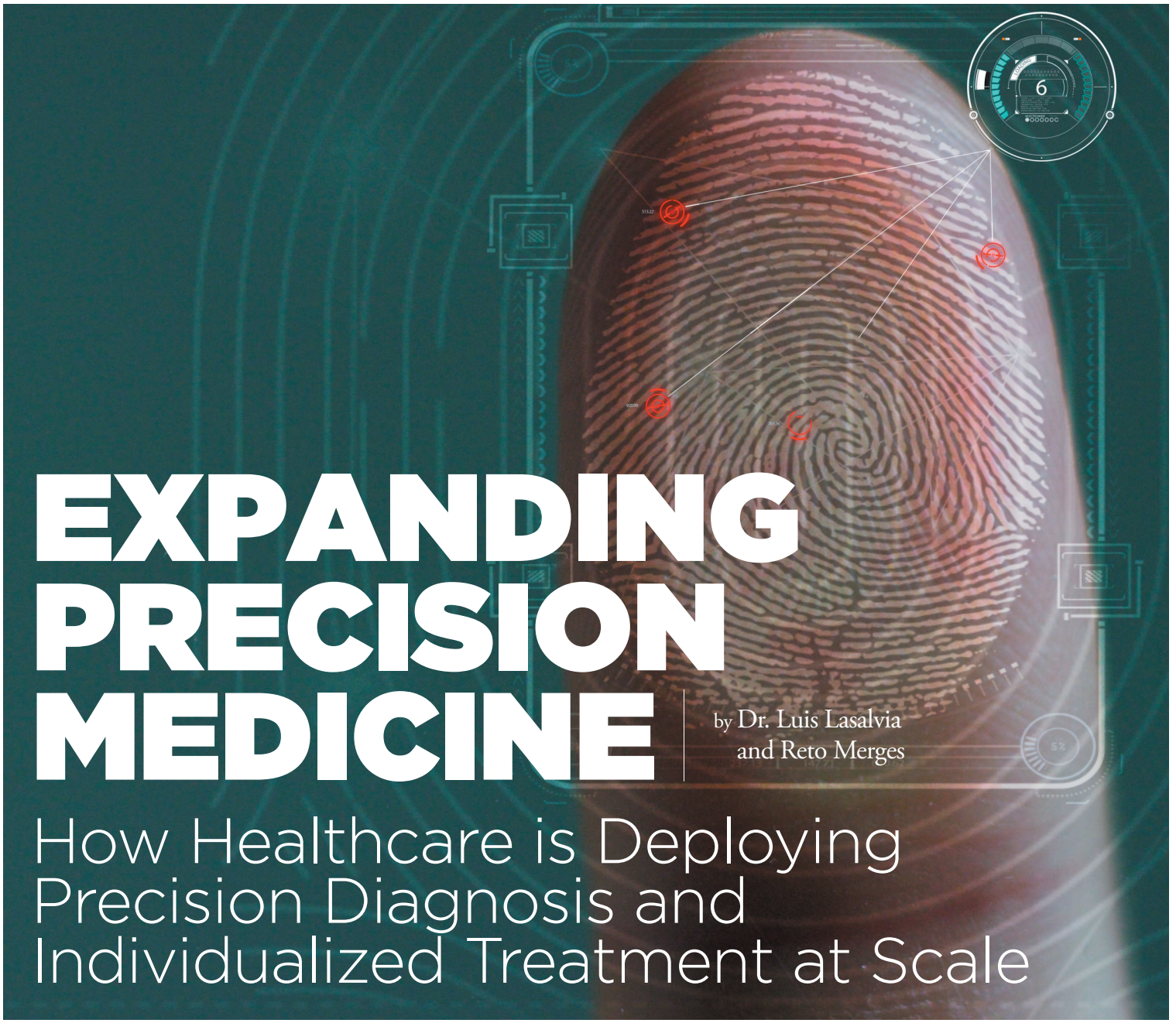


EXPANDING PRECISION MEDICINE

by Dr. Luis Lasalvia and Reto Merges

How Healthcare is Deploying Precision Diagnosis and Individualized Treatment at Scale

How is it possible to improve patient outcomes in the face of relentless pressure to contain costs? As populations continue to age and advanced therapies continue to grow more expensive, scaling up precision in medicine is a recommended approach that can help healthcare executives to add value, reduce costs and improve clinical results.

The age of precision medicine – tying pinpoint diagnoses to individualized treatment – has already begun. The trick now is to find cost-effective ways to scale up this potential game changer so its transformative power can be unleashed on a larger scale.

