# HealthSpan 360°







Die Young, as late as possible\*

HealthSpan 360° Clinic

"An Institute of Longevity and Wellness"

# Mission Statement

"At HealthSpan 360° Clinic, part of the X-Health Inc. family, our mission is more than longevity: it's about thriving in every dimension. We champion the philosophy to 'Die Young as Late as Possible'<sup>1</sup>, ensuring that each individual doesn't merely extend their years, but enriches them. We cater to those who see beyond just an absence of disease, to those who aspire for a 360° healthspan—cognitively, physically, emotionally and spiritually. For the driven, the passionate, and the 'Marginal Decade Athlete', we are here to guide, support, and transform your coming years into a time of true vitality with the help of data and scientific principles."

We are excited for you to embark on this journey of empowerment and self discovery.

Best,

Fahim Rahim, MD FASN Founder- CEO X-Health Inc. HealthSpan 360° Clinic

Sharla Clark, DO Co-Founder & Chief Medical Officer HealthSpan 360° Clinic

<sup>&</sup>lt;sup>1</sup> In our journey with HealthSpan 360°, we are inspired by the profound words of Ashley Montagu, who said, "The idea is to die young as late as possible." This eloquent statement captures the essence of our mission.

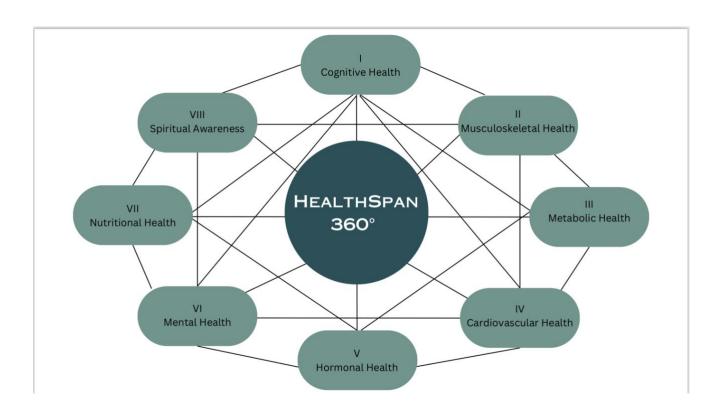
# HealthSpan 360° Value Statement: (Why Us)

At HealthSpan 360°, we recognize the complex challenge of aging gracefully. While scientific advancements have extended the lifespan of lab-mice significantly, translating these breakthroughs to human longevity remains a distant dream. The quest isn't merely about reaching a century; it's about enriching those years with vitality and health. Our approach diverges from elusive promises of extreme longevity. Instead, our focus is on the proactive approach towards prevention of the most prevalent age-related chronic diseases, such as type-II diabetes, cardiovascular disease, kidney disease, cognitive decline, and musculoskeletal deterioration.

We believe addressing dyslipidemia, metabolic syndrome and insulin resistance – the key factors leading to diabetes, heart disease, and kidney problems – is critical. **Our objective is simple yet profound:** to live into our late 90s, free from the burdens of chronic diseases, maintaining our cognition, mobility, happiness, and a purposeful life.

At HealthSpan 360°, we are a team of medical doctors and scientists grounded in the belief that access to accurate and personalized data and established scientific principles can pave the way to therapies that ensure a full, vibrant life span. We don't offer magic pills or potions. Instead, we partner with you, forming your personal "Healthcare Advisory Team." Our approach is rooted in scientific principles and tailored to your unique health profile, focusing on achieving your optimal health span.

Getting older may be inevitable, but falling apart isn't. As the CEO of your health, you will have a dedicated team of doctors and specialists – your **HealthSpan Board of Directors** – guiding you through the ever-expanding Geroprotective data and anti-aging landscape. We commit to finding unique solutions that align with your specific lab data, needs and goals, and hence ensuring a healthier, happier life, free from the clutches of age-related chronic diseases."



# Leadership Vision: Revolutionizing Healthcare with HealthSpan 360° Clinic

The last 25 years of my career and 15 years of Dr. Clark's medical career, we have spent managing chronic disease like hypertension, dementia, diabetes and its complications like advanced cardiovascular diseases and chronic kidney failure; but in the next five years, we envision ourselves at the helm of a transformative shift in healthcare with HealthSpan 360°, a startup wellness company we founded in 2023. This journey represents not just a career pinnacle but the embodiment of our life's work — blending medical expertise with a fervent commitment to proactive health management based on evidence based scientific research and individual client's health data. Where we transform our current state of "disease-care" to a "proactive healthcare" journey for our clients. Our mission at HealthSpan 360° Clinic, to 'Die Young as Late as Possible,' transcends the traditional paradigm of healthcare. It's about enriching the marginal decades of life with vitality and purpose.

We've pioneered a team-based healthcare approach, integrating specialists across disciplines to form a comprehensive "health advisory board" for our clients. This model guarantees a complete, individualized, and proactive health journey for each person we serve, reaffirming the core reasons behind our path: *Transforming the narrative of aging, ensuring a future where longevity is accompanied by unyielding vitality - physical, cognitive and spiritual.* Where health is not just defined by sheer absence of symptoms but actual realtime data that supports and guides an individual's healthspan.

By summer 2024, HealthSpan 360° Clinic's official launch will mark a new era in "precision healthcare." Over the next five years our ambitious plan includes establishing 10 clinic locations, each serving only 500 concierge wellness clients and thus impacting their lives directly with personalized, transformative care. Concurrently, our innovative digital engagement platform will extend our reach, providing accessible preventative care, education, and remote management to those beyond our physical clinics.

Looking forward, HealthSpan 360° Clinic is set to be a beacon in healthcare transformation. Our goal transcends treating diseases; it's about preventing them, enhancing life quality, and redefining aging. We're committed to making the 'Blue Zone' lifestyle attainable, by helping our clients move from their existing "Red Zones" to "Green Zones" and then embarking on a lifelong "Blue Zone" journey — "living into the late gos imbued with cognitive, physical and spiritual health." By proactively avoiding chronic diseases of aging like cardiovascular disease, diabetes type 2, hypertension, chronic kidney disease, dementia and cognitive impairment a "Blue Zone" lifespan is achievable. The upcoming launch, learning from our existing Beta-clients' transformative experiences, and the development of our extensive nutritional and supplement research and industry partnerships all contributes to a 360-degree approach to wellness. This isn't just about managing a clinic; it's about catalyzing a global shift towards wellness, well-being, and proactive health management, hence democratizing healthcare and individual wellbeing.

Our leadership vision is driven by a passion to make a profound difference in client's lives. It's a journey towards a future where aging is redefined, and each individual can realize their full health potential. HealthSpan 360° Clinic is more than a healthcare initiative; it's a movement towards a future where longevity and vitality are intertwined, creating a legacy of health, happiness, and fulfillment.

# The HealthSpan 360° provider's Team

# Fahim Rahim, MD FASN

25+ yrs in healthcare. Board certified in Nephrology and Internal Medicine, Passionate about functional medicine and wellness. <a href="https://www.linkedin.com/in/fahimrahimmd">https://www.linkedin.com/in/fahimrahimmd</a>



# Sharla Clark, DO

15+ years board certified Family Medicine. Specializing in Metabolic Syndrome, Women's health and male & female hormone therapy.

https://www.clarkdpc.com/about



# Samir Damani, MD PharmD

https://www.linkedin.com/in/samirdamani

Doctorate in Pharmacy and a Doctorate in Medicine from the University of Georgia and Georgia Health Sciences University, respectively. He also has a Master's in Clinical Investigation from The Scripps Research Institute. 15+ yrs clinical practice in Cardiology and vascular diseases.



