Biomarkers of Longevity, Healthspan, and Performance

From Disease Detection to Defining Health

Brooks Leitner, MD, PhD | Co-Founder, CEO VO Health

Prepared for: MEDICALFITNESS Association

Content of Today's Presentation

- Why Do Biomarkers Matter for Healthcare & Performance?
- Why Biomarkers of Disease Detection are Failing at Mitigating Chronic Disease
- A Case Study on Insulin Resistance
- Biomarkers that Enable Measurement of Health Rather than Disease
- How Technology is Enabling the Future of Biomarkers
- Implementations of Biomarker-Driven Preventive and Performance Medicine
- Real-World Partnership for Fitness in Cancer Survivors (VO Health & Yale School of Public Health)

Content of Today's Presentation

- **Why Do Biomarkers Matter for Healthcare & Performance?**
- Why Biomarkers of Disease Detection are Failing at Mitigating Chronic Disease
- A Case Study on Insulin Resistance
- Biomarkers that Enable Measurement of Health Rather than Disease
- How Technology is Enabling the Future of Biomarkers
- Implementations of Biomarker-Driven Preventive and Performance Medicine
- Real-World Partnership for Fitness in Cancer Survivors (VO Health & Yale School of Public Health)

What is a Biomarker?

Any characteristic that serves as an indicator of a **biological function**, state of **health**, or metric reflecting a health-related **process**.




Uses:

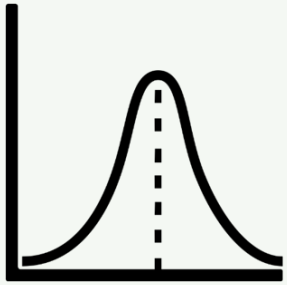
- **Diagnosis**
- **Disease/Risk Prediction**
- **Safety**
- **Monitoring**
- **Treatment Response**
- **Prognosis**

What Makes a Great Biomarker?

An ideal biomarker **maximizes benefits**, clarifies **how individuals and healthcare teams should proceed,** is **easy to measure and track**, and **responds** to specific interventions

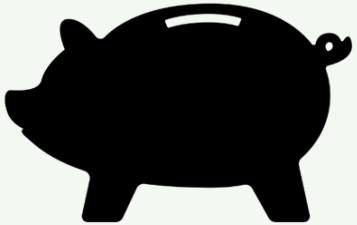
- **Predictive**
- **Actionable**
- **Responsive**
- Explainable
- Feasible
- Minimally Invasive

Biomarkers are Necessary for the Allocation of Attention and Resources at the System Level



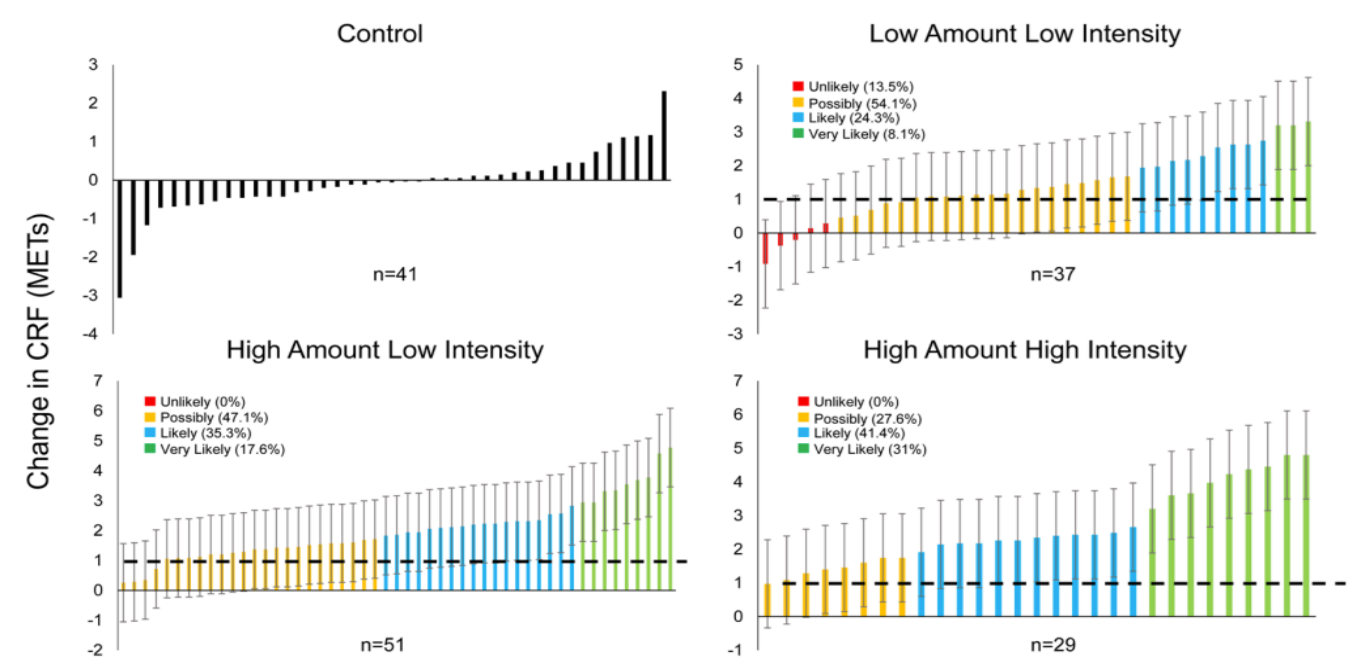
Standardization of Disease Measures for Population Health Studies

Government's Incentives to Contain US Healthcare Costs



Payer Incentives to Mitigate Costly Short Term Outcomes by Normalizing Biomarkers

Biomarkers Can Inform Variability in Response to Training or Treatment



Ross R, et al. Br J Sports Med 2019

Content of Today's Presentation

- Why Do Biomarkers Matter for Healthcare & Performance?
- **Why Biomarkers of Disease Detection are Failing at Mitigating Chronic Disease**
- A Case Study on Insulin Resistance
- Biomarkers that Enable Measurement of Health Rather than Disease
- How Technology is Enabling the Future of Biomarkers
- Implementations of Biomarker-Driven Preventive and Performance Medicine
- Real-World Partnership for Fitness in Cancer Survivors (VO Health & Yale School of Public Health)

Evolution of Biomarkers in US Healthcare

	Early 20th Century (Acute disease era)
Health Challenges	 Nutrient deficiencies  Infectious diseases
Major Causes of Disability, Mortality	1.Influenza/pneumonia 2.Tuberculosis 3.Diarrhea/enteritis *(1900)*
Technology & Trends	• Microbiology testing • Biochemical assays
Exemplar Biomarkers	• ABO Blood typing • Blood test of syphilis • BUN, Creatinine, glucose • Vitamin B12, Folate

