XONE

PRECISION   MEDICINE

Understanding Precision Medicine

By: Karan Shinde & Nicholas Wynne

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Introduction to Precision Medicine

- Current Healthcare Limitations: Traditional healthcare focuses on treating symptoms, leading to overworked providers and long patient wait times. This results in worsened conditions and comorbidities.
- Precision Medicine Approach: Precision medicine offers personalized, predictive, and preventive care using big data, innovative diagnostics, and real-time health monitoring to improve outcomes and extend healthspan.

A New Field of Research

- Lifespan vs. Healthspan: While life expectancy has increased, age-related diseases have surged, emphasizing the need for healthy aging.
- Research on Aging: New studies aim to treat aging processes to delay or prevent age-related diseases, employing diverse methodologies from clinical trials to computational analyses.

Wearable Health Technology
- Wearable Technology: Devices like smartwatches and glucose monitors revolutionize health management with real-time data.
- Data Integration: Combining wearable data with traditional diagnostics provides a comprehensive view of health, though data complexity remains a challenge.

System of Systems

- Interconnected Systems: Human health involves interconnected biological systems. Precision medicine addresses imbalances across these systems for better long-term outcomes.
- Role of the Microbiome: The microbiome influences inflammation and interacts with the nervous and immune systems, playing a key role in health and disease prevention.

Early Detection

- Screening and Prevention: Early and frequent screening helps detect diseases early, enabling better treatment. Precision medicine uses multiple data sources to optimize disease detection.
- Lifestyle Modifications: Preventive measures like exercise, diet, and sleep are crucial in reducing age-related disease risks and extending healthspan.

Conclusion
- Revolutionizing Healthcare: Integrating precision medicine with personalized lifestyle changes can promote healthy aging, prevent chronic diseases, and enhance quality of life.

Early detection significantly improves disease prevention

● **Cancer diagnostic**

99%

99% survival rate for Stage 1 breast cancer drops to 27% at Stage 4. Early detection is critical.

Currently, healthcare focuses on diagnosing and treating illnesses only when symptoms emerge. This approach, while providing a high standard of care for many, is not without limitations:

- Healthcare workers tasked with fixing these problems are overstaffed, overworked, and burned out in our hospitals, community clinics, and long-term care.
- Patients often face long waiting periods for healthcare procedures that could significantly enhance their quality of life. These delays can predictably lead to:
    - Progression of their condition
    - Development of comorbidities
    - Decline in patient health outcomes

The Canadian healthcare system is primarily geared towards addressing the most pressing and immediate health concerns. Any additional care is considered beneficial but not essential and is only feasible if there is surplus time, money, and resources. As a result of these standardized and more traditional treatment protocols, which emphasize acute symptom reduction, doctors do not have the opportunity to focus on long-term health outcomes. Temporary solutions which alleviate symptoms do not address the underlying causes of a condition, potentially leading to a lifelong dependency on therapeutic interventions:

- Identifying and treating the root cause of a condition can be more complex than managing symptoms.
- Ignoring or failing to address the underlying causes of today's symptoms could result in a lifelong dependency on therapeutic interventions.

An emerging healthcare philosophy, known as precision medicine, introduces an opportunity to shift our perspective towards patient-centric, predictive, and preventive care (1). Precision medicine leverages our capacity to collect and analyze big data at the individual level. This allows for:
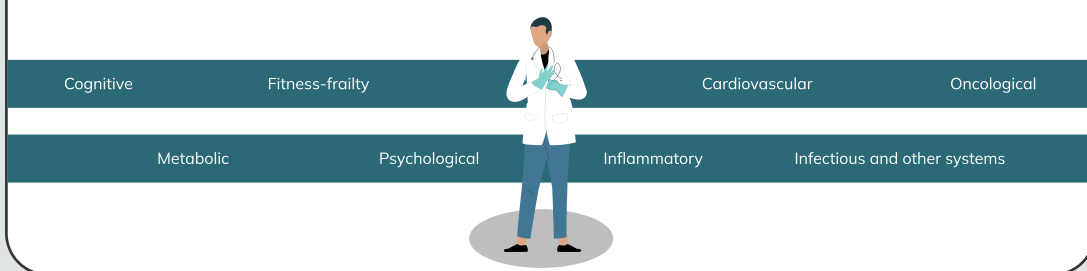
- Creation of rich datasets
- Development of personalized protocols to reduce disease risk
- Overall improvement of patient outcomes

Precision medicine deploys cutting-edge medical research, rigorous diagnostic screening, and real-time health-monitoring with the aim of designing the most optimal treatment strategies with minimal patient risk.

