diagnostics can aid in the risk-benefit decision making regarding the use of a particular therapy.¹⁰

Healthcare stakeholders are navigating regulatory, coverage, and reimbursement changes

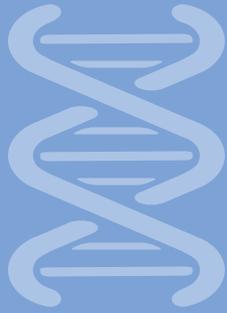
Recent trends indicate growth and uptake of precision medicine; however, regulatory and coverage challenges remain. Draft FDA guidance for the development of companion diagnostics was published in 2016, indicating motion toward adapting to new developments in precision medicine. Coverage and reimbursement challenges also exist as payers seek evidence of the clinical and economic impact of precision medicine in practice. Value-based payment models, value assessment frameworks, and payment and coding standards may all influence the adoption of precision medicine in clinical practice.²

>25%

of new FDA drug approvals in 2016 were personalized medicines.²

~40%

of drugs in the development pipeline include biomarkers in their R&D design.²



THE SCIENCE OF GENETIC AND GENOMIC TESTING AND THEIR USE IN CLINICAL PRACTICE HAS EVOLVED

Select types of molecular diagnostic tests¹¹

The identification and measurement of changes in DNA, RNA, or specific genes are accomplished using molecular tests, which analyze organisms at the molecular level. Molecular tests often focus on single genes or mutations or gene by-products, such as proteins.

Fluorescence and flow cytometry — Early measurements of DNA used ultraviolet absorption methods to identify areas of interest. Fluorescence began to be used in combination with flow cytometry methods, which suspend particles in fluid for analysis.

- Flow cytometry and molecular genomics have been integral to the diagnosis of hematologic malignancies¹²

DNA and sequencing tools — Some testing tools manipulate (cut and copy) DNA material. This allows scientists to “cut” DNA strands at specific places using enzymes and produce fragments that they can separate and reproduce.

- Next-generation sequencing (NGS) techniques are rapid and automated. This sequencing process is important in lung cancers. The identification of oncogenic drivers has redefined how these illnesses are described and treated¹³

Fluorescence in situ hybridization (FISH)

— FISH is a method of detecting mutations, deletions, and other genetic changes on chromosomes. A fluorescent tag is added to a complementary sequence of DNA or RNA that binds, or hybridizes, to a chromosome and can be seen using fluorescence microscopy.

- FISH-based testing has been in the mainstay of HER2-gene testing in breast cancer and in the selection of anti-HER2-targeted therapies¹⁴

Microarray technology, DNA amplification, and polymerase chain reaction (PCR)

— Multiple tests of DNA or RNA can now be performed at the same time using a microarray analysis platform consisting of thousands of different DNA sequences. Microarrays of DNA depend on DNA amplification by PCR, which replicates strands by many orders of magnitude for analysis.

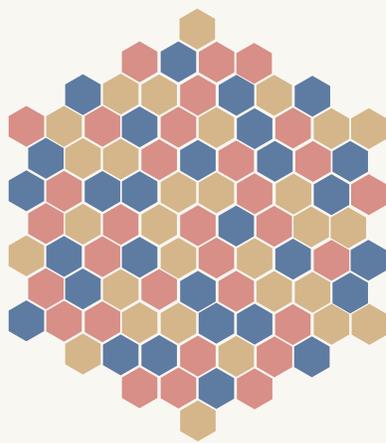
- PCR has applications in infectious disease diagnosis, and in the diagnosis and treatment planning for cancers, such as non–small-cell lung cancer¹¹

Precision medicine advances are important to the evolution of healthcare

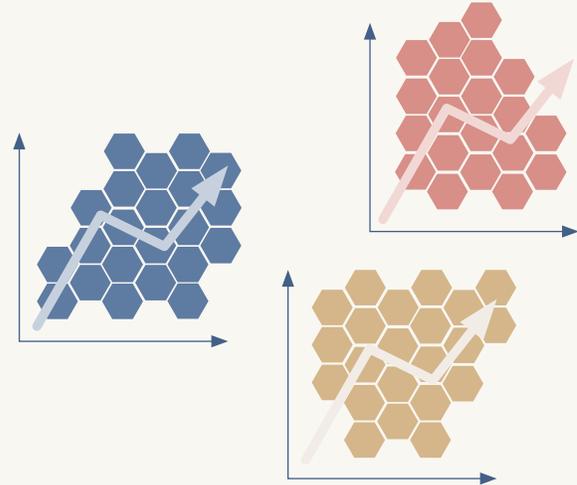
Using the power of big data to propel care forward

Breaking down broad sets of data into clusters of relevant information helps practitioners to formulate real-world insights, and identify and implement tailored treatment plans based on individual circumstances.¹⁵ Patient registries such as the *All of Us* Program support a new approach to research, where the intersection of research data, clinical data, drug data, and patient data may reveal more targeted treatment options. Beyond the advancements in genome sequencing, improved technologies for biomedical analysis and new tools for navigating expansive data sets are helping advance precision medicine.⁹

TURNING BROAD SETS OF DATA INTO CLUSTERS OF RELEVANT INFORMATION



DATA



ANALYSIS OF DATA CLUSTERS YIELDS RELEVANT INFORMATION

Evolving clinical trial designs match patients with experimental therapies

Researchers are using two types of clinical trial designs to improve the matching of genetically profiled cancer patients to beneficial experimental therapies.¹⁶ These trial designs are not without challenges — one being the difficulty in finding adequate numbers of patients with the same cancer subgroups.