# Whitney Tolpinrud, MD FAAD

https://www.linkedin.com/in/whitney-tolpinrud-md-faad-

bo31b61bb?utm source=share&utm campaign=share via&utm content=profile&utm medium=ios app

Dr. Tolpinrud began her career as a Dermatologist at Bruder Dermatology and then founded the Dermatology Clinic at Chickasaw Nation Medical Center in the same year. In 2020 she was appointed as Medical Director and Associate Medical Director at Curology. Whitney attended Yale University School of Medicine and obtained her Doctor of Medicine. Following this, she completed an Internal Medicine Internship at Brigham and Women's Hospital, Harvard University and a Dermatology Residency at Columbia University.



**Sherwin Dsouza, MD** (Endocrinology & Lipidologist) 20+ years of practice in endocrinology and metabolic syndrome. <a href="https://www.stlukesonline.org/health-services/providers/dsouza-sherwin">https://www.stlukesonline.org/health-services/providers/dsouza-sherwin</a>



Saira Hussain, MD
Founder Wellness Health Solutions.
Fellow at Andrew Weil Center for Integrative Medicine
Food is Your Medicine, Founder.
https://awcim.arizona.edu



Integrative Medicine is healing-oriented medicine that takes account of the whole person, including all aspects of lifestyle. It emphasizes the therapeutic relationship between practitioner and patient, is informed by evidence, and makes use of all appropriate therapies.

Kasie Vaughan, (Client Care Co-ordinator)



Jessica Lewis, RN (Client Clinical Coordinator)



# Simon Sinek's Golden Circle for HealthSpan 360° Clinic

# WHY - Our Purpose, Cause and Belief:

Twenty years ago, I founded the Idaho Kidney Institute to serve the people of Idaho. Every day in our seven different locations, we see between 120-150 patients grappling with varying degrees of chronic kidney disease. Tragically, 80% of these patients are battling either diabetes, hypertension, or a combination of both as their underlying cause for their chronic kidney disease and cardiovascular disease. An even more startling revelation is that about half of this group could have been spared from these afflictions if only there had been early interventions decades prior. These individuals might never have needed to become my patients. Such reflections were the catalyst behind the inception of HealthSpan 360° Clinic. We believe in a world where early and "proactive" health interventions can prevent the onset of chronic life-threatening conditions. Our mission is to transform the health trajectories of future generations, emphasizing prevention and ensuring they lead the healthiest, most fulfilling lives possible. And hence maximizing your HealthSpan.

# **HOW** – Our Process and Approach:

At HealthSpan 360° Clinic, we've revolutionized the traditional approach to healthcare. Instead of a single physician deciphering your health needs and evaluations, we embrace a team approach. Our clients benefit from a **council of healthcare advisors**, each a specialist in their respective field of medicine. Working in harmony, they function as counselors, advisors, and supporters, managing your health span and the potential risks of the future. With their combined expertise, they harness the latest interventions, information, and technology to shape your health journey. Think of this council not just as healthcare providers, but as your personal health coaches, committed to guiding you towards achieving a comprehensive, 360-degree health span.

This approach emphasizes the collaborative, cutting-edge, and personalized nature of the HealthSpan 360° Clinic's methodology. This does not replace the important relationship that you should have with your own primary care physician. However, allow this to enrich that relationship with additional resources and physicians on your healthcare team.

# WHAT - Our Products, Services, and Results:

HealthSpan 360° Clinic offers specialized health assessment programs targeting cardiovascular disease risk, insulin resistance, metabolic syndrome, and cognitive health. Through a combination of advanced diagnostics, personalized testing, individualized health plans, wellness education, and ongoing support, we provide a unique healthcare experience aimed at extending and enhancing the quality of our clients HealthSpan.

# A journey from "Red Zones" to "Green Zones" towards "Blue Zones":

Example of a client journey from "Red Zones" to "Green Zones" towards "Blue Zones" Active data collection from blood and urine testing, body composition, VO<sub>2</sub> max and other imaging are incorporated into our proprietary HealthSpan 360° approach.

Phase 1: Our initial testing both blood, urine and imaging helps us identify our clients **Red Zones**.

Phase 2: We utilize the input of our advisory team therapeutics and lifestyle interventions to help the journey of our clients into **Green Zone**.

Phase 3: This is where the real work begins for us to help our clients embark on a true longevity and wellness journey into the **Blue Zone**.

	Goal	6/8/23	12/20/23	
LIPIDS				
Particles				
APOE Genotype		E3/E3		
Apolipoprotein A	>115 mg/dl			
Apolipoprotein B	<70 mg/dl	76		
Apo B/A1 ratio	<0.77	0.37		
LDL-P	<1000 nmol/L	1032	1356	
HDL-P	>30.5 micromol/L	35.5	35.6	
Small LDL-P	<527 nmol/L		<90	
LDL size	>20.5 nm	21.6	21.6	
Cholesterol				
LDL-C	70 mg/dl		135	
HDL-C	> 55 mg/dl	87		
Triglycerides	<100 mg/dl	68	60	
Total Cholesterol	<150 mg/dl	207	233	
LP-IR Score	<25	<25	<25	
Metabolic				
A1c	<5.3	5.6	5.6	
Fasting Blood Su	<100	112		
AST	<20	26	23	
ALT	<20	21	20	
Insulin	<7	8.9	4.8	
Hormones				
Testosterone	>600	285	500	
Nutrition				
Vitamin D	50-70	29.2	39.5	
Vitamin B12	>500			
Ferritin	>100	31.6	32	
Inflammation				
Uric Acid	<4	4.5	4.5	
Homocysteine	0		9.9	
CRP	0	<0.03	<1	
ESR	0	11	8	

# A stair-step approach moving patients from Red Zones to Green, and subsequently Green to Blue Zones:

A Danish twin study looking at nearly 3000 twins born between 1870 and 1900 found that *only 20% on how long someone lives is dictated by our genes, while nearly 80% was attributed to lifestyle.* More recently, a national geographic expedition investigating the secrets to longevity led to the discovery of 5 places in the world linked to exceptional longevity. The 5 areas in Loma Linda, CA, Nicoya, Costa Rica, Sardinia, Italy, Ikaria, Greece, and Okinawa Japan have been designated blue zones (BZs), with centenarians present at 10x the rate of most places around the world.

The inhabitants of these geographies not only survived but thrived living active lifestyles well into their 100s. **Several key modifiable areas were identified to slow the aging process:** 

- Moving naturally. The blue zones inhabitants didn't pump iron or belong to gyms, but rather moved naturally
  and frequently throughout the day. Gardening, house work, and walking were frequent staples of their daily
  routine
- 2. Having purpose: Knowing your "why"
- 3. Coping with stress:
- 4. 80% rule, eat till you're 80% full.
- 5. Plant slant diets
- 6. Belonging & Community: over 90% of centenarians belonged to a closed nit community.
- 7. Family: Most BZ households lived with aging grandparents and invested significant time with a life partner and their children and grandchildren
- 8. Positive outlook on life: Depression is far below developed world averages in BZs and is thought to be secondary to the community, purpose, frequent social interactions, and increased movement.

As we move you from your health 'red zones' to green, we will simultaneously assess how we can successfully nudge you from green to blue while addressing key areas on movement kinetics, nutrition, fitness levels (VO<sub>2</sub> max), sleep, social support networks, and mental health.

This transformation will be lifelong and focused on areas 1-8 noted above, but also supported by the latest in science and technology including wearables for sleep, glucose, nutrition and fitness tracking apps and devices.

Evidence-based biohacking techniques will be reviewed and integrated where appropriate including the use of trauma informed breath-work, sound therapy, sauna, cold water immersion, stretching, and high intensity interval (HIT) training.