Phenotyping

| Metabolome | Genome | Proteome | Immunome | Microbiome | Transcriptome |

| Physiological | Exposome | Imaging | Clinical | Behavioral | Family History | Personal History |

Health Status or Risk

| Cognitive | Fitness-frailty | Cardiovascular | Oncological |

| Metabolic | Psychological | Inflammatory | Infectious and other systems |

Modifiable Trajectory

Additional screening Genetic counseling Diet and lifestyle modification Personalized medical theory
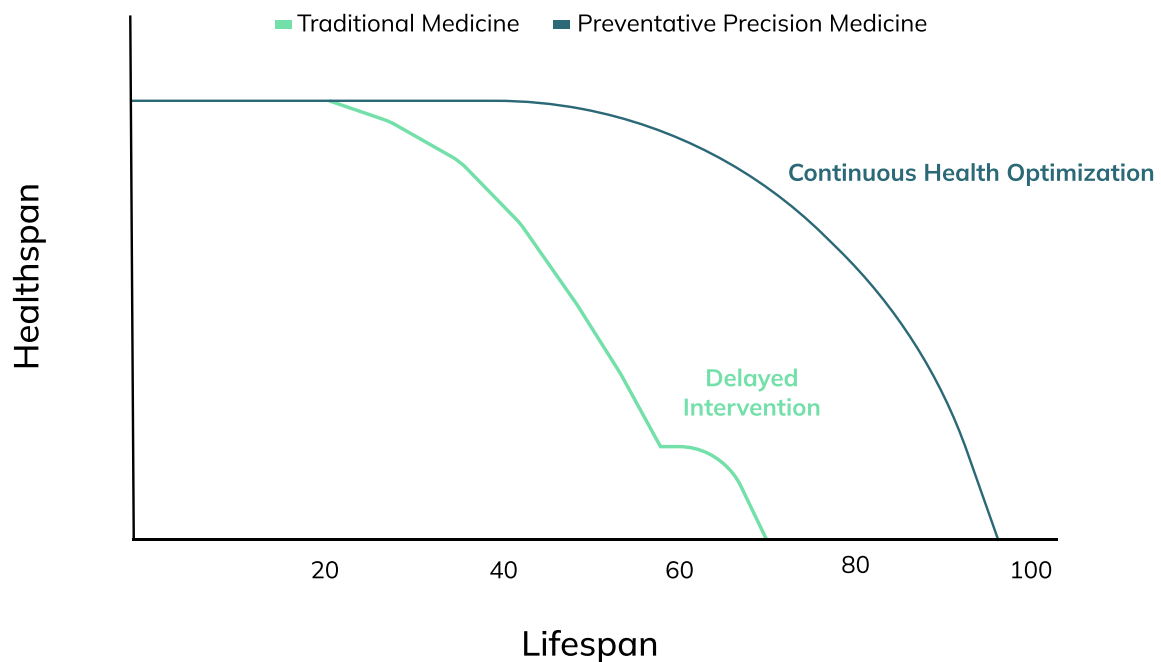
The advent of innovative diagnostic methods and the improved accessibility of biometric data from wearable devices have simplified the process of identifying complex pathologies. The incorporation of multi-omic data from sources like genetic testing, microbiome assessments, and sleep and metabolic data from wearable devices can facilitate a comprehensive phenotypic understanding and provide a unique opportunity to optimize a patient's health. While addressing these issues remains challenging, a multidisciplinary approach focused on various facets of both physical and mental health will enhance the potential to improve patient quality of life.

The precision medicine approach advocates for the use of diverse multi-omic data to construct a comprehensive picture of an individual's health. Leveraging rich datasets from sources such as whole-genome sequencing, broad-spectrum blood biomarker analysis, microbiome assessment, cardiometabolic exercise testing, liquid biopsy cancer screening, full-body imaging scans, and wearable biometric devices presents a unique opportunity to discover novel strategies for disease management and prevention. The primary objective is to extend the number of healthy years experienced by the patient, also known as healthspan.

Beyond the increased effectiveness of care at an individual level, sharing new data and disease management strategies will enhance our overall understanding of patient health and the system's ability to improve patient outcomes on a broader scale.

Healthspan (y-axis)

Legend: Traditional Medicine — Preventative Precision Medicine

Continuous Health Optimization

Delayed Intervention

Lifespan (x-axis): 20 40 60 80 100

A New Field of Research

Human life expectancy has been rising since the earliest records in the 1800s. This substantial increase in global human lifespan aligns significantly with the evolution of healthcare strategies. Key developments, such as antibiotics and vaccinations, have considerably reduced the rates of infectious diseases, historically one of the primary causes of death. As innovative therapeutics have emerged to combat major diseases of the past, and the average lifespan continues to rise, there has been a concurrent transformation in the nature of age-related health threats faced by an aging population.
Regrettably, this rise in average life expectancy is shadowed by a dramatic surge in age-related diseases. While life expectancy has remarkably increased over the past 150 years (2), the added years are not invariably healthy. This implies that a higher proportion of life is now being spent in poor health, suggesting that the value of lifespan extension is compromised if most of the additional time is spent in a state of illness or disease.