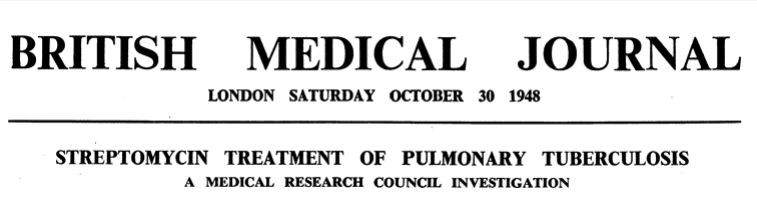
Evolution of Biomarkers in US Healthcare

	Early 20th Century (Acute disease era)	**Mid 20th Century** (Expansion of chronic diseases)
Health Challenges	 Nutrient deficiencies  Infectious diseases	 Smoking (in 1955, 56.9% of men and 28.4% of women)  Heart disease
Major Causes of Disability, Mortality	1.Influenza/pneumonia 2.Tuberculosis 3.Diarrhea/enteritis *(1900)*	1.Heart Disease 2.Cancer 3.Stroke *(1950)*
Technology & Trends	• Microbiology testing • Biochemical assays	• Framingham Heart Study • Shift towards early risk screening (proactive) • Multiplexed biochemical assays • Hypercholesterolemia & hypertension classified as "disease"
Exemplar Biomarkers	• ABO Blood typing • Blood test of syphilis • BUN, Creatinine, glucose • Vitamin B12, Folate	• Lipid and cholesterol panels • Basic Metabolic Panels • Thyroid function testing • Newborn screening (e.g. phenylketonuria)

Evolution of Biomarkers in US Healthcare

	Early 20th Century (Acute disease era)	Mid 20th Century (Expansion of chronic diseases)	Late 20th Century (Era of precision medicine)
Health Challenges	 Nutrient deficiencies  Infectious diseases	 Smoking (in 1955, 56.9% of men and 28.4% of women)  Heart disease	 Cancer (emerging understanding of immune system)  Metabolic Syndrome
Major Causes of Disability, Mortality	1.Influenza/pneumonia 2.Tuberculosis 3.Diarrhea/enteritis *(1900)*	1.Heart Disease 2.Cancer 3.Stroke *(1950)*	1.Heart Disease 2.Cancer 3.Low Back Pain (3rd leading contributor to DALYs) *(1990)*
Technology & Trends	• Microbiology testing • Biochemical assays	• Framingham Heart Study • Shift towards early risk screening (proactive) • Multiplexed biochemical assays • Hypercholesterolemia & hypertension classified as "disease"	• Human Genome Project • Polymerase chain reaction (PCR) • Genomic testing (risk alleles, etc.) • Companion Diagnostics • Proteomics (early) • Epigenomics (early)
Exemplar Biomarkers	• ABO Blood typing • Blood test of syphilis • BUN, Creatinine, glucose • Vitamin B12, Folate	• Lipid and cholesterol panels • Basic Metabolic Panels • Thyroid function testing • Newborn screening (e.g. phenylketonuria)	• HER2+ IHC test (Breast Cancer) • PD-L1 Expression (Cancer Immunotherapy) • Cologuard (epigenetic colon cancer screening test)

The Chronic Disease Management Toolkit is Based on Model of Infectious Disease

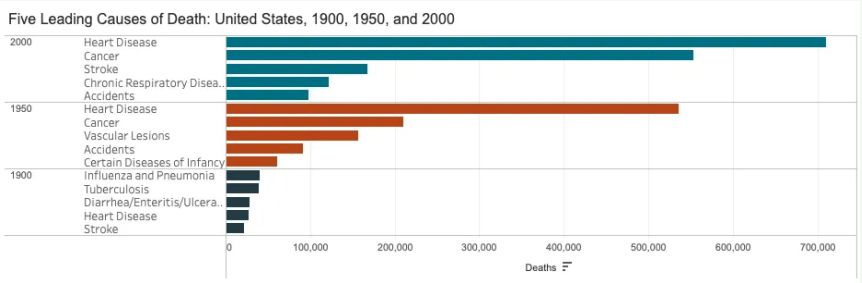


BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 30 1948

STREPTOMYCIN TREATMENT OF PULMONARY TUBERCULOSIS

A MEDICAL RESEARCH COUNCIL INVESTIGATION



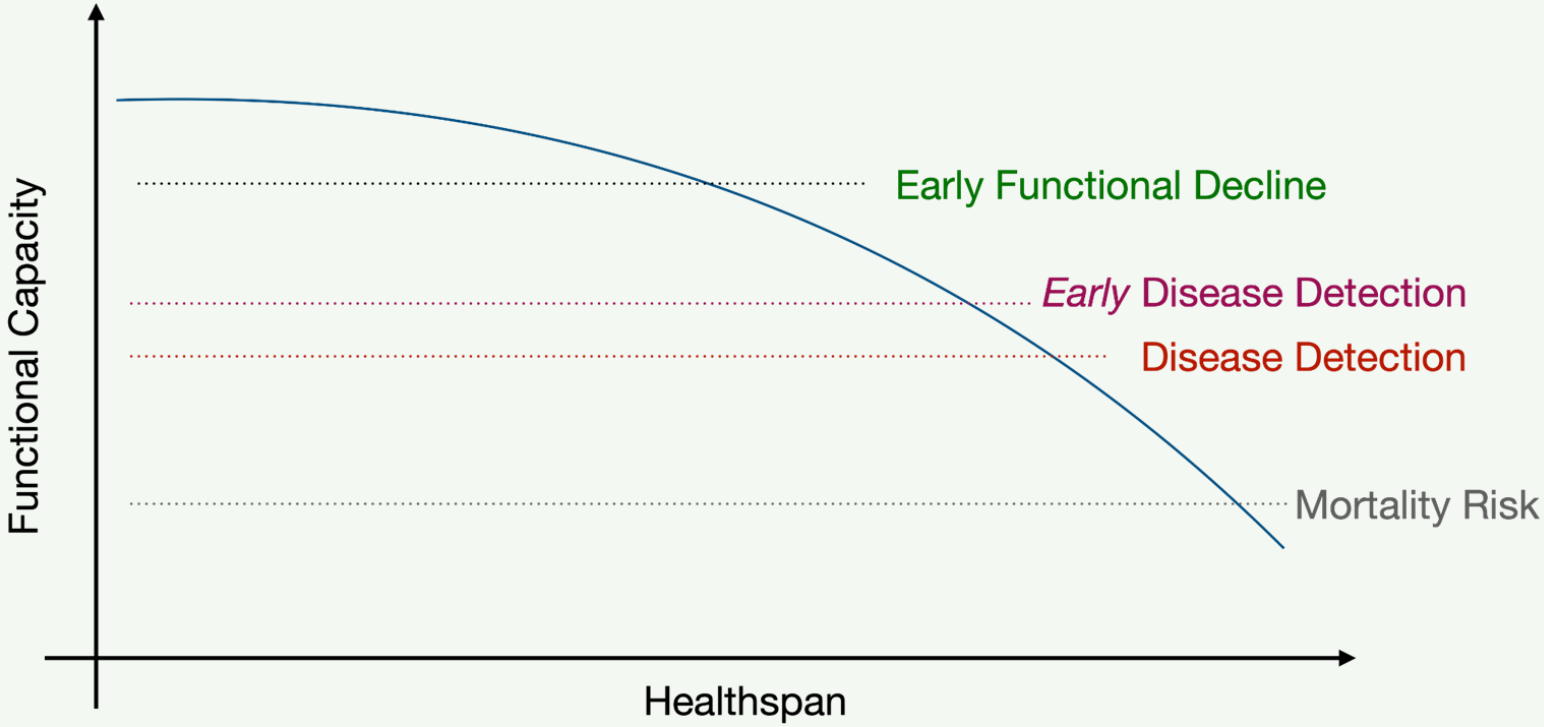
Success in Infectious Disease Mitigation & Vitamin Deficiency Treatment in early 1900s