During this process, you will be optimally equipped to be more aware and intervene early when your daily micro-environments are having deleterious effects on your physical, emotional, and/or mental health. This early response system will minimize long term stress, elevated cortisol, and maximize your opportunity for long term healthspan and happiness.

# Understanding the science of aging and Geroprotective effects of lifestyle changes.

At HealthSpan 360°, our healthcare advisory team is committed to guiding you through the complexities of aging, leveraging the latest scientific data to optimize your health journey. Understanding the multifaceted nature of aging, we focus on individualized strategies for optimal health outcomes, including enhancing the levels of key anti-aging proteins such as UCP1 (Uncoupling Protein 1), GPLD-1 (Glycosylphosphatidylinositol-Specific Phospholipase D1), and Irisin through lifestyle interventions.

Regular exercise and specific dietary choices are known to boost these proteins, each playing a significant role in combating aging-related insulin resistance, metabolic syndrome, and other age-related changes. UCP1, a mitochondrial protein, increases with exercise, guarding against metabolic syndrome. GPLD-1, measurable in plasma, also rises with physical activity, contributing to improved metabolic functions. Irisin, enhanced by Zone-II exercise and lifestyle modifications, aids in metabolic regulation. Additionally, dietary practices like caloric restriction, intermittent

fasting and a methionine-restricted diet, often low in red meat, have been linked with increased longevity and improved metabolic health.

To achieve these outcomes at HealthSpan 360°, we begin with a thorough assessment of your VO2 max, Lactate threshold and heart rate-based Zones, (VAT) Visceral adipose tissue, A/G ratio - Android fat (Abdomen region) to your Gynoid fat (hip region) and RMR resting metabolic rate. This approach allows us to craft exercise and nutritional plans uniquely tailored to your individual needs and physiological profile. By integrating this precise data with our understanding of aging biology, we design interventions that not only decelerate the aging process but also boost your overall vitality. Whether fine-tuning your diet to enhance metabolic health or developing a fitness regimen to elevate your VO2 max, our strategies are rooted in scientific evidence and personalized to your unique health parameters. We believe that aging gracefully is not just a possibility but a science, and with the right guidance, it's an achievable goal. Our healthcare advisory team is committed to partnering with you on this journey, ensuring that every step is informed, effective, and aligned with your health aspirations.

# HealthSpan 360° Clinic-Client Experience

# Step 1:

The Client Coordinator Specialist will contact you with instructions on how to register for our electronic system. You will be sent electronic forms to fill out your health history. The following HealthSpan 360° lab tests will be ordered for you and coordinated for you to get them drawn near where you live. These lab tests should be performed in the morning (7-10AM) and fasting for at least 8 hours.

#### **General Health Panel**

- Comprehensive Metabolic Panel
- Direct-Indirect Billirubin

- ❖ UA w/ Micro, reflex to Urine Culture if indicated.
- ❖ Micro-ALBUMIN URINE (Protein-Creatinine Ratio Spot)
- CREATININE, URINE
- ❖ MAGNESIUM
- PHOSPHORUS
- CBC & PLATELETS(AUTO)

# Metabolic Syndrome and Insulin Resistance

- HEMOGLOBIN GLYCLATED (HGB A1C)
- 2Hr Glucose Tolerance Test. With both Insulin and Glucose levels (75gm Glucose load)
- CGM- Continuous Glucose Monitoring (if indicated)
- Gut micro-biome evaluation.

#### Hormones:

- ❖ TSH (THYROID STIMULATING HORMONE)
- Free T<sub>3</sub>, Free T<sub>4</sub>
- Testosterone Free, Testosterone Total, SHBG, % Free Testosterone (Male)
- LH, FSH, Progesterone, Testosterone, Estradiol (Female)
- ❖ AM Cortisol Level

# **Inflammatory Markers:**

- CRP High Sensitivity
- Homocysteine
- ❖ ESR
- Uric Acid

#### Vitamin Levels:

- Vitamin D 25-OH (ng/ml)
- ❖ IRON
- ❖ IRON BINDING CAPACITY (TIBC)
- FERRITIN
- Vitamin B12/Methylmalonic Acid

# Cardiovascular risk assessment and understanding genetic predisposition.

- NMR Lipoprotein Fractionation, with Lipid Panel and Graphs
- Apolipoprotein B (Apo B)
- ❖ Apolipoprotein A1
- ❖ Apo B/A1 ratio
- Cardio IQ Apo-E Genotyope

# **Preventative Health Screening Recommendations:**

#### Males

- ❖ PSA (PROSTATE SPECIFIC ANTIGEN)
- Colonoscopy
- Low dose Chest CT (history of smoking)

#### **Females**

- Mammogram
- Pap Smear
- Colonoscopy
- Low dose Chest CT (history of smoking)

#### Step 2:

Your results will be evaluated by your HealthSpan 360° Provider's Team, and a treatment plan will be formulated based on your specific areas of HealthSpan needs. The team will consult with a Lipidologist, Diabetes and Metabolic Syndrome Physician if

needed. The Team will set up a virtual consult with you and then discuss the findings and plan of care. Any further testing if indicated at this point like the following will be addressed.

- CGM Continuous Glucose Monitoring and food diaries.
- Coronary CT scan to evaluate Coronary Calcium Scoring
- DEXA Scan/Full Body Scan
- X-Ray Chest
- Total Body MRI as needed.
- Vitamin Supplementations and Hormone supplements etc.
- Comprehensive Physical Activity Plan and coaching directions.
- Need to see a dietician.
- Pro-biotic supplementation.

# Step 3: Follow up and evaluation phase.

Your progress will be monitored with the help of our care coordinator any barriers to achieving your optimal HealthSpan goals will be discussed, and solutions provided via email and phone communication.

# Step 4: Repeat Testing and further evaluation. (6-8 months milestone)

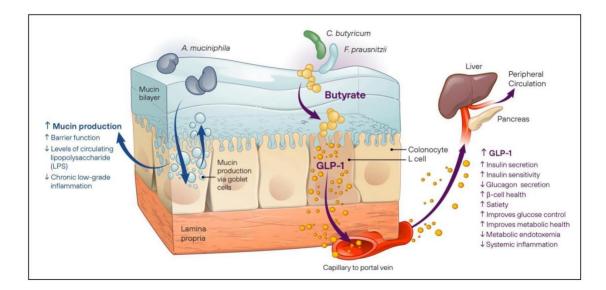
Total Duration to achieve HealthSpan 360 is about 24 months.

# Revolutionizing Wellness: GLP-1 and Microbiome Harmony at HealthSpan 360°

At HealthSpan 360°, our pioneering vision is set to transform wellness and preventative healthcare through innovative gut biome research, with a special emphasis on the crucial role of GLP-1 (Glucagon-Like Peptide-1). Recognizing the profound influence of the gut microbiome on overall health, we are advancing through strategic partnerships with leading academic and commercial experts in gut microbiome research, probiotics, and GLP-1 therapies. Our integrated approach is specifically designed to combat and prevent chronic illnesses such as insulin resistance and metabolic syndrome, drawing on the latest findings that highlight the gut's pivotal role in producing GLP-1. This hormone, crucial for glucose metabolism and insulin modulation, can be naturally stimulated by a well-balanced gut biome, offering a novel way to manage metabolic health. By analyzing and tailoring the gut microbiota of our clients, we aim to develop personalized nutrition and lifestyle plans that not only foster a beneficial microbiome environment but also optimize GLP-1 production. This strategy is deeply rooted in the latest scientific insights, underscoring the gut microbiome's significant impact on immune function, metabolic health, and even mental well-being. Our commitment transcends traditional healthcare methods, focusing on proactive measures to nurture and balance the gut biome, thereby enhancing our

clients' healthSpan. At HealthSpan 360°, we are dedicated to delivering a holistic and scientifically grounded wellness experience, empowering our clients to lead healthier, more vibrant lives through the targeted management of their gut health and the innovative use of GLP-1 enhancing strategies.<sup>2</sup>