Doing so requires four things: improving the accuracy of diagnoses, reducing unwarranted variations in diagnosis, personalizing treatment when it can make a difference, and finally, taking advantage of today's progress in advanced therapy intervention to maximize outcomes.

Achieving these four goals – known as the Four Pillars of Expanding Precision Medicine – is the recipe for enabling healthcare executives to fulfill the promise of implementing precision in medicine and empowering its adoption at scale around the world.

Why Precisely Do We Need Precision Medicine?

The answer is simple: medicine, for all its advances, is still hobbled with inconsistency in both diagnosis and treatment. Although it is a cost problem, this is a human problem as well.

Suboptimal precision in medicine is visible across the continuum of care. Diagnoses that are not precise, timely, or accurate negatively affect patients' results.

Even when the appropriate diagnosis is being made, unwarranted variations can add at least 25% to the cost of healthcare, with negative impact in outcomes too. Medically justified treatments that aren't individualized or unnecessary invasive procedures put people's health at risk.

Lack of precision exacts a price both clinically and financially. A study by *U.S. News* and *World Report* found that in some regions of the U.S., Medicare patients underwent 450% more coronary artery angioplasty procedures than in other parts of the country.[1] Many of those patients, the article noted, had unnecessary invasive procedures that can be both risky and costly.

The Right Treatment at the Right Time for Every Patient

As a goal, it sounds simple. In practice it's one of healthcare's biggest challenges, with systemic effects on medicine around the world.

Thanks to the explosion of clinical data available from new technologies, it is easier to tailor treatments that take a patient's unique phenotype and genetic makeup into account.

Contextually relevant data is gold when it comes to reducing inaccuracies in diagnosis. It's one of the reasons the National Institutes of Health's *All of Us Research Program* is now gathering lifestyle, environmental, and biological data from one million U.S. volunteers. While *All of Us* is a user-friendly name, it's worth noting that it used to be called the *Precision Medicine Initiative Cohort Program* – a government commitment to advancing the field. Similar initiatives have been launched in the private sector. Healthcare companies and institutions such as Geisinger, Kaiser Permanente, and Johns Hopkins Hospital are leading the way in the U.S.

Researchers in Europe are also taking up the challenge of using data to scale up healthcare's ability to more fully characterize the determinants of health and disease. U.K.'s Biobank has a study that is looking at ways to clarify the specific roles that an individual patient's imaging and genetics make up, together with lifestyle and environmental factors, in the development of disease. In Germany, the Study of Health in Pomerania (SHIP) is currently assessing the "prevalence and incidence of common risk factors, subclinical disorders and clinical diseases" and using data to investigate associations and reactions between them.[2] In addition, in 2016, the Chinese government started the China Precision Medicine Initiative, pledging to invest 9.2 billion USD between now and 2031.

When massive datasets such as these are analyzed with the help of AI technologies, connections and patterns begin to emerge. The medical community is then able to determine optimal therapeutics based on an individual's phenotype, disease subtype, tumor signature, and other biomarkers so that the best therapy can be implemented as soon as possible. Just as exciting is the ability to use predictive analysis to enable earlier, more effective intervention.

Scaling up these capabilities will give healthcare providers significantly enhanced capabilities to diagnose based on synthesizing all relevant patient data and insights at the point of decision. Then the most appropriate treatment can be chosen.

Scaling Up the Four Pillars of Precision Medicine

The promise of precision medicine is founded on four pillars:

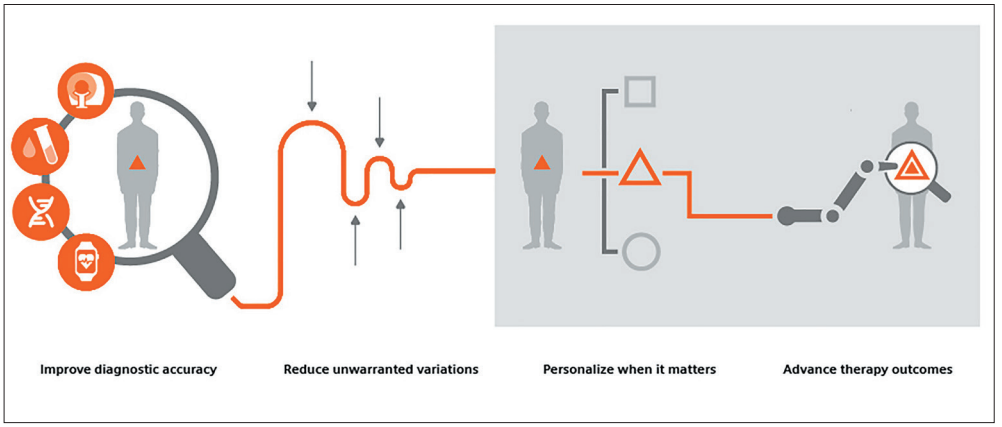
- Improve Diagnostic Accuracy
- Reduce Unwarranted Variations
- Personalize When It Matters
- Advance Therapy Outcomes

The first two are about increasing precision in diagnosis; the second two focus on choosing the right therapy individualized for each patient. Expanding precision medicine to scale means scaling up both categories – all four pillars, and for all patients.