- Age is among the greatest risk factors for many diseases.
- Healthy individuals in older age groups often face a greater risk of all-cause mortality compared to their younger, less healthy counterparts.
- This raises the question: why is age so strongly correlated with disease?

Modern geriatric medicine aims to enhance the quality of life for aging individuals by reducing the risks of developing age-associated diseases and treating their symptoms which inevitably occur. If the diseases of aging could be effectively managed, would it be possible for individuals to live indefinitely? This would not be the case as humans eventually yield to the aging process, often described as 'death by natural causes.' Although aging is an inescapable process experienced by all living beings, there is still significant potential to modify the natural trajectory of aging.

An emerging wealth of research focusing on the biology of the aging process continues to underscore the importance of healthy aging. If age is a dominant risk factor for disease, directly treating processes of aging could hold promise in:

- Delaying the onset of age-associated decline
- Preventing age-related diseases entirely (3)

Geriatric science researchers globally have adopted diverse sophisticated approaches to unravel the intricacies of the human aging process. Experimental methods for studying aging span a wide spectrum, ranging from pre-clinical studies of model organisms and computational analyses of aging processes to clinical trials in human patients and even studies of the aging process in unique environmental conditions such as space (4). Over recent decades, the field has agreed on a series of processes, widely known as the hallmarks of aging (5), that underlie the aging process. These hallmarks illustrate a decline in fundamental cellular processes essential for human function, revealing a potential pathophysiology linked to the increased risk of age-related disease.
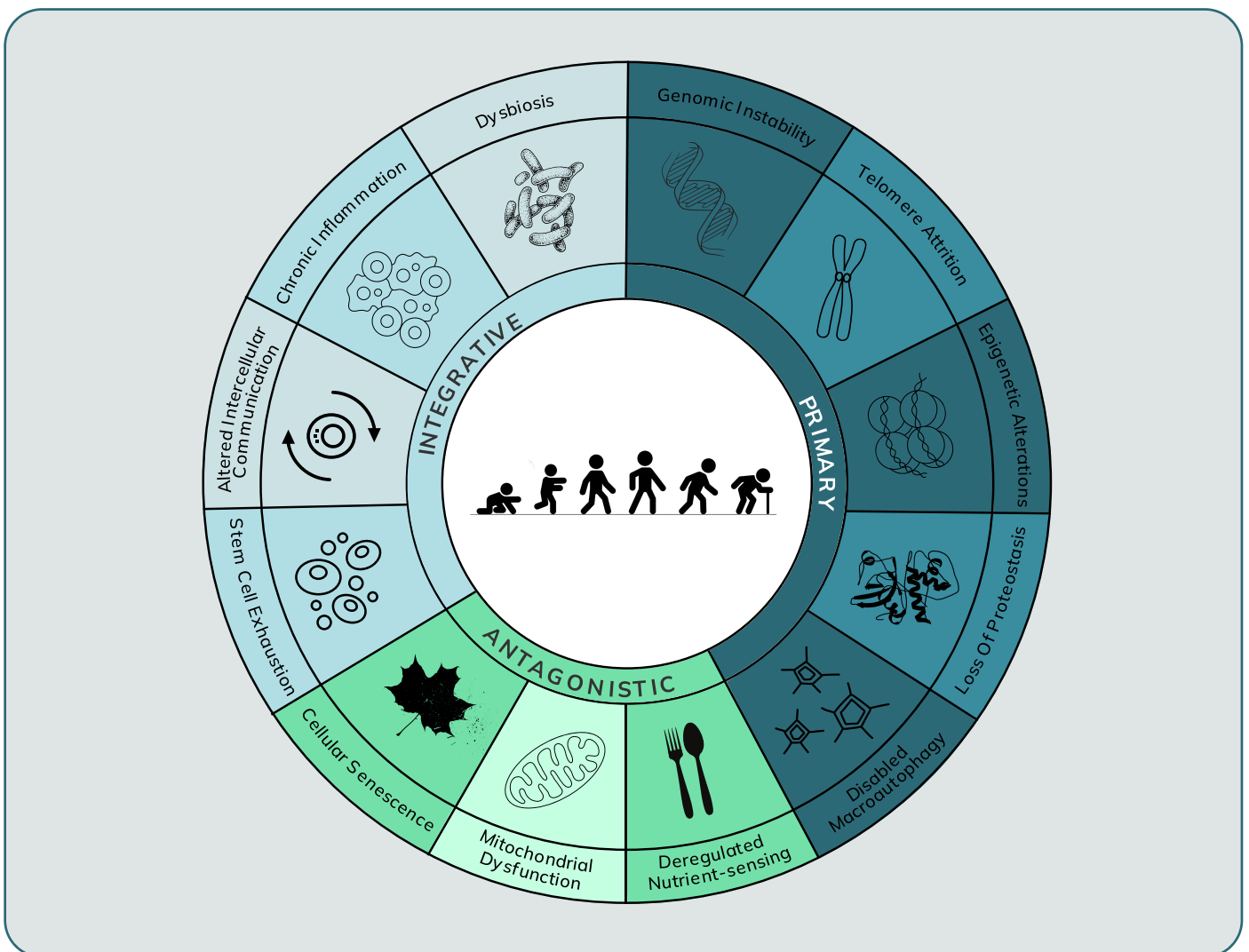
Adopting an 'aging-first' approach offers a new path for patient care, presenting unique opportunities to significantly alter an individual's health trajectory with the aim of optimizing patient healthspan. While there remains much progress to be made in geriatric research, the goal is to:

- Keep up-to-date with scientific advancements
- Incorporate emerging healthcare technology to equip patients with the most effective tools to positively influence their long-term health trajectory

Endurance exercise is key

Studies indicate that engaging in regular endurance exercises, such as cycling or walking, can reduce the risk of sarcopenia by up to 50%, making it an essential component of any strategy aimed at maintaining muscle health and function in the elderly population.

● **Reduce muscle loss**

50%

This reduction is particularly important as sarcopenia is a leading cause of frailty and loss of independence in older adults, and its prevention through exercise can significantly enhance quality of life.

Wearable Health Technology

Wearable devices have held an invaluable role in the development of human society beginning with the invention of the first wristwatch in 1810. From facilitating research and education to enabling social networking and military operations, the development of wearable technology has had far-reaching implications. As the technology of wearable sensors continues to evolve, new data sources are revealed, offering innovative approaches to some of society's most pressing problems.

Recently, the personal health sector has witnessed a substantial increase in the use of wearable devices. New technologies, including:

- Smartwatches
- Continuous glucose monitors
- Sleep trackers
- Electronic weight scales equipped with biometric sensors

These technologies are revolutionizing health management (6,7). Combined with cloud-based data consolidation, these devices offer the convenience of tracking personal health metrics directly from a smartphone. The ability to gather health data on a 24-hour basis offers a newfound perspective into personal health. It allows individuals to:

- Obtain a more detailed view of their biometric data
- Monitor changes in health metrics
- Gain real-time insights into their overall wellbeing

While the popularization of wearable technology has empowered individuals to take health initiatives themselves, the abundance of data generated can be overly complex and overwhelming for the average person. Significant strides have been made in integrating wearable health devices into everyday life, and few barriers remain on the path to their widespread utilization in healthcare. As devices continue to improve in sensitivity, accuracy, and availability, leaders in the healthcare space must champion the education of healthcare providers to fully understand the capabilities and limitations of wearable health devices used today. The real potential of wearable health data lies in multivariate analysis of diverse data sources, combined with traditional diagnostic methods. This approach:

- Facilitates a comprehensive view of patient health
- Enables tracking of health outcomes over time
- Underscores the impact of lifestyle interventions, such as diet and exercise, on overall wellbeing.

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System of Systems

Throughout our lives, we as humans are susceptible to a number of diseases that can compromise our physical and mental well-being. Some of the most prevalent diseases include:

- Cardiovascular disease
- Cancer
- Dementia
- Metabolic syndrome

Although these diseases have distinct pathologies, they share more commonalities than may initially appear.

The human body is a complex network comprising several subsystems, including the musculoskeletal, respiratory, circulatory, digestive, nervous, endocrine, and reproductive systems. Conventionally, when patients present with symptoms indicative of disease or dysfunction, physicians employ diagnostic testing to pinpoint the affected system and formulate an optimal treatment plan to alleviate symptoms. This approach often overlooks the substantial interconnectedness between these systems and the possibility that underlying factors may simultaneously impact multiple systems.

Our approach to precision medicine seeks to address this oversight by underscoring the interconnectedness of these disparate systems. This includes adopting a systems biology approach to examine how different biological systems — such as the immune, nervous, and endocrine systems — interact with each other and the environment. By assessing the underlying imbalances and dysfunctions in these systems, practitioners can devise a comprehensive treatment plan that tackles the root causes of a patient's illness, thereby aiming for improved long-term patient outcomes.