The gut-metabolism axis: How gut microbes help regulate metabolic functions, affecting body weight, glucose control, obesity and overall health.<sup>3</sup>



<sup>&</sup>lt;sup>2</sup> https://drc.bmj.com/content/bmjdrc/8/1/e001319.full.pdf

 $<sup>^3</sup> https://cdn.shopify.com/s/files/1/0175/3104/3894/files/Gut\_metabolism\_axis\_White\_Paper\_Final-v1.docx.pdf?v\%3D1675729218\&sa=D\&source=docs\&ust=1680096582858507\&usg=AOvVaw2vWTeMIOlaWqsZEKL-sWFu$ 

# Our Fee Structure at HealthSpan 360°

As we gear up for the official launch of HealthSpan 360°, we're currently in an exciting phase of beta testing with our pioneering clients. Our official annual subscription<sup>4</sup>, set to commence with our grand opening August 2024, will be \$10,000/year with a 2-year membership. This fee reflects the comprehensive and personalized healthcare services we provide, centered around prevention and wellness. However, as part of our beta phase, we are offering a reduced fee of \$5500/yr to our early adopters (Closed Now). This special rate is our way of saying thank you to those who are helping us refine and perfect our services. By joining us now, you become a crucial part of our journey towards transforming healthcare, and you get to enjoy the benefits of our concierge medicine services at this exclusive rate. After two years the fee is dropped to \$3000 per year for our optimal maintenance phase.

# HealthSpan 360° Background Information

The following information is to expand your knowledge base about the importance and reasoning behind why each of the tests ordered will affect longevity. This is just informational so do not feel overwhelmed by the material discussed. As your advisors we will discuss in detail your results and develop an individualized plan of care.

#### General Health Panel

- Comprehensive Metabolic Panel
- Direct-Indirect Billirubin
- ❖ UA w/ Micro, reflex to Urine Culture if indicated.
- ❖ Micro-ALBUMIN URINE (Protein-Creatinine Ratio Spot)
- CREATININE, URINE
- ❖ MAGNESIUM
- PHOSPHORUS
- CBC & PLATELETS(AUTO)

A Comprehensive Metabolic Panel (CMP) provides crucial information about body's chemical balance and metabolism. It encompasses a variety of tests that offer insights into various functions and parameters of your body.

Liver Function: The liver is pivotal in processing nutrients, producing proteins, and detoxifying the body. Tests such as AST, ALT, ALK, and Direct-Indirect Bilirubin offer a window into liver health and function. Abnormalities in these markers might point to liver diseases or damage. ALT goal < 30 in Males and <20 in Females.

Kidney Function: The kidneys are responsible for filtering waste products from the blood. The CMP includes parameters like Creatinine with Glomerular Filtration Rate (GFR) which provides insights into kidney function. A reduced GFR can indicate compromised kidney function. Additionally, the Micro-ALBUMIN URINE test (Protein-Creatinine Ratio Spot) and the CREATININE, URINE test can detect early signs of kidney damage, often before other symptoms appear.

UA w/ Micro: A urinalysis with microscopy examines urine for signs of kidney disease or urinary tract infections. If abnormalities are found, a reflex to urine culture is done to identify potential pathogens.

Electrolyte Balance: Electrolytes help maintain the body's fluid balance, muscle action, and other processes. Magnesium and phosphorus are among the key electrolytes evaluated in the CMP to ensure they're at proper levels.

Fasting Blood Sugar and Proteins: Blood glucose levels provide insights into sugar metabolism, and protein levels (like albumin) can give clues about nutrition and liver function.

CBC & PLATELETS(AUTO): This test evaluates components of blood, including red blood cells, white blood cells, and platelets. It can diagnose conditions like anemia, infection, and many other blood disorders.

<sup>&</sup>lt;sup>4</sup> Annual fee includes all physicians' consultations, 24/7 access to a fully dedicated family doctor, initial screening and 2 follow up labs through LabCorp, VO<sub>2</sub> testing and DXA scan. Medications, supplements and additional specialized imaging like Ultrasound Liver Total Body MRI, CT Coronary screening, Vascular imaging like carotids and peripheral vascular screening incurs additional cost (or through insurance) which will be discussed prior to any specialize imaging.

By weaving together insights from these tests, the General Health Panel offers a holistic view of one's metabolic health. It delves deep into liver and kidney functions and provides a comprehensive overview of the body's metabolic processes. Such a panoramic view is instrumental in early disease detection, monitoring existing conditions, and guiding treatment plans.

# Metabolic Syndrome and Insulin Resistance

- HEMOGLOBIN GLYCLATED (HGB A1C)
- 2Hr Glucose Tolerance Test. With both Insulin and Glucose levels (75g Glucose load)
- CGM- Continuous Glucose Monitoring (if indicated)
- Gut health and the Microbiome.

The prevalence of pre-diabetes, metabolic syndrome, and insulin resistance is alarmingly rising, with forecasts suggesting that as many as 1 in 3 American adults could have diabetes by 2050, according to a recent analysis by the Centers for Disease Control (CDC). This is a stark escalation from the current statistic where one in 10 adults is living with the condition. Ann Albright, PhD., RD, director of the CDC's Division of Diabetes Translation, highlighted that approximately 23.6 million people in the United States are currently diagnosed with diabetes, and shockingly, up to a quarter of them might be unaware of their condition. Moreover, another 57 million Americans are on the precipice of developing diabetes, classified as pre-diabetic.

Beyond the immediate threat of diabetes, these metabolic disorders have broader health implications. Insulin resistance significantly contributes to Non-Alcoholic Fatty Liver Disease (NAFLD), which can progress to the severe Non-Alcoholic Steatohepatitis (NASH) and, if untreated, lead to liver cirrhosis, a leading cause of liver transplants.

Against this backdrop, tools like the HEMOGLOBIN GLYCLATED (HGB A1C) test and the 2Hr Glucose Tolerance Test become even more critical. The HGB A1C offers a glimpse into average blood glucose levels over the preceding 2-3 months, indicating compromised glucose control if elevated, suggestive of prediabetes or diabetes. In contrast, the 2Hr Glucose Tolerance Test, which assesses insulin and glucose levels post a 75g glucose challenge, can detect insulin resistance—a precursor state of elevated blood sugars.

Given these testing results and a comprehensive risk factor assessment, your HealthSpan 360\* provider's team may recommend Continuous Glucose Monitoring (CGM). CGM provides instantaneous insights into glucose dynamics, offering patients and medical professionals the information needed to adjust treatment regimens, dietary practices, and lifestyle decisions. In summary, early detection and proactive intervention, leveraging tests like HGB A1C, Glucose Tolerance, and tools like CGM, are essential not just for curbing the diabetes epidemic but also for safeguarding comprehensive metabolic and liver health.

We will be paying special attention to your ALT (Liver Function test) and that might lead us to consider doing an Ultrasound of Liver if needed to rule out fatty liver.

# Hormones:

- ❖ TSH (THYROID STIMULATING HORMONE)
- Free T<sub>3</sub>, Free T<sub>4</sub>
- Testosterone Free, Testosterone Total, SHBG, % Free Testosterone (Male)
- LH, FSH, Progesterone, Testosterone, Estradiol (Female)
- ❖ AM Cortisol Level

#### **Thyroid**

The thyroid hormone affects every organ in our body in different ways. It is a complex cycle but in the simplest terms, TSH (thyroid stimulating hormone) is released from the pituitary gland in the brain which then will "turn on" or "turn off" the thyroid gland to make the active forms of thyroid hormone. T4 is solely a product of the thyroid gland, whereas T3 is a product of the thyroid and of many other tissues, in which it is produced/converted by deiodination of T4. If there is a deficiency of active hormone, it will activate the pituitary gland to increase TSH. In contrast, if there is an excess of active thyroid hormone, it will deactivate the pituitary gland and decrease the TSH. There are various thyroid disorders and if there is an overproduction or deficiency of thyroid hormone it can affect us in different ways.