Let's examine these one by one.

Improve Diagnostic Accuracy

It is not possible to choose the right treatment with the wrong diagnosis. Accurately pinpointing what's wrong with a patient is the starting point for everything. Yet, in their 2015



The Four Pillars

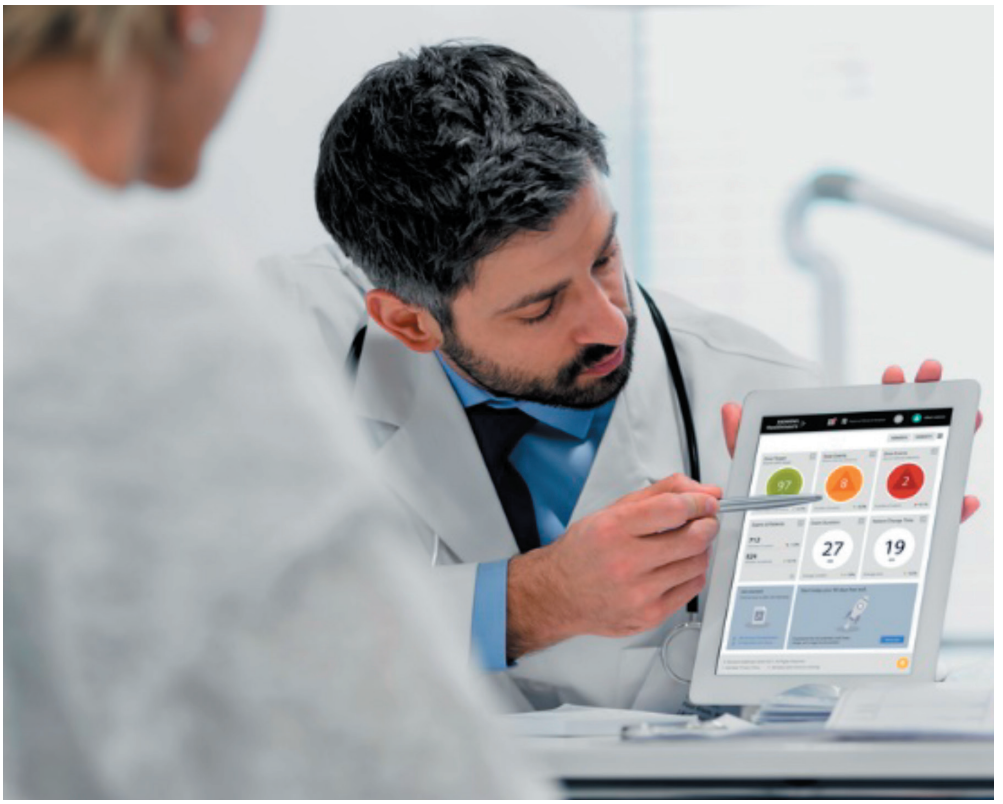
report "Improving Diagnosis in Healthcare," The Institute of Medicine and The National Academies of Sciences, Engineering, and Medicine found that 5% of U.S. adults who received outpatient care that year – millions and millions of patients – had errors in their diagnoses. Those errors led to 10% of patient deaths and accounted for as much as 17% of adverse events in hospitals.[3]

It doesn't have to be that way. Today's advanced laboratory and imaging technologies can yield significantly more actionable information than ever before. And this information has the power to yield rich patient insights at the point of decision.

In neurology, current imaging technologies with high resolution, for instance, can help in making the differential diagnosis between multiple sclerosis lesions and other inflammatory and non-inflammatory conditions.

In cardiology, suboptimal diagnosis can lead to non-adequate use of implantable defibrillators. More precise identification of patients at risk for sudden cardiac arrest can help make sure the right patients receive these life-saving devices at the right time. Running diagnostic processes based on imaging and laboratory tests can allow people who actually need defibrillators to get them – and people who don't need them don't wind up with them unnecessarily.