One pivotal node within the interconnected systems of human biology is the microbiome. Microbes inhabit every body cavity exposed to the external environment, including:

- Nasal cavity
- Mouth
- Skin
- Gastrointestinal tract

They serve as the primary filter for everything we encounter, from foreign pathogens in the air we breathe to essential nutrients in the food and water we consume. These microbes possess the remarkable capability to identify foreign entities and emit chemical signals to other systems within our body to stimulate an appropriate response. For instance, the gut microbiome communicates with the nervous system via the gut-brain axis — a bidirectional communication pathway between the gut and the brain (8). The gut microbiome can generate neurotransmitters and other signaling molecules that influence mood, behavior, and cognitive function. Conversely, the brain can also impact gut function and the composition of the gut microbiome. This interplay can act as a form of nutrient sensing, resulting in specific metabolic and emotional responses.

Furthermore, the gut microbiome communicates with the immune system by producing various metabolites and signaling molecules that modulate immune function. For instance, some gut bacteria can generate short-chain fatty acids that regulate the function of immune cells in the gut and other parts of the body.
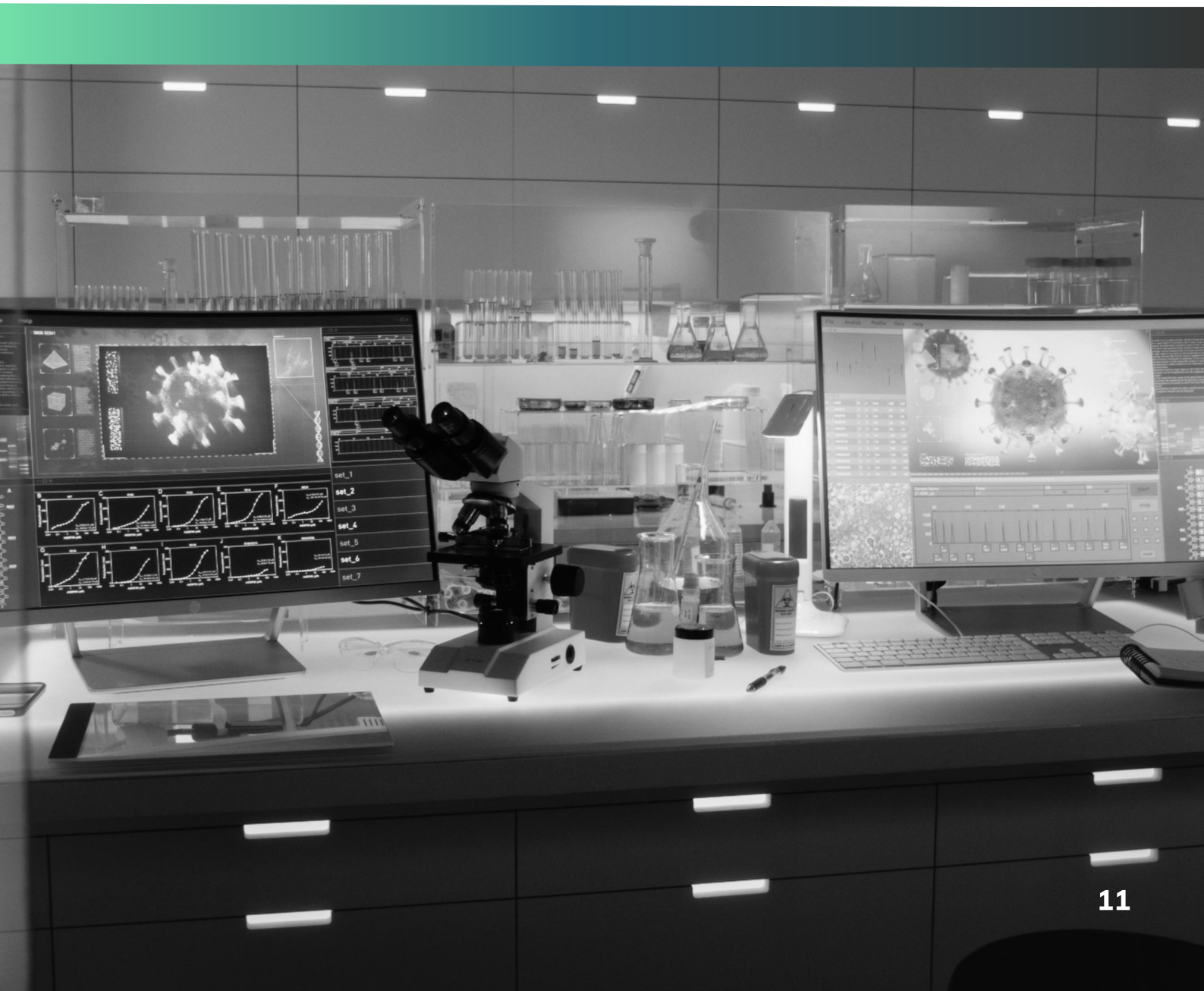
Given its strategic position as the first line of defense against all foreign bodies entering our system, the microbiome plays a crucial role in mediating inflammation, a process associated with many systems in our body. Acute inflammation typically ensues during times of infection, whereas systemic chronic inflammation (SCI) is triggered by long-term exposure to unhealthy environmental factors such as obesity, poor diet, sedentary lifestyle, and various others (9). SCI, which escalates with age, inflicts damage to tissues and organs through oxidative stress. Though inflammation is an integral component of our immune system, it assumes a broader role in our health as it is associated with a wide array of medical conditions including:

- Hypertension
- Hyperglycemia
- Dyslipidemia
- Type 2 diabetes
- Non-alcoholic fatty liver disease and alcoholic cirrhosis
- Cardiovascular and chronic kidney disease
- Various types of cancer
- Depression
- Neurodegenerative and autoimmune diseases
- Osteoporosis
- Sarcopenia (9)

The association of inflammation with a broad spectrum of diseases renders it an ideal marker of disease. However, the lack of specificity in the inflammatory response can make it challenging to identify the source of inflammation. Inflammation, which can be assessed by measuring pro- and anti-inflammatory cytokines, acute phase proteins, and immune cell fractions, can appear remarkably similar across a wide range of diseases. Inflammation can be caused by a poorly tolerated diet, autoimmune disease, accumulation of senescent cells due to aging, and many other conditions.
In isolation, assessing the microbiome or the inflammatome can be complicated as they are parts of a much larger system and can be influenced by a variety of factors. When assessed in combination, it can be a lot easier to identify the cause of systemic disruption, prescribe the optimal treatments, and assess patient progress over time to achieve further health optimization.
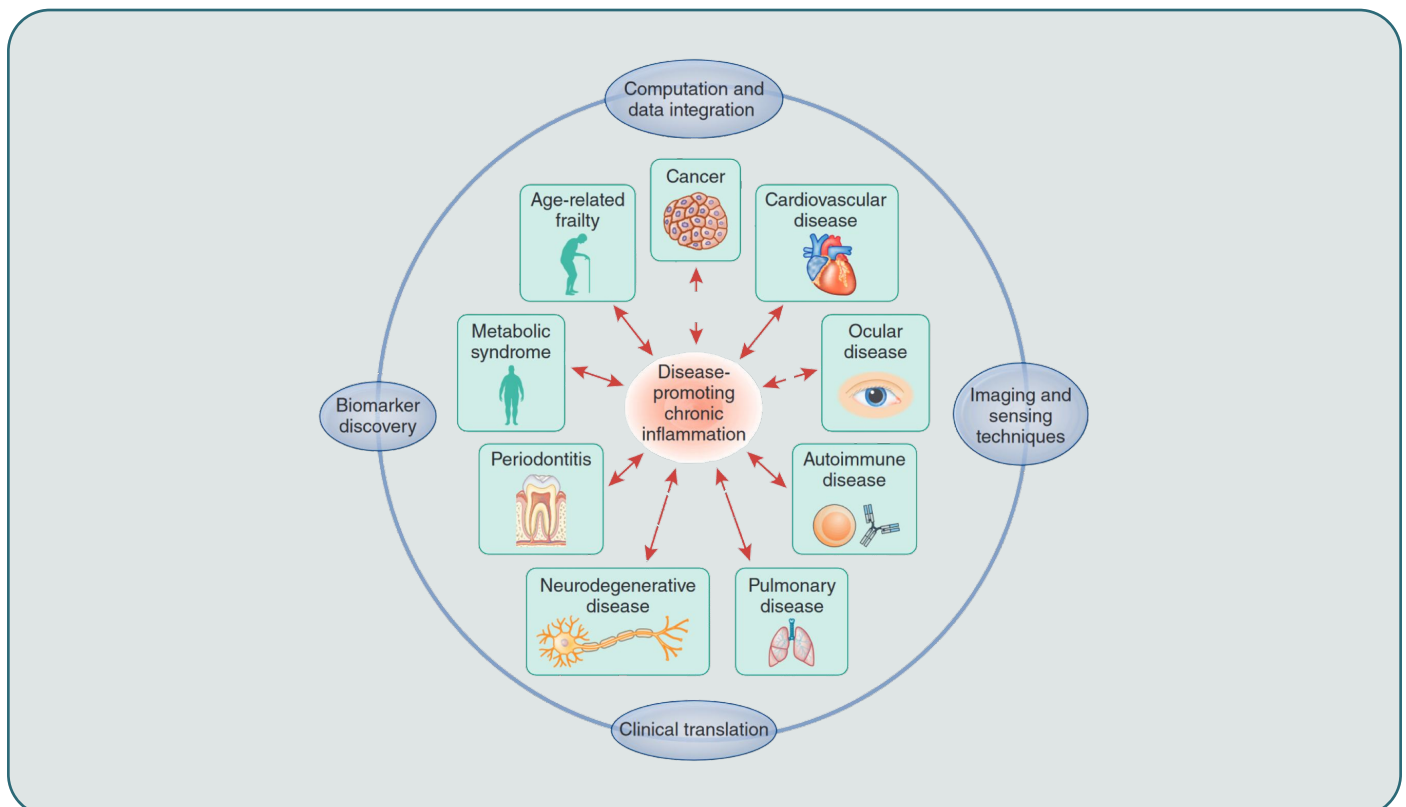
Early detection significantly improves disease prevention