Common symptoms of hypothyroid (low thyroid) disease are:

- Fatigue and weakness
- Cold intolerance
- Dyspnea on exertion

- Weight gain
- Cognitive dysfunction
- Intellectual disability (infantile onset)
- Constipation
- Growth failure
- Dry skin
- Hoarseness
- Edema
- Decreased hearing
- Myalgia and paresthesia
- Depression
- Menorrhagia
- Arthralgia
- Pubertal delay

Common symptoms of hyperthyroid (high thyroid) disease are:

- Anxiety & Emotional lability
- Weakness
- Tremor
- Palpitations
- Heat intolerance
- Increased perspiration
- Weight loss despite a normal or increased appetite. However, some patients gain weight.
- Increase in stooling (not necessarily diarrhea)
- Urinary frequency
- Abnormal or lack of periods in women
- Gynecomastia (increased breast tissue) in men
- Erectile dysfunction in men

However, these are "classic" symptoms. Both hypothyroid and hyperthyroid symptoms can occur in a person who has high or low thyroid function. It is important to individualize diagnosis and treatment based on both the clinical picture and laboratory data.

# Late-Onset Hypogonadism (LOH): (Male Menopause)

Clinical Presentation of Male Late-Onset Hypogonadism (LOH):

- Primary Symptom: Reduced libido.
- Erectile dysfunction
- Muscle mass and strength reduction
- Increased body fat
- Osteoporosis onset due to decreased bone mineral density
- Reduced overall vitality
- Mood disturbances such as depression.
- Differential Diagnosis: Prior to establishing a LOH diagnosis, it's crucial to rule out:
- Depression
- Hypothyroidism
- Chronic alcohol use
- Medication effects (corticosteroids, antidepressants, etc.)
- Temporary testosterone decline due to acute illnesses.

# Laboratory Diagnosis:

Testosterone Measurement Timing: Circadian rhythms can affect testosterone levels. Hence, blood samples should be taken between 0700 and 1100 h.

# <u>Understanding Testosterone in the Blood:</u>

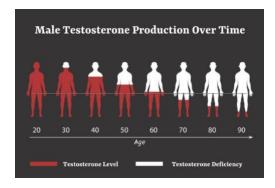
- Total Testosterone
  - o A combination of unbound and protein-bound testosterone.
- Bioavailable Testosterone
  - o Comprises the free testosterone and that bound loosely to albumin.
  - Note: The majority of testosterone is tied to SHBG and albumin.

#### Reference Values:

- Low: Below 350 ng/dl
- Normal: Above 350 ng/dl (Goal: >450)
- Borderline: Between 230 ng/dl and 350 ng/dl.
  - o In such cases, SHBG levels should also be measured to evaluate bioavailable testosterone.

# Identifying Hypogonadism Type:

- Measurement of LH and FSH levels helps determine if the hypogonadism is primary (elevated LH & FSH) or secondary (low LH & FSH).
- Normal LH and FSH levels combined with low testosterone could indicate issues with the hypothalamus or pituitary gland.



#### Male Andropause

Andropause, stemming from Greek "Andras" (human male) and "pause" (cessation), refers to a syndrome in older men marked by decreased sexual satisfaction and general well-being due to low testosterone levels. In 1946, a paper titled "The male climacteric" identified symptoms of andropause such as nervousness, decreased libido, irritability, fatigue, depression, memory problems, and sleep disturbances. Hypogonadism is a broad term for a syndrome resulting from androgen deficiency impacting multiple organ functions and quality of life. Unlike the well-defined and universal nature of menopause in women, andropause has a more gradual onset and progression. True andropause is limited to men who have lost testicular function due to diseases, accidents, or advanced prostate cancer treatments.

- Testosterone Levels: Testosterone levels naturally decrease with age, dropping at a rate of 1% annually. This decline is sharper in free testosterone levels due to shifts in sex hormone binding globulin (SHBG). However, the rate of decline varies among individuals and can be influenced by factors such as obesity, illness, stress, medications, and lifestyle.
- Symptoms & Detection: The testosterone level at which symptoms appear varies among individuals. Some may not show symptoms even with low testosterone levels. Declining testosterone can affect body functions, including frailty, obesity, cognitive decline, and erectile dysfunction. Studies have linked testosterone insufficiency in older men to a higher risk of death over subsequent years, though this association hasn't been universally confirmed.
- Prevalence & Treatment: LOH is a common yet often under-diagnosed condition in aging men. Prevalence rates range from 3.1–7.0% in men aged 30–69 years, and up to 18.4% in those older than 70 years. The European Male Aging Study reported a 2.1% prevalence based on low testosterone and specific sexual symptoms. Despite these figures, only 5–35% of hypogonadal males receive treatment.

However, just because a male's testosterone is low does not automatically mean that you need to be treated with actual testosterone. There are a lot of factors that will go into this decision. For example, adipose tissue carries estrogen which can decrease the testosterone. If we work on dietary and lifestyle changes to decrease the adipose tissue, then testosterone can increase naturally. In general, males under the age of 35 and those desiring future fertility should not be on testosterone therapy. There are other medications if needed that may be able to increase testosterone. There are long- and short-term side effects that need to be discussed at length to weigh risks vs benefits for this decision to make sure it is the right one for the individual.

# Female Perimenopause and Menopause

Female hormones play a crucial role in regulating various physiological functions within a woman's body, influencing aspects such as the menstrual cycle, fertility, and overall well-being. The primary female hormones are estrogen and progesterone, produced by the ovaries. These hormones work together in a delicate balance to maintain reproductive health, bone density, and cardiovascular function.

Perimenopause marks the transitional phase leading up to menopause, typically starting in a woman's late 30s or early 40s. During perimenopause, hormone levels fluctuate, leading to irregular menstrual cycles and various symptoms. Women may experience hot flashes, night sweats, mood swings, changes in libido, and sleep disturbances. The duration of perimenopause varies, but it usually lasts several years before menopause, which is officially diagnosed when a woman has not had a menstrual period for 12 consecutive months.

Menopause itself signifies the end of a woman's reproductive years, usually occurring around the age of 51, although it can happen earlier or later. Estrogen and progesterone levels decline significantly, leading to a range of symptoms such as vaginal dryness, thinning of the skin, mood changes, and an increased risk of osteoporosis and cardiovascular disease.

Managing the symptoms of perimenopause and menopause involves various treatment options. Hormone replacement therapy (HRT) is one common approach, which aims to replenish declining estrogen levels. HRT can alleviate hot flashes, improve bone density, and reduce the risk of heart disease. However, it is not suitable for everyone and may carry certain risks, so it's essential to discuss the potential benefits and drawbacks with a healthcare provider.

While testosterone is often associated with males, it also plays a crucial role in the female body, albeit in smaller quantities. Produced in the ovaries and adrenal glands, testosterone contributes to maintaining bone density, muscle mass, libido, and overall vitality in women. Low testosterone levels in females can lead to symptoms such as fatigue, reduced sexual desire, and mood changes. When testosterone levels drop, especially during perimenopause and menopause, some women may benefit from testosterone replacement therapy (TRT). This involves the administration of synthetic testosterone, typically through patches, gels, or injections, under the guidance of a healthcare provider. TRT aims to restore hormonal balance and alleviate symptoms associated with testosterone deficiency. However, it is essential to approach testosterone replacement with caution, as excessive levels can have adverse effects. Therefore, any consideration of testosterone therapy should involve a thorough evaluation by a healthcare professional to determine the appropriate dosage and duration based on individual health needs and considerations.