Population Wide Datasets Enabling ID of Chronic Disease "Risk Factors" *(e.g. 1948 Launch of Framingham Heart Study)*

Life Expectancy in US
1900: 47 years
1950: 68 years

Smoking, high blood pressure, obesity, high cholesterol, and physical inactivity as risk factors for heart disease

Traditional Biomarkers are Designed to Detect Disease Well After Decline in Function



Content of Today’s Presentation

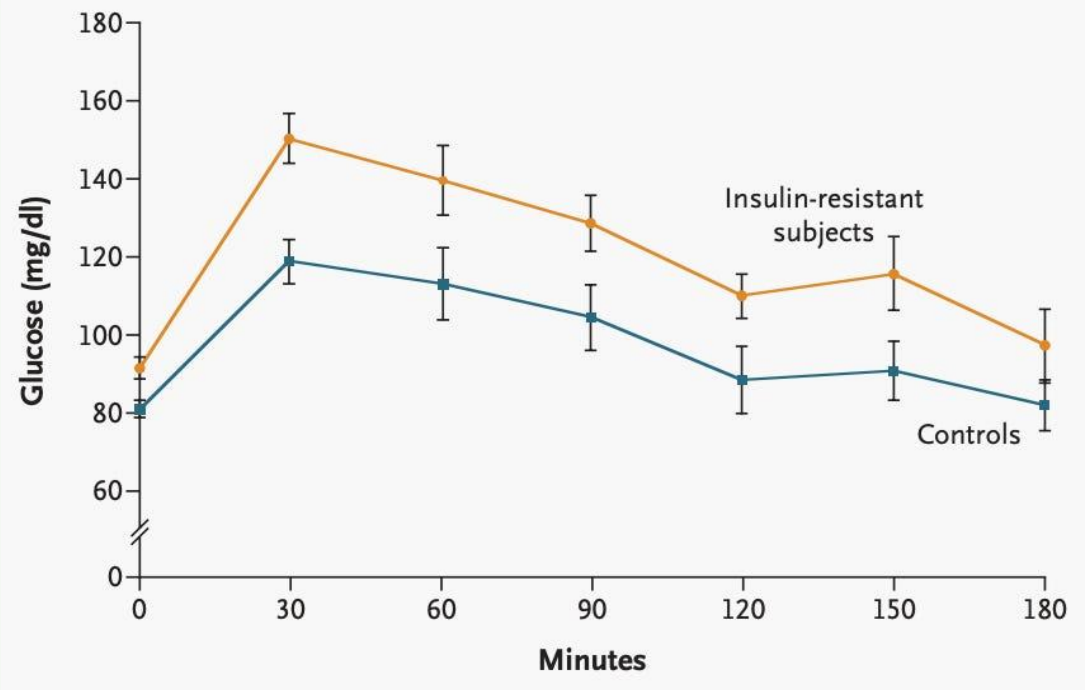
- Why Do Biomarkers Matter for Healthcare & Performance?
- Why Biomarkers of Disease Detection are Failing at Mitigating Chronic Disease
- **A Case Study on Insulin Resistance**
- Biomarkers that Enable Measurement of Health Rather than Disease
- How Technology is Enabling the Future of Biomarkers
- Implementations of Biomarker-Driven Preventive and Performance Medicine
- Real-World Partnership for Fitness in Cancer Survivors (VO Health & Yale School of Public Health)

A Case Study of Insulin Resistance in Young Healthy Adults

	Insulin Sensitive	Insulin Resistant
Age (yr)	28±7	26±7
Weight (kg)	60±13	64±9
Height (m)	1.69±0.11	1.65±0.09
Body-mass index	21±2	23±2
Activity index†	2.6±0.5	2.4±0.4
Glycosylated hemoglobin (%)‡	5.1±0.3	5.2±0.4
Adipocyte-derived factors		
Adiponectin (μg/ml)	12±4	11±4
Tumor necrosis factor α (pg/ml)	1.5±0.3	1.8±0.9
Interleukin-6 (pg/ml)	0.52±0.31	0.68±0.42
Resistin (ng/ml)	0.77±0.24	0.79±0.24

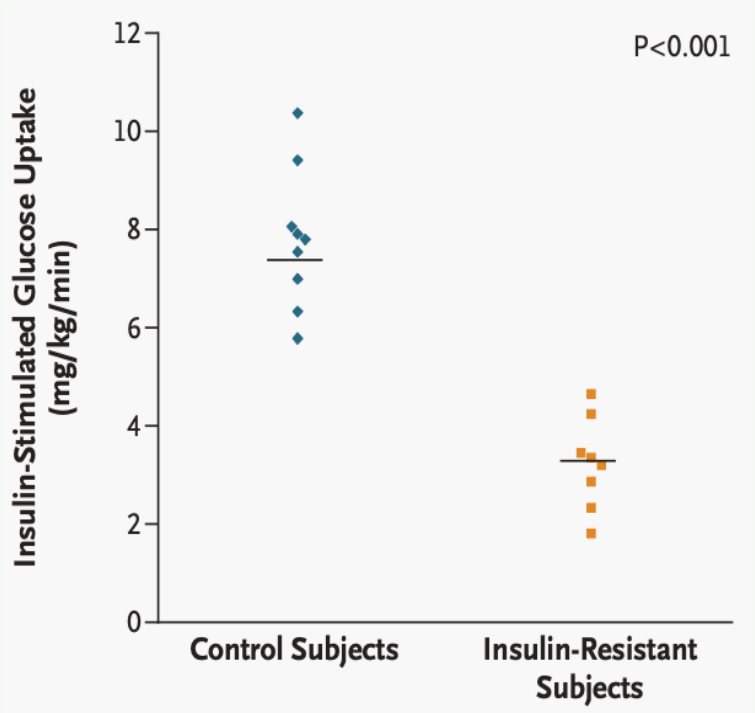
Petersen et al. NEJM 2004

Impaired Glucose Tolerance Upon Functional Assessment (Oral Glucose Tolerance Test)