In oncology, rich clinical insights drawn from advanced imaging technologies are already improving the screening and diagnosis of many kinds of cancers. Multi-parametric Magnetic Resonance Imaging (mpMRI), for example, allows for more precise identification of prostate cancer versus standard transrectal ultrasonography-guided biopsies. The U.K. National Health Service estimates that "between 33% to 40% of patients who have an mpMRI scan will find out on the same day that they don't have prostate cancer." That means they can avoid an unnecessary biopsy.[4]



In lung cancer, emerging radiomics digitally extract and analyze disease-related data from images. It can make lung cancer screening faster and more accurate by using machine learning when applied to the right set of high-risk patients.

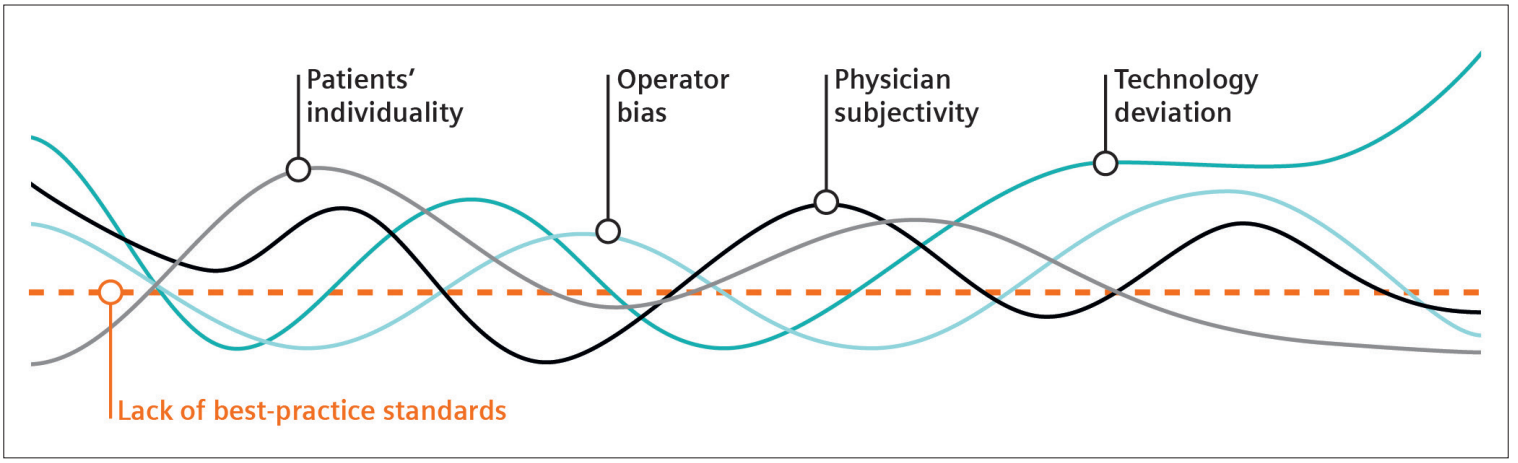
Laboratory tests have become more sensitive and precise in the vast majority of clinical conditions. Standardization allows for additional consistency in their interpretation. On top of that, automation in the laboratory adds accuracy by removing operation and manual handling risks.

One of the most fertile avenues for scaling up diagnostic accuracy lies in leveraging the power of digitalization and artificial intelligence. Technologies driven by quantified markers and machine learning are able to process vast sets of data from imaging, laboratory, socio-determinants, and other sources. That gives healthcare providers an expanded ability to pinpoint parameters that define subgroups of patients or disease states. The integration of data and artificial intelligence can be used in decision support systems to make suggestions for next steps. Add to that the ability of new networked medical technologies that enable physicians to share data from peers around the world, and you have a recipe for significantly more accurate diagnoses.

The bottom line is more precise diagnosis can be achieved for a broad range of conditions.

Reduce Unwarranted Variations

Accuracy is clearly important. But without consistent accuracy – accuracy independent of who's doing the testing, who's reading the results, and where and when the testing occurs – the notion of "precision medicine"



Sources of unwarranted variations in diagnosis: Improving diagnostic consistency is possible through standardization, adaptation to the patient, automation, clinical decision support, and ensuring reliable and comparable results, when technology is applied.

becomes meaningless. One of the biggest opportunities to improve outcomes while reducing costs is the reduction of unwarranted variations. Precision medicine can only expand when clinicians and patients can count on consistent results across different operators and institutions.

Unwarranted variations are the variations in medical practices that cannot be explained by illness, medical need, patient preferences, or the recommendations of evidence-based medicine.