Non-hormonal interventions also exist, such as lifestyle modifications, including a healthy diet, regular exercise, and stress management, which can help alleviate symptoms. Additionally, there are medications available to address specific symptoms, such as antidepressants for mood swings or vaginal estrogen for vaginal dryness.

Navigating perimenopause and menopause involves a personalized approach, taking into account an individual's health history, preferences, and symptoms. Regular communication with a healthcare provider is crucial to developing a tailored plan that optimizes well-being and quality of life during this natural life stage.

# **AM-Cortisol Level and Its Significance:**

Cortisol, often referred to as the "stress hormone," plays a pivotal role in our body's response to stressful situations. Produced by the adrenal glands, its release is part of the body's natural rhythm, peaking in the morning and declining throughout the day. This diurnal variation is why the AM-Cortisol Level is frequently tested, as it gives an indication of the body's cortisol production pattern.

Impact of Stress & Elevated Cortisol:

As revealed by several clinical trial the human body tries to adjust to stressful situations with physiological and psychological defenses. When these defenses are overwhelmed, cortisol levels can spike. Their study found that during periods of stress, cortisol levels in healthy young individuals rose significantly, with some individuals experiencing about a 9-fold increase compared to relaxed periods. This aligns with other studies, such as those on medical students, where elevated cortisol levels were observed during exams.

Such elevated cortisol levels, especially when chronic, have several implications:

- Weight Gain: High cortisol levels have been linked to an increased appetite and cravings for sugary or fatty foods. Over time, this can lead to weight gain, particularly around the abdominal area, due to the storage of visceral fat.
- Sleep Disruptions: Chronic stress and elevated cortisol levels, especially in the evening, can interfere with the body's sleep-wake cycle. This can lead to difficulties falling asleep, frequent awakenings, or non-restorative sleep.
- Impact on Balance and Physical Responses: As observed in the clinical trial, stress can result in various physical symptoms like muscle spasms, numbness, and even balance disruptions. The study noted significant differences in both dynamic and static balance scores during stressed states compared to relaxed periods. These findings suggest a potential connection between stress-induced cortisol spikes and balance, which could be particularly relevant for athletes and individuals engaged in physical activities.
- Mood and Mental Health: Chronic elevated cortisol levels can also affect mood, leading to feelings of irritability, anxiety, or depression.

#### Conclusion:

Managing stress and monitoring cortisol levels is crucial, especially considering the extensive physiological and psychological impacts that chronic stress can have. Regular testing, understanding the body's responses, and implementing stress-reducing strategies specially 8hrs sleep nightly can be beneficial for overall health and well-being. The connection between cortisol spikes and balance disruptions, as highlighted by the research, underscores the multifaceted impacts of stress on the human body and aging.

# Vitamin D 25-OH (ng/ml)

Vitamin D 25-OH (25-Hydroxyvitamin D) holds immense significance in various physiological functions. Experts typically advocate for maintaining its serum levels between 50-70 ng/ml to reap its optimal health benefits:

- Bone Health: Within these levels, Vitamin D aids calcium absorption in the intestines, ensuring strong bones and teeth and preventing conditions like osteoporosis, osteomalacia, and rickets.
- Immune System Boost: Vitamin D augments the defensive capabilities of monocytes and macrophages against pathogens. Furthermore, it mitigates inflammation, strengthening the immune system and potentially offering protection against infections and select autoimmune diseases.
- Mood and Brain Health: Adequate Vitamin D levels have correlations with mood stabilization, potentially assisting in combating depression. Vitamin D receptors present in the brain underline its crucial role in cognitive functions and mental wellness.
- Diabetes Management: Preliminary research indicates that vitamin D, within the 50-70 ng/ml bracket, might influence insulin regulation, potentially assisting in diabetes management.
- Cardiovascular Health: Healthy Vitamin D levels correlate with cardiovascular wellness, potentially aiding blood pressure management and diminishing the risk of conditions like coronary artery disease.
- Lung Function and Respiratory Health: Vitamin D fortifies lung function, potentially offering a defense against respiratory diseases.
- Reduced Cancer Risk: Some research suggests that maintaining Vitamin D within optimal levels might relate to a diminished risk of certain cancers, possibly owing to its role in modulating cellular growth and communication.

A worrying trend, however, is the widespread Vitamin D deficiency seen globally. Studies estimate that around one billion people worldwide suffer from Vitamin D deficiency. In the US, a staggering 42% of adults are deficient. Alarmingly, 50% of children between one and five years of age and 70% between six and 11 years exhibit low Vitamin D reserves. Additionally, the prevalence of severe and moderate Vitamin D deficiency (VDD) tends to be higher in women, making it crucial for this demographic to be particularly vigilant about their Vitamin D levels.

Ensuring Vitamin D concentrations stay within the 50-70 ng/ml range is paramount. Regular monitoring and appropriate supplementation, when necessary, can help strike this balance for holistic health.

# **Inflammatory Markers:**

- CRP High Sensitivity
- Homocysteine (LabCorp)

- ESR
- B12 and Folate level
- IRON
- ❖ IRON BINDING CAPACITY (TIBC)
- ❖ FERRITIN
- ❖ URIC ACID BLOOD

# CRP High Sensitivity (hs-CRP):

What It Is: C-reactive protein (CRP) is produced by the liver in response to inflammation. The high-sensitivity test (hs-CRP) is used to detect low levels of inflammation and is particularly useful in evaluating the risk of cardiovascular disease.

Clinical Significance: Elevated hs-CRP levels have been associated with an increased risk of heart attacks, strokes, and arterial disease. Some guidelines recommend its use in conjunction with traditional risk factors to determine the risk of cardiovascular disease.

#### Homocysteine:

What It Is: Homocysteine is an amino acid in the blood. Elevated levels can result from dietary deficiencies, particularly in vitamin B12, folic acid (vitamin B9), and vitamin B6.

Clinical Significance: High homocysteine levels have been linked to atherosclerosis (hardening and narrowing of the arteries) and an increased risk of heart attacks, strokes, blood clot formation, and possibly Alzheimer's disease.

#### Erythrocyte Sedimentation Rate (ESR):

What It Is: ESR measures the rate at which red blood cells settle in a tube over a specified period. It's a non-specific measure of inflammation.

Clinical Significance: An elevated ESR can indicate inflammation in the body, but it doesn't pinpoint its cause. It might be raised in conditions like rheumatoid arthritis, giant cell arteritis, and other inflammatory states. However, many factors can influence ESR, so it's often used in conjunction with other tests.

#### Uric Acid:

What It Is: Uric acid is a waste product formed from the breakdown of purines, which are substances found naturally in the body as well as in certain foods. Uric acid is filtered by the kidneys and excreted in the urine.

Clinical Significance:

- Gout: Elevated levels of uric acid in the blood can lead to a type of arthritis known as gout. In gout, uric acid crystallizes in the joints (especially the big toe), leading to intense pain, swelling, redness, and warmth.
- Kidney Stones: High uric acid levels can also lead to the formation of kidney stones. Uric acid stones are one type of kidney stone that can form when there's an excess amount of uric acid in the urine.
- Other Conditions: Elevated uric acid levels can be seen in conditions such as:
  - Metabolic syndrome
  - High blood pressure
  - Chronic kidney disease
  - o Diuretic use (medications that help the body get rid of excess salt and water)
- Cardiovascular Disease: Some studies have suggested a link between high uric acid levels and cardiovascular disease, although the exact relationship remains a topic of research.
- Assessment & Treatment: It's essential to determine the cause of elevated uric acid levels. Lifestyle modifications, such as limiting high-purine foods and alcohol, can help reduce uric acid levels. Medications, such as allopurinol or febuxostat, may also be prescribed to lower uric acid levels or treat gout.