Petersen et al. NEJM 2004

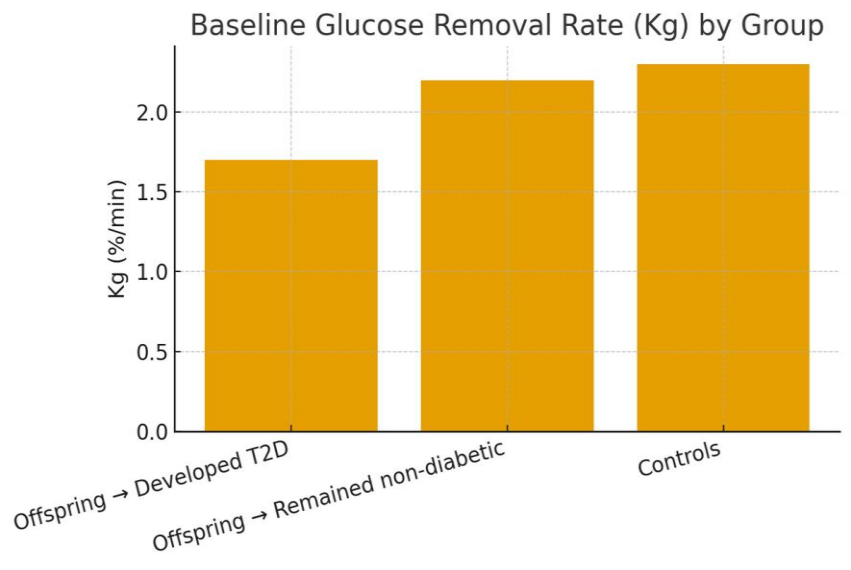
Impaired Insulin Sensitivity Upon Functional Assessment (Hyperinsulinemic Euglycemic Clamp)



Petersen et al. NEJM 2004

“**One to two decades before type II diabetes is diagnosed,** reduced glucose clearance is already present”

Average 13 Year Follow-Up



Warram et al. Ann. Int. Med. 1990

If We Can See Metabolic Dysfunction in Young People, *and* Have an Effective Preventive Intervention, What's the Issue?

- Biomarkers that determine resource allocation (e.g. eligibility for coverage of diabetes prevention program) are **based on lagging indicators** of functional decline
- The toolkit for functional capacity assessment exists in research facilities or performance fitness centers, and is **underutilized in clinical settings**
- Biomarkers of functional capacity are **not easily scalable, or implemented into routine clinical practice**

Content of Today's Presentation

- Why Do Biomarkers Matter for Healthcare & Performance?
- Why Biomarkers of Disease Detection are Failing at Mitigating Chronic Disease
- A Case Study on Insulin Resistance
- **Biomarkers that Enable Measurement of Health Rather than Disease**
- How Technology is Enabling the Future of Biomarkers
- Implementations of Biomarker-Driven Preventive and Performance Medicine
- Real-World Partnership for Fitness in Cancer Survivors (VO Health & Yale School of Public Health)