Umbrella trials enroll patients with one specific tumor type, profile the tumor, and treat with different therapies (each targeting a different biomarker profile) in the same trial.



Basket trials group together patients with several different types of cancers, but with a similar biomarker profile in their tumors so they can receive a treatment that targets those molecular drivers.

New clinical trials explore the promise of precision medicine

Trials sponsored by the National Cancer Institute (NCI) are advancing precision medicine research

With support from the NCI, scientists are pursuing new technologies and collaborations, and are conducting new kinds of clinical trials to explore the promise of precision medicine. A new precision medicine strategy is being tested through genotype-to-phenotype and phenotype-to-genotype research initiatives. Genotype-to-phenotype trials screen for molecular features that may predict treatment response to a drug with a particular mechanism of action. Phenotype-to-genotype trials use retrospective genotype analysis of a patient's tumor to discover if molecular factors may explain why the patient responded well to a particular treatment.¹⁷

Funded in part by the Precision Medicine Initiative, the NCI-supported precision medicine trials include the Lung-MAP, ALCHEMIST, NCI-MPACT, and NCI-MATCH studies. The NCI-MATCH (Molecular Analysis for Therapy Choice) study is unique in assigning adult patients to targeted treatments based on the genetic abnormalities in their tumor, regardless of cancer type.^{17,18} The expanded availability of tumor sequencing through commercial vendors has given patients broader access to information about clinical trials, in turn allowing NCI-MATCH to access thousands of patients who would not otherwise be available for screening and enrollment. These developments have increased participation in the rare variant arms of clinical trials.¹⁷

Genentech is committed to bringing innovation to clinical trial design

Genentech is implementing innovative clinical trial designs that aim to bring individualized medicine to each patient by simultaneously¹⁹:

- Testing a single drug in multiple diseases
- Testing several drugs against a single disease
- Condensing the traditional 3-phase clinical trial into a fluid, adaptive process

Spotlight on innovation and partnerships to advance cancer treatment¹⁹

Flatiron Health was founded on the premise of leveraging big data to help researchers discover more effective therapies and better match cancer patients with life-saving treatments. The company recognized that much of the collected real-world data were stored across thousands of disconnected care settings such as medical centers, hospitals, and community clinics.²⁰ Through its OncoCloud™ platform, Flatiron captures real-world data from cancer patients who are *not* in clinical trials, transforming previously unstructured data into validated data in a registry.

The focus on precision medicine is increasing across various stakeholders

As the benefits of precision medicine are gaining traction and underlying testing costs are lowered, various healthcare stakeholders are exploring the opportunity to improve patient outcomes through this approach to care.



BIOPHARMACEUTICAL COMPANIES | R&D PIPELINE

- The number of personalized medicines has increased steadily since 2008²
- R&D investment in precision medicine is anticipated to increase by 33% in the next 5 years²
- Of the 74 new molecular entities in the Roche clinical pipeline, 30 are personalized healthcare products¹⁹



REGULATORS AND POLICY MAKERS | GUIDELINES AND APPROVALS

- A 2016 perspective highlighted the FDA's belief that "the desire to provide earlier access to highly effective drugs should encourage further use of seamless expansion-cohort trials, particularly as drugs with unprecedented levels of efficacy advance into clinical trials"²¹
- The FDA released "Principles for Codevelopment of an In Vitro Companion Diagnostic Device with a Therapeutic Product" in July 2016. This draft guidance assists therapeutic product and in vitro diagnostic device sponsors with the development process¹⁰
- May 2017 marked the first time the FDA granted accelerated approval to a cancer treatment (pembrolizumab) based on a common biomarker rather than the location in the body where the tumor originated²²



MANAGED CARE ORGANIZATIONS (MCOs) | COVERAGE

- Two-thirds of MCOs and more than 50% of specialty pharmacies identified balancing treatment standardization (i.e., guidelines and pathways) with personalization (i.e., molecular/biomarker testing) as one of the most pressing challenges in cancer care in 2016²³
- Among surveyed MCOs²³:
 - 30% restrict drug coverage to favorable/biomarker test results
 - 28% require a PA/precertification for molecular/biomarker tests
 - 24% restrict molecular/biomarker test coverage based on evidence supporting the validity and cost effectiveness of the test