When assessing inflammation or the risk of cardiovascular disease, we often look at a combination of these and other markers. It's essential to interpret these values in the context of the whole clinical picture, considering other symptoms, risk factors, and diagnostic tests.

# Cardiovascular risk assessment and understanding genetic predisposition:

- ❖ Apolipoprotein B (Apo B)
- ❖ Apolipoprotein A1
- ❖ Apo B/A1 ratio

Apolipoprotein B (Apo B) and the Apo B/A1 ratio are important markers in the assessment of cardiovascular risk. Here's why:

# o. Apolipoprotein B (Apo B):

- Function: Apo B is a primary protein found in LDL (low-density lipoprotein) and VLDL (very low-density lipoprotein). Every LDL and VLDL particle contains one molecule of Apo B. Therefore, the Apo B level provides a direct measure of the total number of atherogenic (artery-clogging) particles in the blood.
- Clinical Significance: Elevated levels of Apo B indicate a higher number of these atherogenic particles, which
  increases the risk of atherosclerotic diseases. Some research suggests that Apo B might be a better indicator of
  cardiovascular disease risk than LDL cholesterol alone, especially in people with metabolic abnormalities like
  diabetes or insulin resistance.

# Apolipoprotein A1 (Apo A1):

- . Function: Apo A is a primary protein component of high-density lipoprotein (HDL) cholesterol. HDL cholesterol is often referred to as "good cholesterol," and Apo A1 plays a significant role in its function and overall cardiovascular health.
- a. Clinical Significance of Apolipoprotein A1 (Apo A1): HDL Component: As mentioned, Apo A1 is the main protein component of HDL particles. HDL has a protective role in the cardiovascular system, helping to transport cholesterol from the arteries and tissues back to the liver for excretion, a process known as reverse cholesterol transport.
- b. Cardiovascular Protection: High levels of Apo A1 are generally associated with a decreased risk of cardiovascular disease. This is because Apo A1, through its role in HDL, helps to prevent the buildup of cholesterol in arterial walls, reducing the risk of atherosclerosis.
- c. Assessment of Cardiovascular Risk: Apo A1 levels can be used alongside other lipid markers to assess an individual's risk of cardiovascular disease. A decreased Apo A1 level might indicate reduced HDL levels and, hence, a potential increased risk for heart disease.
- 2. <u>Apo B/A1 Ratio</u>: As previously discussed, the Apo B/A1 ratio provides a balance between atherogenic (harmful) and protective lipid particles. A higher ratio indicates a higher risk for cardiovascular events. Inflammatory Marker: There's ongoing research into the role of HDL and Apo A1 in inflammation, which is a key component of atherosclerosis. Some studies suggest that HDL and Apo A1 have anti-inflammatory effects.

  While increasing Apo A1 and HDL levels theoretically should reduce cardiovascular risk, attempts to raise HDL pharmacologically (with drugs) have not shown consistent benefits in cardiovascular outcomes. This suggests that the
  - function of HDL and Apo A1 might be as important as their levels.

    Lifestyle factors such as diet, exercise, and avoiding tobacco can positively influence Apo A1 and HDL levels.

#### **Overall Implications:**

Both Apo B levels and the Apo B/A1 ratio provide a more nuanced understanding of an individual's risk for atherosclerotic
cardiovascular disease than traditional cholesterol measures alone. They can be especially valuable in patients with
conditions like diabetes, metabolic syndrome, or other situations where traditional cholesterol measurements might be
misleading.

# NMR Lipoprotein Fractionation, with Lipid Panel and Graphs (LabCorp)

The NMR (Nuclear Magnetic Resonance) Lipoprotein Fractionation test, combined with a standard lipid panel, offers a detailed assessment of a person's lipid and lipoprotein profile. Let's break it down:

# **Standard Lipid Panel:**

This typically includes:

Total Cholesterol: Measures the sum of all cholesterol in your blood.

LDL-C (Low-Density Lipoprotein): High levels are associated with an increased risk of atherosclerosis and cardiovascular disease. HDL-C (High-Density Lipoprotein): High levels are associated with a reduced risk of cardiovascular disease.

Triglycerides: A type of lipid in the blood. High levels can increase the risk of atherosclerosis and are often seen in conditions like metabolic syndrome.

# NMR Lipoprotein Fractionation:

NMR spectroscopy is used to identify the size and number of lipoprotein particles, which can provide more detailed information about cardiovascular risk than standard lipid levels alone.

- LDL-P (LDL Particle Number): Refers to the actual number of LDL particles in the blood. Some people might have normal LDL cholesterol levels but a high LDL-P, which could increase their cardiovascular risk.
- HDL-P (HDL Particle Number): The total number of HDL particles. HDL-P might give additional information about cardiovascular risk beyond standard HDL cholesterol measurements.
- Particle Size: NMR can determine the size of LDL and HDL particles. Small, dense LDL particles are believed to be more atherogenic (prone to cause plaque formation) than larger LDL particles. Conversely, larger HDL particles might offer more protection against cardiovascular disease than smaller ones.
- LP(a) Lipoprotein: Some NMR panels may also include LP(a), a lipoprotein linked to increased cardiovascular risk.

# **Clinical Significance:**

- Comprehensive Risk Assessment: The combination of a standard lipid panel with NMR lipoprotein fractionation
  provides a comprehensive assessment of cardiovascular risk, capturing both the quantity and quality of
  lipoproteins.
- Customized Treatment: This detailed insight can guide more personalized treatment strategies. For instance, someone with normal LDL cholesterol but a high LDL-P might benefit from interventions to reduce cardiovascular risk
- High-Risk Populations: The NMR test is particularly beneficial for individuals with a family history of premature heart disease or those with metabolic disturbances, like insulin resistance, where standard lipid panels may not fully capture their risk.

As with all diagnostic tests, it's crucial to interpret the results in the context of the individual's overall health, family history, and other risk factors. It's also important to work with a healthcare professional to understand the results and their implications for treatment or lifestyle changes.

# Cardio IQ Apo-E Genotyope (LabCorp)

The Apo-E genotype test is a genetic test that identifies variations in the APOE gene. These variations can influence cholesterol metabolism and are associated with the risk of cardiovascular disease and other conditions.

# Apo-E Genotyping:

- The APOE gene provides instructions for making a protein called apolipoprotein E (Apo-E). This protein combines with fats (lipids) in the body to form molecules called lipoproteins. Lipoproteins are responsible for packaging cholesterol and other fats and carrying them through the bloodstream.
- The APOE gene has several variants, but the three most common are e2, e3, and e4.

# Genotypes:

- E2/E2, E2/E3: These combinations are associated with reduced levels of total and LDL cholesterol. People with an E2 allele might have a reduced risk of cardiovascular disease but may be at an increased risk for type III hyperlipoproteinemia, a rare condition associated with increased triglycerides and cholesterol.
- E<sub>3</sub>/E<sub>3</sub>: This is the most common genotype and is often considered the "neutral" genotype in terms of cardiovascular risk.
- E<sub>3</sub>/E<sub>4</sub> and E<sub>4</sub>/E<sub>4</sub>: The presence of the E<sub>4</sub> allele has been associated with higher levels of LDL cholesterol and an increased risk of cardiovascular disease. Moreover, the E<sub>4</sub> allele is also linked to an increased risk of Alzheimer's disease.