Functional Physiological Toolkit for Health Assessment

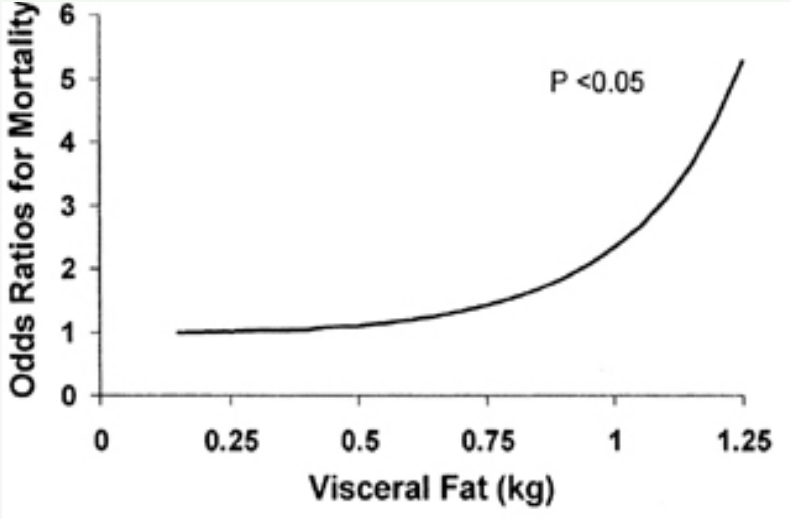
Cardiorespiratory Fitness

Body Composition

Insulin Sensitivity

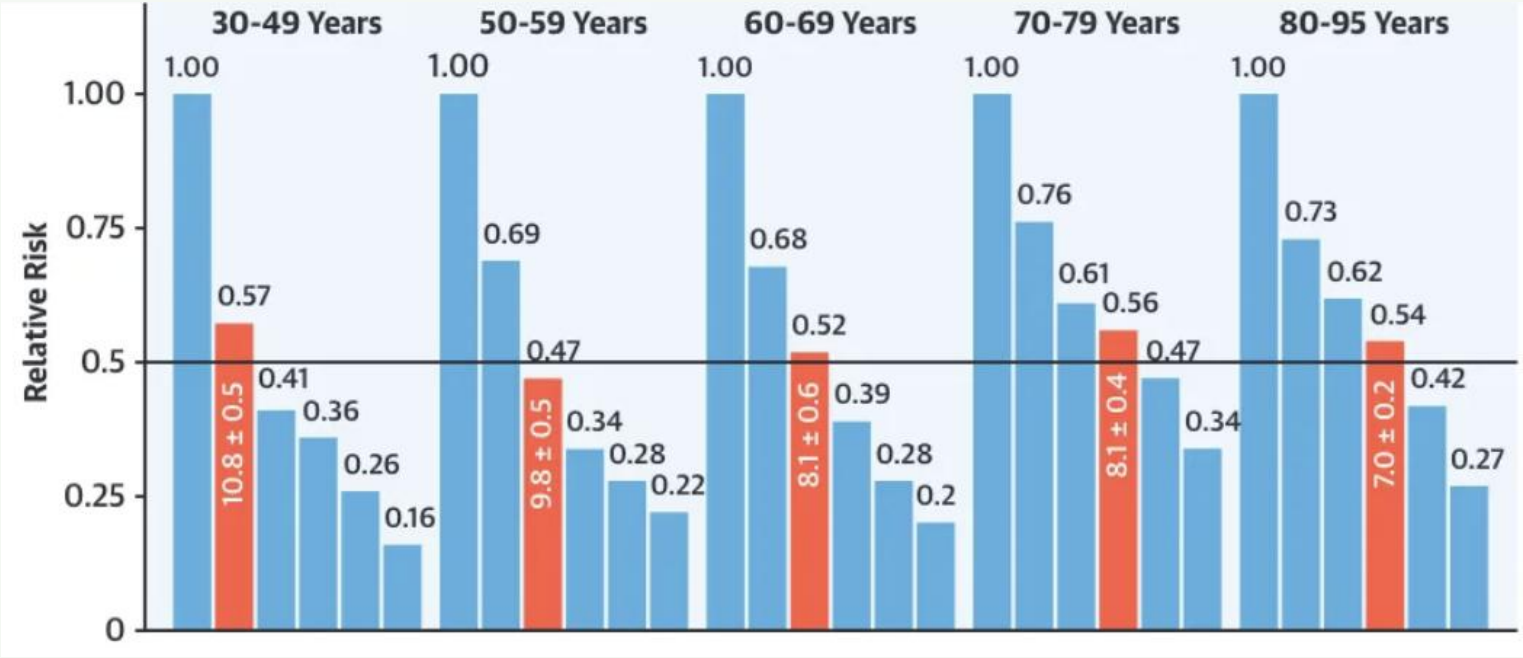
Strength

Visceral Fat is a Strong, Independent Predictor of All-Cause Mortality



Kuk et al. J. Obesity 2012

VO2max: The Strongest Independent Predictor of All Cause Mortality at All Ages

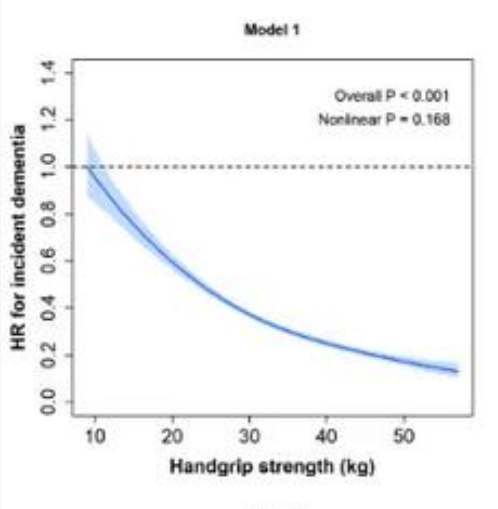


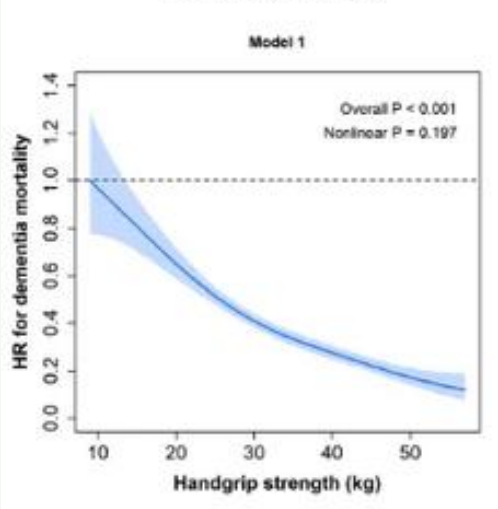
Kokkinos et al. JACC 2022

VO2max: Inversely Associated with All Chronic Disease Risk Factors and Diagnoses

Kokkinos et al. JACC 2022

Grip Strength: Not Just for Deadlifts





Esteban-Cornejo et al. J. Cach, Sarc, Musc 2022

Evolution of Biomarkers in US Healthcare

	Early 20th Century (Acute disease era)	Mid 20th Century (Expansion of chronic diseases)	Late 20th Century (Era of precision medicine)	Frontier Biomarkers (Early diagnosis & healthspan)
Health Challenges	 Nutrient deficiencies  Infectious diseases	 Smoking (in 1955, 56.9% of men and 28.4% of women)  Heart disease	 Cancer (emerging understanding of immune system)  Metabolic Syndrome	 Mental and Cognitive Health  Obesity & Metabolic Syndrome (*cont.*)
Major Causes of Disability, Mortality	1.Influenza/pneumonia 2.Tuberculosis 3.Diarrhea/enteritis *(1900)*	1.Heart Disease 2.Cancer 3.Stroke *(1950)*	1.Heart Disease 2.Cancer 3.Low Back Pain (3rd leading contributor to DALYs) *(1990)*	1.Heart Disease 2.Cancer 3.Mental Health & Cognitive Disorders/Dementia *(2025)*
Technology & Trends	• Microbiology testing • Biochemical assays	• Framingham Heart Study • Shift towards early risk screening (proactive) • Multiplexed biochemical assays • Hypercholesterolemia & hypertension classified as "disease"	• Human Genome Project • Polymerase chain reaction (PCR) • Genomic testing (risk alleles, etc.) • Companion Diagnostics • Proteomics (early) • Epigenomics (early)	• Scalable assessments of functional capacity • At home, continuous monitoring • Integrated multi-omics • **The need to define "health"**
Exemplar Biomarkers	• ABO Blood typing • Blood test of syphilis • BUN, Creatinine, glucose • Vitamin B12, Folate	• Lipid and cholesterol panels • Basic Metabolic Panels • Thyroid function testing • Newborn screening (e.g. phenylketonuria)	• HER2+ IHC test (Breast Cancer) • PD-L1 Expression (Cancer Immunotherapy) • Cologuard (epigenetic colon cancer screening test)	• Digital biomarkers (e.g. wearable for Parkinsonism) • Plasma MTBR-tau243 for Alzheimer's • Biological Age

Content of Today's Presentation

- Why Do Biomarkers Matter for Healthcare & Performance?
- Why Biomarkers of Disease Detection are Failing at Mitigating Chronic Disease
- A Case Study on Insulin Resistance
- Biomarkers that Enable Measurement of Health Rather than Disease
- **How Technology is Enabling the Future of Biomarkers**
- Implementations of Biomarker-Driven Preventive and Performance Medicine
- Real-World Partnership for Fitness in Cancer Survivors (VO Health & Yale School of Public Health)