HEALTHCARE PROVIDERS | CLINICAL PRACTICE

- Oncologists are increasingly turning to precision medicine to help identify appropriate treatments for their patients²³
 - 76% of oncologists rated the impact of molecular biomarker testing and NGS on patient outcomes as moderate to significant when used to identify mutations for prognosis and treatment planning
 - More than 50% of oncologists frequently discuss molecular testing with their patients



PATIENTS | TREATMENT

- Continued education of patients is needed to inform consumers about precision medicine. A 2014 survey revealed that 38% of patients had heard of precision medicine, but only 16% felt they were very informed on the subject²⁴
- Major concerns identified by patients in the survey were insurance coverage, affordability, and how collected personal information would be used²⁴
- The Personalized Medicine Coalition advocates for policies and practices for patient engagement, privacy, and data protections that ensure appropriate consent and are acceptable to patients²

The evolving healthcare environment aligns with precision medicine objectives

The shift to value-based care aligns with the goals of precision medicine: disease prevention, effective treatment, improved outcomes, and potential cost reduction.

PRECISION MEDICINE MAY HELP TO ADVANCE AND IMPROVE BOTH PATIENT HEALTH AND THE OVERALL HEALTH SYSTEM BY²:



SHIFTING FOCUS TO PREVENTION



USING A TARGETED VERSUS A TRIAL-AND-ERROR APPROACH



REDUCING ADVERSE DRUG REACTIONS



IDENTIFYING ADDITIONAL TARGETED USES FOR DRUGS



SUPPORTING INCREASED PATIENT TREATMENT ADHERENCE



DECREASING USE OF HIGH-RISK, INVASIVE TESTING



HELPING CONTROL COST OF CARE

Collective efforts across healthcare stakeholders may help advance precision medicine

The success of precision medicine is predicated on the collaboration of multiple healthcare stakeholders to pursue innovation and support the evolution of care to drive improved patient outcomes and healthcare system efficiencies.

Payer and health system organizations are exploring the use of precision medicine

Payer perspective: adapting to the rapid advancements in precision medicine

NGS-based clinical testing challenges traditional payer coverage frameworks. Many payer organizations classify NGS testing as investigational rather than medically necessary and therefore do not offer coverage. Research suggests that payer organizations may postpone evidence review of genetic and pharmacogenomic tests due to the lack of clinical study support. Oncology has been identified as a key area of growth for the clinical application of NGS and is the first area where policy solutions will be essential.²⁵

Priority Health was the first insurer in the U.S. to implement a formal coverage policy for the use of genomic profiling for members with aggressive forms of cancer. “By covering genomic profiling in specific circumstances, we can help identify alternative and potentially more effective treatment options for those diagnosed with aggressive or difficult-to-treat cancer,” said John Fox, M.D., senior medical director and associate vice president of medical affairs at Priority Health.²⁶ Its medical coverage policy outlines 7 specific criteria for coverage of NGS testing in the diagnosis and treatment of cancer.²⁷

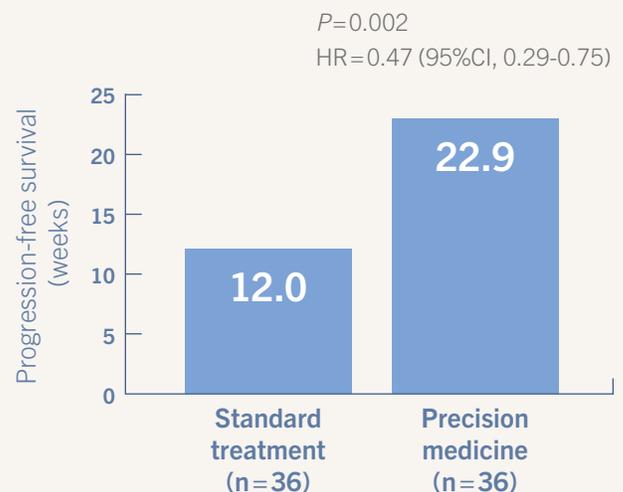
In July 2016, UnitedHealthcare released a medical policy to cover molecular profiling using NGS testing for patients with metastatic stage IV non-small cell lung cancer that met specific criteria.²⁸

NGS enables rapid review of many genes simultaneously using a single test, and it has extended the use of sequencing beyond research and into clinical practice.⁵

Case study: improved outcomes without increased healthcare costs

Intermountain Healthcare recently conducted a retrospective analysis of precision medicine outcomes within one region of its delivery system. The matched-cohort study assessed outcomes and total costs in patients with advanced, refractory cancer who underwent genomic testing and received targeted treatment in the precision medicine program compared with control patients receiving standard chemotherapy or supportive care. Patients in the precision medicine group had an average progression-free survival of 22.9 weeks versus 12.0 weeks in the control group. Costs in the 2 groups were similar, with per patient charges per progression-free survival week of \$4,665 for the precision medicine group and \$5,000 for the control group.²⁹

PRECISION MEDICINE IMPROVED OUTCOMES IN ADVANCED CANCER²⁹



What does the future hold?

The future of precision medicine may offer unprecedented opportunities to match the right patient with the right treatment, ultimately improving outcomes for many.³⁰

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