68%

Individuals have shown a large degree of variability in postprandial glucose response. After consuming identical meals, variation in postprandial responses was found to be 68% for glucose, 103% for blood triglycerides, and 59% for insulin.

Early Detection

Leveraging the tools now at our disposal in conjunction with a precision-based approach, we have an unprecedented opportunity to detect diseases either before they manifest or in their earliest stages, thereby enabling the best prognosis. Early and frequent screening can help identify biological perturbations in an individual, which paves the way for the development of optimal protocols to mitigate disease risk and positively influence their health trajectory. For instance:

- Cardiovascular disease can start to manifest in the body through arterial calcification as early as one's 20s or 30s (10).
- Understanding an individual's specific etiology of cardiovascular disease creates a path for numerous effective treatment strategies (10).
- In the context of diabetes, prevention becomes key when realizing that nine out of ten individuals with pre-diabetes are unaware of their prediabetic status (11).

There can be a substantial lag time between the molecular manifestation of disease and the presentation of clinical symptoms detectable by diagnostic testing. If a disease is diagnosed decades after its onset in the body, the efficacy of available treatments is drastically diminished.
The integration of multiple data sources offers a high-definition picture of a patient's biology. This strategy optimizes the trade-off between the sensitivity and specificity of each screening tool we implement for a given disease, with the intention of achieving the highest positive predictive value:

- Sensitivity refers to the likelihood of a test to yield a true positive result among individuals with a disease, genetic variant, or risk factor.
- Specificity pertains to the frequency at which a test yields a true negative result in individuals without any disease, genetic variant, or risk factor.
- The trade-off between sensitivity and specificity acknowledges that enhancing the detection rate of true positives (sensitivity) curtails the test's capacity to identify false positives (specificity).

For this reason, layering multiple tests to create a comprehensive screen provides the highest probability of detecting any early manifestations of disease. For example, over 50% of cancers are diagnosed at a late stage, presenting a challenging battle, whereas early detection could potentially reveal a less genetically complex tumor that is more susceptible to treatment (12).

Conclusion

Geriatric medicine, which targets aging-associated diseases, aims to enhance the quality of life and health span for elderly patients. While such care is crucial, there is a need for greater emphasis on prevention. Simple lifestyle modifications, such as:

- Regular exercise
- Healthy balanced diet
- Quality sleep
- Supplementation

These can significantly mitigate the risk of developing age-related diseases. As we continue to invest resources into developing new therapeutics to treat aging-related diseases, pivoting towards prevention holds great potential for reducing disease prevalence and extending average healthspan.

The significance of regular exercise and healthy eating habits in medicine is not a novel concept. Doctors have advocated for these lifestyle choices for centuries. However, patients often find themselves lost amidst the plethora of recommended diets and contradictory advice surrounding optimal dietary approaches.

Exercise can be similarly intimidating given the various forms and the potential to miss out on benefits or even risk injury if appropriate programs are not employed.

Frailty is the leading cause of accidental death in adults over 65. Muscular strength and bone mineral density, which are primarily developed earlier in life, become challenging to improve significantly after a certain age. Maximizing physical function is vital for healthy aging and maintaining independence. As we age, physical dysfunction often leads to dependence. To counter this, we must:

- Maintain muscle and bone mass
- Enhance physical strength and function

Mobility training, an effective method to preserve physical function, becomes essential in lowering frailty risk. Not to be confused with flexibility, mobility involves actively moving through a joint's full range of motion with strength to reduce injury risk.

In addition to mobility training, attention should be focused on two other key physical health metrics: bone density and muscle mass. Large-scale population studies have revealed:

- Decline in bone mineral density after the age of 35 for men and 40 for women, with women experiencing a more significant decline during perimenopause (13).
- Muscle mass steadily decreases after age 50, increasing the risk of falls and fractures.