We all pay a price for these unwarranted variations. Twenty-five percent of hospital costs are wasted due to variations, and some estimates even go up to 65% of HC costs, based on the "Five steps every hospital CEO should start today".[5]

In the U.K., for example, the 2017 Diagnostic Atlas of Variation for England found a nine-fold variation in the acquisition of brain imaging for stroke patients within an hour of arrival at the hospital.[6] In the U.S., the Dartmouth Atlas of Health Care found a greater than two-fold variation in per capita Medicare spending across the country driven by the rate of care utilization rather than price. And at least three groups have concluded that 30% of U.S. spending on healthcare is unnecessary.[7]

Building best-practice standards along the continuum of care is a prerequisite for consistent, evidence-based care. The key levers for reducing variations are adapting to patients' individual needs and reducing the subjectivity of operators and physicians. Correspondingly, automation and assisted decision-making based on reproducible technology activate these levers to create consistent diagnostic results. Steady, iterative improvements using this approach effectively reduce unwarranted variations.

Efforts to reduce unwarranted variations are beginning to bear fruit. Mercy Health in St. Louis, Mo., USA, was able to improve patient outcomes after total knee replacement (TKR) by analyzing a wide variety of data associated with the procedure. TKR patients with the shortest hospital stay, it turns out, had all been administered pregabalin prior to surgery based on published data that it can improve post-op pain management. Mercy Health, as a result, was able to improve patient outcomes for TKR patients, including reducing length of stay, for a total savings of more than $1 million per year in direct costs.

Personalize When It Matters

Medical treatments are best when they're custom-tailored to individuals and their conditions. Today, advances in biomarkers, genomics, proteomics, metabolic science, and AI-assisted data processing are enhancing the ability of healthcare providers to offer genuinely personalized care.

High-quality imaging technologies, for example, now allow for personalized radiation planning for patients undergoing radiation treatment based on their unique anatomical and functional imaging profile. Companion diagnostics – tests to determine which patients are likely or unlikely to be helped by a particular drug – are now required by the U.S Food & Drug Administration for drugs designed to work on a specific genetic or biological target typically present in small portions of the population. Herceptin, a HER2/neu inhibitor, is a good example of a therapy that takes this model.[8]

In oncology, liquid biopsies (using simple blood samples instead of the more invasive traditional biopsy) combined with genomic analyses are able to identify the genomic makeup of circulating DNA or cancer cells, thus helping physicians to identify precise and effective individualized treatments, even in cases when tumors are not directly accessible.

The quantitative analysis emerging in radiology – known as radiomics – also shows promise in giving physicians greater insights into tumor biology and genetic diversity that can correlate with tumor aggressiveness and response to treatment.

The move to personalized treatment has begun. Deploying such personalized approaches at scale is a clear requirement for improving clinical and financial outcomes for patients and hospitals around the world.

Advance Therapy Outcomes

Today, physicians performing minimally invasive surgeries are able to turn to image-guided therapies for unprecedented accuracy over traditional surgeries. The results: shorter hospital stays and less post-operative pain.

Many opportunities to enhance therapy precision lie in the integration of imaging and treatment delivery. Therapeutic procedures from surgery to radiation oncology rely on integrated real-time or multimodal image guidance and robotic assistance. This facilitates minimally and non-invasive interventions that support faster recovery with fewer complications. This enables healthcare providers to advance therapy outcomes and make treatment safer, faster, and less costly.

New advances in medical technology and imaging modalities such as ultrasound, magnetic resonance, CT, endoscopic cameras, and robotic technology are rewriting the rules for precise procedures and improved patient outcomes. Today's leading surgeons regularly rely on computed tomography and angiography systems for high-res images. Real-time imaging is also finding a home in cardiovascular care, oncology, orthopedics, vascular procedures, and the surgical removal of tissue. Constantly improved outcomes at scale are likely to accelerate as these new technologies and procedures continue to mature.

Conclusion

Expanding precision in medicine is opening the door to improving outcomes and reducing healthcare costs unlike anything before. The twin goals of more precise diagnoses and more individualized treatments are clearly within reach.

Expanding precision medicine to a global scale will be further enabled by the continued collaboration of healthcare providers, medical technology companies, and clinical partners to let precision diagnosis and individualized treatment become the default paradigms. The capability is clearly there to improve outcomes and reduce costs. All that's needed now is the will to bring it to scale so that 21st century precision medicine is available to everyone. ■

For more information please visit: siemens-healthineers.com/precision-medicine

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