# Clinical Significance:

- Cardiovascular Disease: The Apo-E genotype can provide insight into an individual's risk of cardiovascular disease based on their genetic cholesterol metabolism. It may influence treatment strategies, especially in those with a family history of heart disease or other risk factors.
- Alzheimer's Disease: The E4 variant is the most significant genetic risk factor for late-onset Alzheimer's disease. Individuals with one E4 allele have an increased risk, and those with two E4 alleles have an even higher risk.

# Lifestyle and Treatment Implications:

- For those with E4, lifestyle interventions like a heart-healthy diet, regular exercise, and avoiding tobacco can be crucial.
- Some studies suggest that E4 carriers might respond differently to dietary fats, so individualized dietary recommendations might be beneficial.
- Knowledge of one's Apo-E genotype can also influence cholesterol-lowering treatment strategies.
- While Apo-E genotyping provides valuable information, it's just one piece of the puzzle. It should be interpreted in the context of other risk factors, family history, and clinical assessments.
- Genetic information can have psychological implications, especially concerning conditions like Alzheimer's. Thus, it's essential to discuss the results with a knowledgeable healthcare provider who can provide context and guidance.

In conclusion, the Cardio IQ Apo-E Genotype test provides insights into genetic factors influencing cholesterol metabolism and disease risk, offering an additional layer of information for *personalized health strategies*.

# Imaging Studies that HealthSpan 360° Clinic Team might consider:

# Coronary CT for Calcium Scoring: Your Key to Early and Effective CAD Management

- Accurate Detection: Coronary CT for calcium scoring provides a non-invasive method to directly visualize and quantify
  calcified plaques in the coronary arteries. These calcified plaques are indicative of atherosclerosis and can be a precursor to
  significant coronary artery disease.
- Risk Stratification: By assigning a numeric value (the calcium score), clinicians can classify patients into different risk categories. A higher score correlates with a higher risk of heart attack or other cardiac events. This helps in tailoring treatment strategies to the individual, optimizing both prevention and intervention methods.
- Pre-symptomatic Detection: Before symptoms even manifest, calcium scoring can identify at-risk individuals. This is particularly valuable for asymptomatic patients who might have risk factors for CAD but don't yet show symptoms.
- Quick and Non-Invasive: The test is fast, usually completed in under 15 minutes, and doesn't require the use of any contrast agents, which can be beneficial for those with allergies or renal impairments.
- Cost-Effective: Compared to more invasive diagnostic procedures like coronary angiography, calcium scoring is a cost-effective method to evaluate the potential risk of CAD in individuals.
- Guided Treatment Plans: The results from calcium scoring can guide therapeutic decisions. For instance, someone with a high calcium score might benefit from more aggressive management, such as statin therapy, even if they're asymptomatic.

• Reassurance: For those with a low or zero calcium score, the test can provide reassurance and potentially lessen the need for other, more invasive diagnostic tests.

In sum, the Coronary CT for Calcium Scoring offers a valuable, efficient, and effective tool for identifying and managing high-risk patients with CAD, making it an indispensable tool in modern cardiology practice.

#### Liver Ultrasound for Hepatic Steatosis Assessment: Comprehensive Guide to Early Liver Health

- Direct Visualization: Ultrasound provides a real-time imaging method to visualize the structure of the liver. It helps in identifying the characteristic bright or "steatotic" appearance of the liver, suggesting fat accumulation.
- Early Detection: Hepatic steatosis, or fatty liver, is a precursor to more severe liver conditions like non-alcoholic steatohepatitis (NASH) or cirrhosis. Detecting it early in insulin-resistant patients can lead to timely interventions, potentially preventing disease progression.
- Non-Invasive & Safe: Liver ultrasound is a non-invasive procedure, eliminating the risks associated with invasive techniques. It doesn't involve radiation or contrast agents, making it safe for repeated evaluations if necessary.
- Correlation with ALT Elevations: In patients with marginally elevated ALT—a liver enzyme often raised in liver diseases—an ultrasound can provide a clearer picture of whether the elevation is due to hepatic steatosis or another liver condition.
- Cost-Effective: As a screening tool, ultrasound is considerably less expensive than other imaging modalities like MRI or advanced elastography- fibrosis scan, making it a cost-effective initial evaluation method.
- Guided Treatment Decisions: Identifying hepatic steatosis in its early stages can guide healthcare providers in tailoring interventions. This could include dietary modifications, weight loss strategies, or specific medications to address insulin resistance and liver health.
- Patient Education: Visual evidence of fatty infiltration in the liver can serve as a powerful motivational tool for patients, emphasizing the need for lifestyle changes or adherence to prescribed treatments.
- Versatility: Beyond assessing hepatic steatosis, liver ultrasound can also identify other liver abnormalities, such as liver cysts, tumors, or vascular issues, offering a comprehensive liver evaluation.

In essence, liver ultrasound stands as a cornerstone tool for the proactive assessment and management of hepatic steatosis, especially in insulin-resistant patients with subtle ALT elevations. It delivers insights that can guide both patient and practitioner toward better liver health outcomes.

#### ❖ Value Proposition of DEXA Scan in Metabolic Health Assessment:

The DEXA scan stands as a pivotal tool in unveiling the nuances of fat distribution, a crucial factor influencing metabolic health. While abdominal obesity might be overt, it's the unseen visceral fat that poses substantial metabolic challenges. Clinical research has illuminated the correlation between visceral fat and metabolic disturbances, even in individuals with a standard BMI. Visceral adipocytes, characterized by enhanced lipolytic activity, lead to metabolic disruptions via lipotoxicity. Moreover, they release proinflammatory cytokines, further perturbing metabolic functions. In contrast, subcutaneous fat emerges as a potential protective shield, with increased amounts correlating with improved metabolic markers. Beyond just identifying risk, DEXA scans can discern the "metabolically healthy" obese individuals, offering a granular understanding of one's metabolic profile and directing tailored health interventions.

- Holistic Health Overview: The DEXA scan offers a detailed breakdown of various body components. This granularity is beneficial for a broad audience, from athletes tracking their muscle mass to individuals simply curious about their health.
- Total Body Fat Percentage (%BF): This metric provides insights into the proportion of one's body composed of fat, influenced by both fat and lean mass amounts.
- Fat Mass Index (FMI): A measure of total fat relative to an individual's height, independent of lean mass. It contextualizes fat amount concerning one's size.
- Visceral Adipose Tissue (VAT): Reflects the amount of internal abdominal fat. Different from subcutaneous fat, elevated VAT is linked with higher cardiovascular and metabolic disease risk, with current research showing elevated risk at around 100-160 cm<sup>2</sup>.
- A/G ratio (Android to Gynoid Ratio) Indicates where fat is predominantly stored. Ideal values are less than 0.8 for women and 1.0 for men.
- Skeletal Muscle Mass (SMM & %SMM): Although direct skeletal muscle mass measurement is challenging, DEXA provides an accurate estimate, comparable to MRI or CT measurements.
- Appendicular Lean Mass Ratios (ALM/Height^2 & ALM/BMI): These ratios assess the risk factor for sarcopenia. They provide insights into lean mass in arms and legs concerning height or Body Mass Index.

- Resting Metabolic Rate (RMR): An estimate of calorie requirements to maintain current body mass under resting conditions. The value is based on tissue amounts and their metabolic rates, indicating the "ideal" RMR.
- Bone Density: A crucial metric to gauge osteopenia and osteoporosis risk. Both z-scores (comparison to age-matched peers) and t-scores (comparison to a 30-year-old) offer insights into bone health.
- Versatile Applicability: Athletes can track muscle and fat percentages for performance optimization. Similarly, any health-conscious individual can use DEXA to gain insights into their body composition and potential health risks, making informed decisions for optimal well-being.