Dual energy X-ray absorptiometry (DEXA) scans are the gold standard for assessing body composition, providing valuable insight into the effectiveness of exercise programs and dietary interventions in mitigating physical decline. Early identification of low bone mineral density allows for more targeted interventions, slowing the rate of bone loss.

Sleep is another crucial factor in healthy aging, impacting physical, cognitive, and emotional well-being. While genetic predisposition might dictate sleep health to some extent, prioritizing healthy sleep habits is often undervalued. Sleep hygiene develops beneficial habits to maximize sleep quality and duration, which can be assessed and optimized with new sleep-tracking technology. Enhancing sleep quality and quantity can:

- Improve memory consolidation
- Enhance learning
- Regulate emotions
- Boost metabolic health

All these factors contribute to improved healthspan.

Precision medicine harnesses the power of deep phenotyping, providing insight into optimal lifestyle habits tailored to the individual. Through diagnostic testing and wearable devices, physicians can devise personalized lifestyle interventions and monitor progress in real-time, encouraging adherence to healthy habits. Advances in precision medicine offer tools for identifying an individual's unique genetic, environmental, and lifestyle factors impacting health. However, these insights must be coupled with actionable lifestyle modifications to be effective. Leveraging deep phenotyping in a patient-centric approach allows us to pinpoint specific areas for improvement, facilitating lifestyle changes that optimize healthspan.

By integrating precision medicine with lifestyle changes, we can devise personalized interventions that promote healthy aging, prevent chronic diseases, and enhance the quality of life. While new technologies can offer valuable insights, it ultimately falls upon the individual to enact necessary lifestyle changes for promoting healthy aging and preventing chronic diseases. The marriage of precision medicine and healthy lifestyle behaviors has the potential to revolutionize healthcare and empower individuals to take control of their health and well-being.
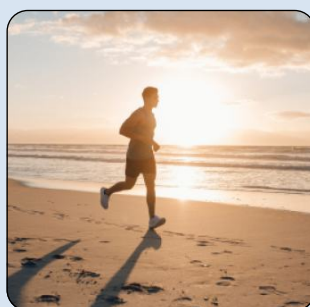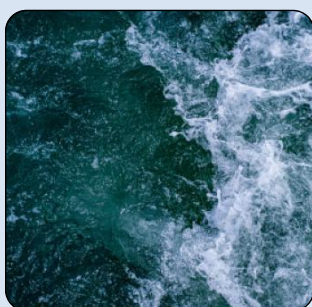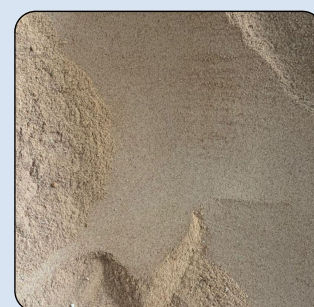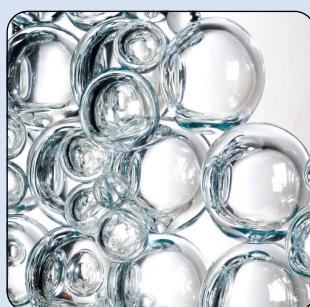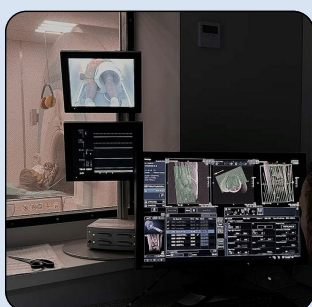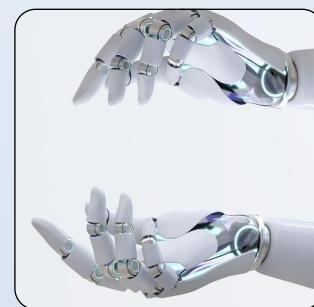
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Hormone Optimization Program

What are Hormones?

Hormones are chemical substances produced by various glands in the body. They act as messengers, traveling through the bloodstream to target cells or organs, where they regulate and control various bodily functions. Hormones are vital in maintaining balance and harmony within the body, influencing processes such as growth, metabolism, reproduction, mood, and overall health.

"Normal is not Optimal"

Hormone optimization aims to balance and improve hormone levels, reducing symptoms and enhancing overall health and quality of life. Our evidence-based treatment program takes an individualized and holistic approach to address hormonal deficiencies and their impact on quality of life. We strive to achieve a level where you feel and function at your best, rather than simply falling within a normal range for the general population. Why? Because normal is not optimal!

What are the Benefits and Risks of Hormone Optimization?

Our hormone optimization program focuses on achieving symptomatic improvement, ultimately enhancing quality of life. Each hormone carries its own set of benefits and risks, and every individual has a unique risk-benefit profile based on their health history, symptoms, and health goals.