Features of Next-Generation Biomarkers

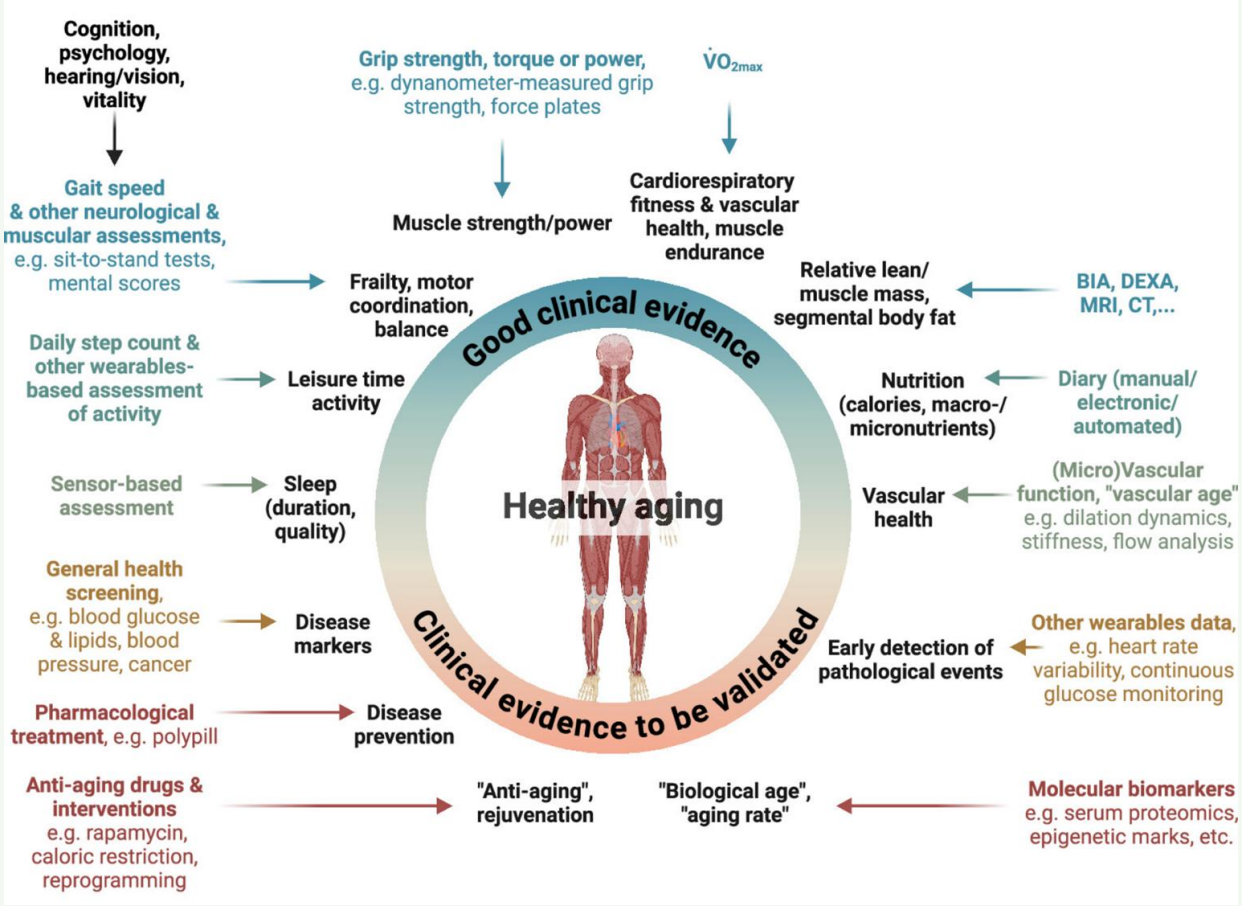
Biomarkers of Disease

- **Genomics driven** (will continue; likelihood of success of therapeutic clinical trials increases when drug target has genetic association)
- **Classify disease subsets** (disease will be classified into specific bins in order to accommodate reductionist mechanism-targeting)
- **Associated with diagnosis or mortality** (marker of disease diagnosis, monitoring, prognosis, drug response, risk, or mortality)

Biomarkers of Healthspan

- **Functional genomics driven** (proteomics, metabolomics, epigenetics, and transcriptomics, microbiome are responsive to health interventions)
- **Disease agnostic** (metrics of health, fitness, and flourishing should be protective regardless of predominant organ system involvement)
- **Associated with functional capacity** (integrated measures of health, such as VO_2max or muscle mass, provide quantitative estimates associated with quality of life)

Molecular Biomarkers and Wearables Will Build Upon Well-Validated Functional Measures of Healthy Longevity



Furrer & Handschin. Phys. Rev. 2025

Pharmaceutical for Body Composition Enhancement Are Here. Fitness is a Primary Endpoint for Emerging Drugs.

Editorial | Published: 12 November 2025

Are GLP-1s the first longevity drugs?

Nature Biotechnology **43**, 1741–1742 (2025) | Cite this article

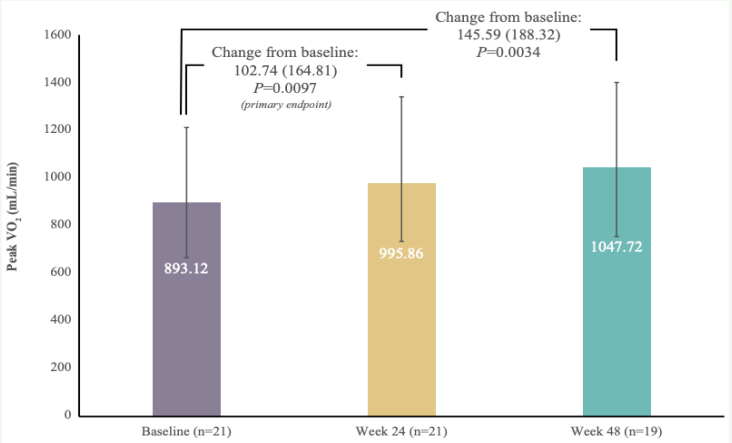
25k Accesses | **1** Citations | **222** Altmetric | Metrics

Circulation: Heart Failure

ORIGINAL ARTICLE

SPECTRA Phase 2b Study: Impact of Sotatercept on Exercise Tolerance and Right Ventricular Function in Pulmonary Arterial Hypertension

Aaron B. Waxman, MD, PhD; David M. Systrom, MD; Solaiappan Manimaran, PhD; Janethe de Oliveira Pena, MD, PhD; Jonathan Lu, MD, PhD; Franz P. Rischard, DO, MSc



Content of Today's Presentation

- Why Do Biomarkers Matter for Healthcare & Performance?
- Why Biomarkers of Disease Detection are Failing at Mitigating Chronic Disease
- A Case Study on Insulin Resistance
- Biomarkers that Enable Measurement of Health Rather than Disease
- How Technology is Enabling the Future of Biomarkers
- **Implementations of Biomarker-Driven Preventive and Performance Medicine**
- Real-World Partnership for Fitness in Cancer Survivors (VO Health & Yale School of Public Health)

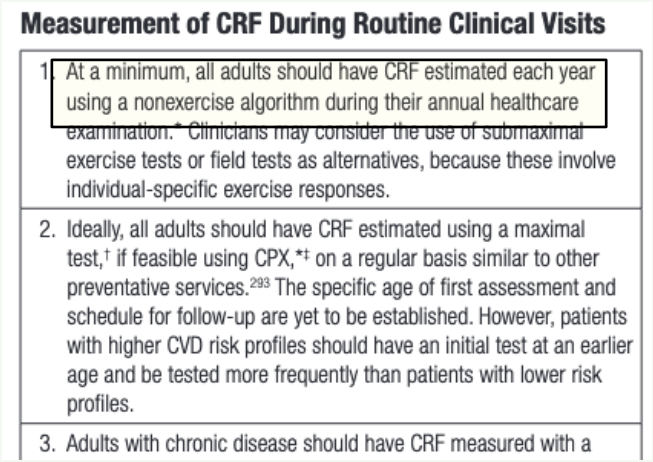
The 2016 AHA Call To Action for Fitness as a Vital Sign

Check for updates

AHA SCIENTIFIC STATEMENT

Importance of Assessing Cardiorespiratory Fitness in Clinical Practice: A Case for Fitness as a Clinical Vital Sign

A Scientific Statement From the American Heart Association

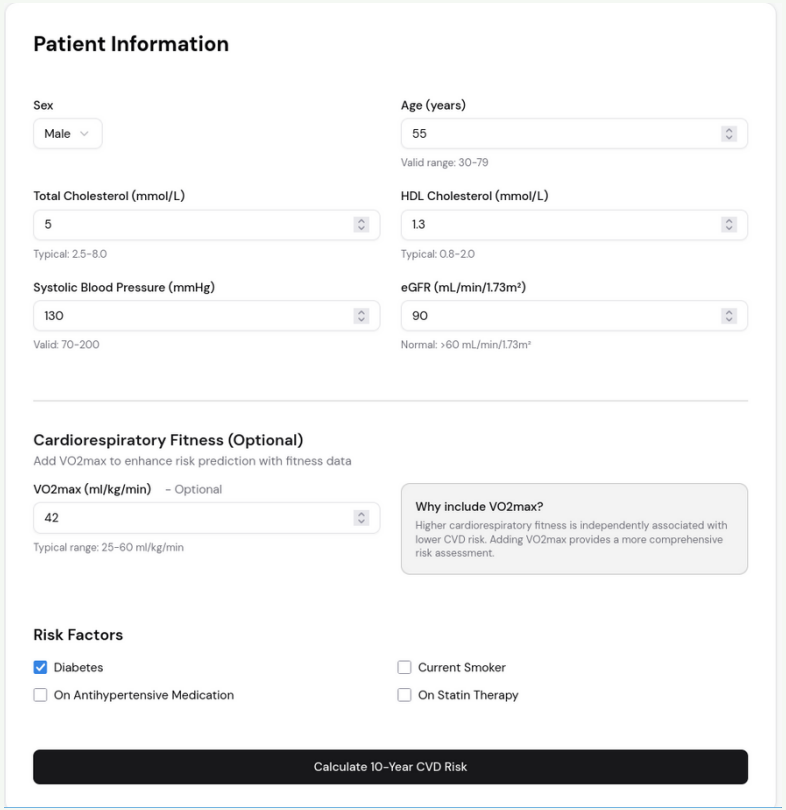


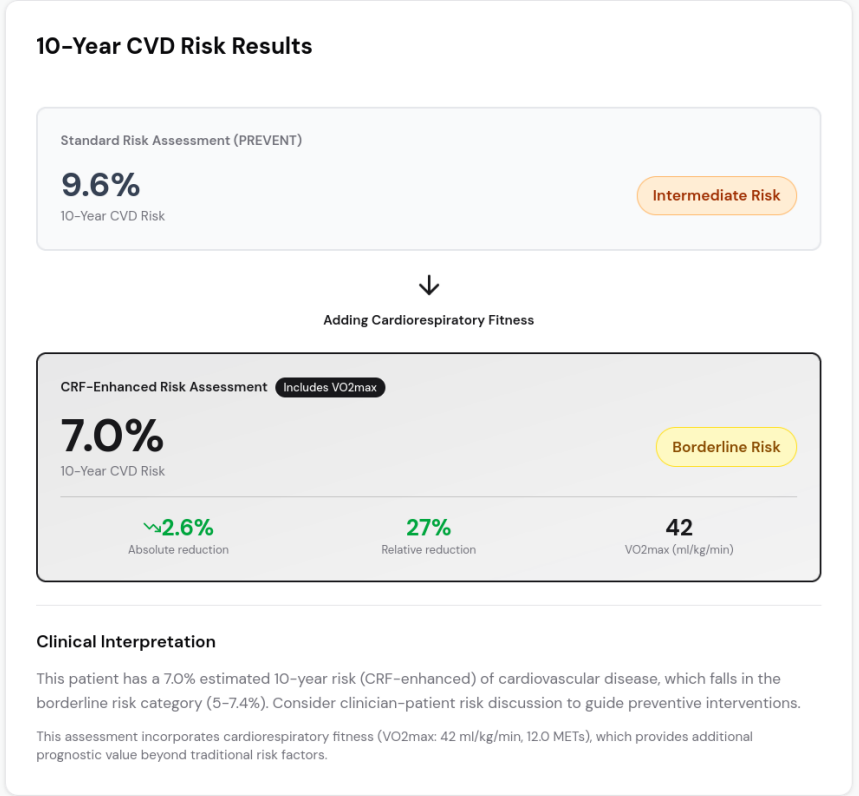
Measurement of CRF During Routine Clinical Visits

1. At a minimum, all adults should have CRF estimated each year using a nonexercise algorithm during their annual healthcare examination.* Clinicians may consider the use of submaximal exercise tests or field tests as alternatives, because these involve individual-specific exercise responses.
2. Ideally, all adults should have CRF estimated using a maximal test,† if feasible using CPX,*‡ on a regular basis similar to other preventative services.[293] The specific age of first assessment and schedule for follow-up are yet to be established. However, patients with higher CVD risk profiles should have an initial test at an earlier age and be tested more frequently than patients with lower risk profiles.
3. Adults with chronic disease should have CRF measured with a

Ross et al. Circulation 2016

VO Health's Real World Implementation of CRF to Enhance Cardiac Risk Stratification





Addressing Limitations of Current Non-Exercise CRF Estimates: Quantitative & Integrated into Clinical Workflows

Research-grade, predictive functional insights are **inaccessible & don't scale** beyond the lab.

VO2 max is the #1 predictor of all-cause mortality & chronic disease risk

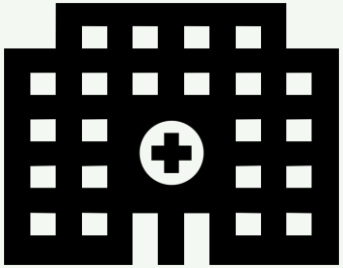
MRI/DXA - muscle mass and visceral fat detect early metabolic disease

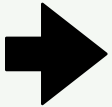
Glucose Clamps measures pre-disease insulin sensitivity

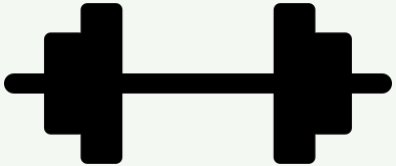
VO's novel biomarkers deliver the **insights of gold-standard tests**, from a routine blood draw.

Increasing Integration of Fitness & Medicine by Expanding The Medical Fitness Model: Gym as Primary Care

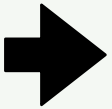
MFA Founding

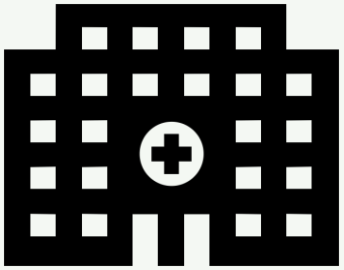






Reversing the Traditional Referral Pathway





Potential Policy Tailwinds for Fitness Biomarkers as CMS-Covered Fitness and Nutrition Interventions


MAKE AMERICA HEALTHY AGAIN MAHA PRESIDENT DONALD J. TRUMP

REALIGN INCENTIVES

Realigning Incentives and Systems to Drive Health Outcomes Research to Drive Innovation

Implement policy reforms, deregulation, and structural improvements that will drive advancements in innovation to

Medicaid Quality: CMS will collaborate with states to establish quality metrics for Medicaid managed care organizations that promote measurable health improvements through nutrition coaching and other fitness indicators (e.g., predicted VO_2 Max).

Content of Today's Presentation

- Why Do Biomarkers Matter for Healthcare & Performance?
- Why Biomarkers of Disease Detection are Failing at Mitigating Chronic Disease
- A Case Study on Insulin Resistance
- Biomarkers that Enable Measurement of Health Rather than Disease
- How Technology is Enabling the Future of Biomarkers
- Implementations of Biomarker-Driven Preventive and Performance Medicine
- **Real-World Partnership for Fitness in Cancer Survivors (VO Health & Yale School of Public Health)**

The Well Known Relationship Between PA, Fitness, and Cancer Outcomes

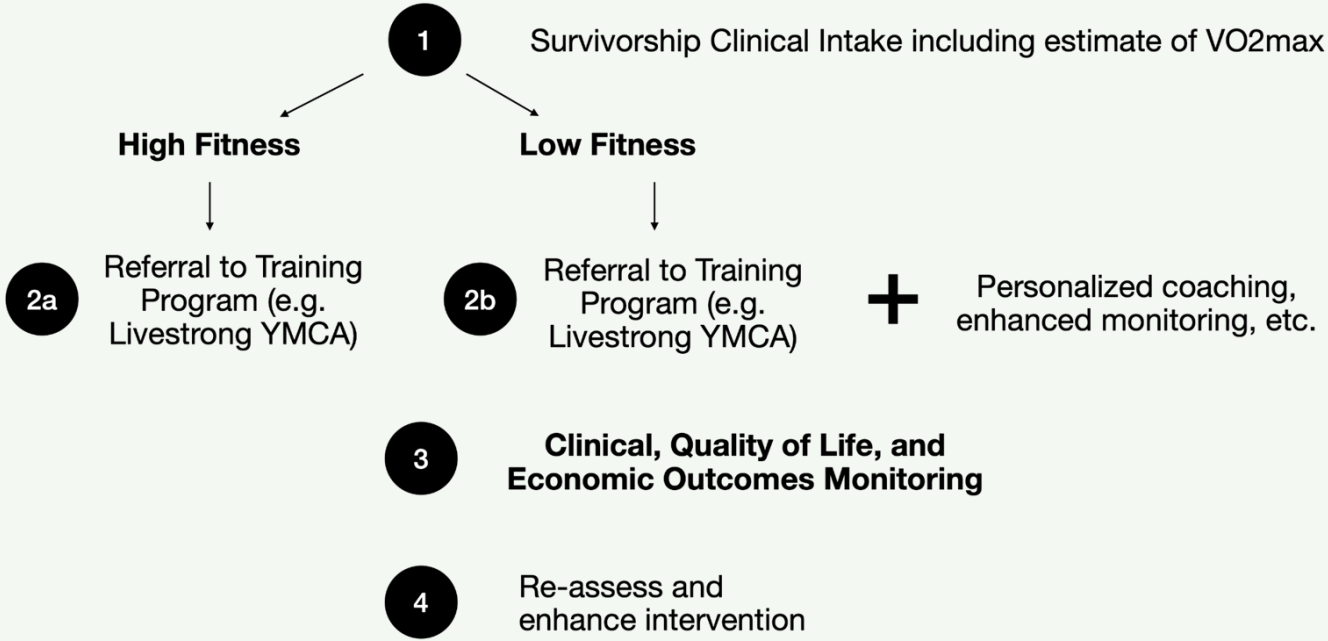
- Regular exercise improves cancer risk[1] and survival[2]
- Fitness is associated with lower risk of multiple cancers[3]
- Fitness associated with lower mortality[3]

[1]Albini et al. Eur. J. Cancer Prevention 2025

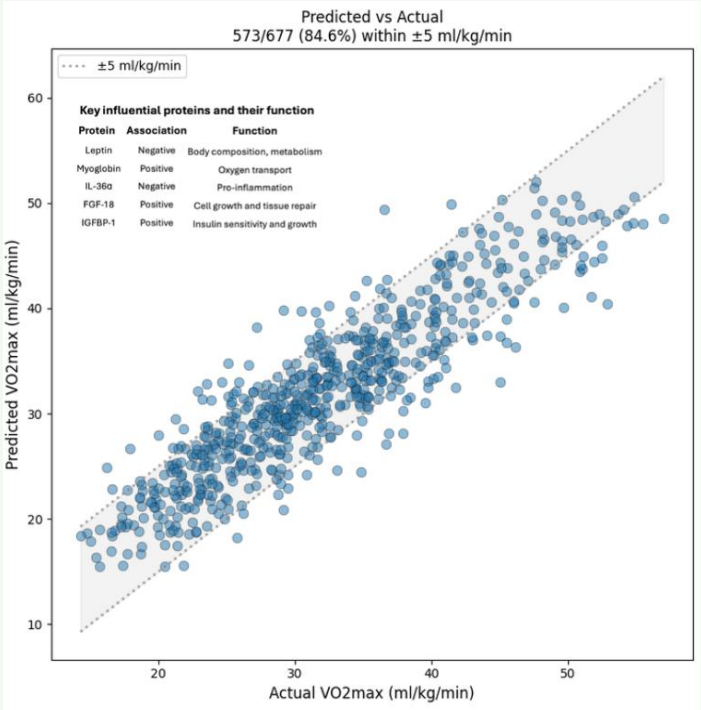
[2]Yu et al. Br. J. Sports Med. 2025

[3]Ekblom-Bak et al. JAMA Net. Open 2023

Fitness as a Benchmark for Cancer Survivorship To Enhance Engagement with Medical Fitness and Quality of Life



Does VO Health's Blood Test Also Predict Fitness in Breast Cancer Survivors?



Retrospective data analysis from banked plasma samples in >100 patients who underwent a year long exercise and nutrition intervention with pre- and post-fitness benchmarks

Takeaways

- Biomarkers play a key role in allocation of healthcare resources
- Traditional biomarkers of disease are based upon the reactive healthcare system
- The functional physiology toolkit can predict diseases well in advance, and omics are unlocking the ability to scale these predictive insights
- Now is the time for biomarkers of fitness to play a role in prevention, longevity, in addition to performance

Interested in Collaborating or Getting Early Access to Our Next-Gen Biomarkers?

Reach out: brooks@vohealth.co

Sign up for waitlist: VOHealth.co