



Longevity Biomarkers Landscape Overview

Teaser
Q4 2021

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www.longevity.international

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This analytical study provides a review of aging-related and Longevity biomarkers. It contains selected lists, rankings, and profiles of more than 100 single biomarkers correlated with age-related diseases and disorders. An increasing role of Artificial Intelligence applications in the field of the biomarkers' industry is also introduced.

Biomarkers are an essential factor in the Aging Analytics Agency's strategic agenda, which includes policy proposals to national and international governance bodies on how to effectively **increase National Healthy Longevity** via practical implementation of P4 medicine technologies. It is essential to develop and promote the widespread use of panels of biomarkers that are validated and actionable.

The report documents various aging-related biomarkers and identifies from among them those which, by the metrics described, belong to the category we have named **Minimum Required: the Most Viable Products for immediate implementation.**

It is our hope and commitment that regardless of whether it is adopted wholesale, the results of the report's analysis can guide relevant counterparties on how to optimally utilize existing technologies to maximize the health of aging populations and aging economies.

Introduction

In 2019, Aging Analytics Agency produced [Biomarkers of Longevity Landscape Overview 2019](#), an open-access special analytical case study that uses comprehensive analytical frameworks to rank and benchmark existing panels of biomarkers of aging, health and longevity according to their ratios of accuracy vs. actionability, identifying the panels of biomarkers that can have the greatest impact on increasing both individual and national healthy longevity in the next few years, for use by a wide variety of strategic decision makers including companies, investors, governments and insurance companies.

The report was designed to make key strategic recommendations regarding technologies and biomarkers implementations within the reach of companies, entities and nations in order to assist them in optimizing their developmental plans and strategies, providing specialized guidance for business and investment core decisions, including a comprehensive list of single biomarkers of aging and panels (their advantages and disadvantages), a concrete analysis of recent novel biomarkers of aging just entering R&D processes today, an overview of why AI platforms will come to be a necessary and indispensable component of longevity biomarker discovery.

Biomarkers of Longevity

Analytical Report

Current State, Challenges and Opportunities
Landscape Overview 2019

Increasing Role of Data Science and Artificial
Intelligence in Biomarker Discovery and
Monitoring



Report Value Proposition

1. What are the current most comprehensive biomarkers and panels to follow the aging trajectory and its related conditions and the most viable or minimum required ones, and how they can be implemented in the most ideal and useful manner?
2. What leading personalised and preventive market-ready health assessments can aging biomarkers and panels dispense to the existing pipeline of healthcare entities to maximize their competitive advantage?
3. What novel updates and advances in biomarker-related research and development will impact the health industry in the next years? Which of those should be watched closely for integration into clinics and biomedical or healthcare companies' existing pipelines as soon as their conditioning is achieved?

We feel that our efforts over the course of the past five years have established a solid foundation of knowledge and expertise upon which we intend to summarize the entire landscape of aging and Longevity biomarker utilities in the health industry: the production of this new report entitled Biomarkers of Longevity Landscape Overview 2019: Current State, Challenges and Opportunities.

This report seeks to answer these three specific questions, with an upcoming +300 pages version that will be produced over the next 3-6 months, and a new edition of its content during each financial quarter, incrementally increasing its breadth and depth as we go along, and with each edition providing a deeper, more comprehensive and more precise understanding of the landscape. It will deliver:

- Concrete deep analysis of which biomarkers and biomarker panels are available today, its strengths and weaknesses, their accuracy, availability and current actionability, and the opportunities and challenges related to its uses for real-time and precision monitoring of health status, and ultimately the reversal of biological age.
- Tangible estimations of which biological age biomarkers and implementations are consolidated, or their current conditioning stage for precision assessment of health status and endpoints of clinical trials and therapies.
- Highlights regarding the role of digital biomarkers and AI platforms and how they will become necessary and indispensable components of aging and Longevity biomarker discovery, research, development and users daily use.

The parties who will have early access to this report will gain deep expertise on how they can optimize their clinics' strategic, technological and scientific prospects in order to deliver the most sophisticated and comprehensive precision health products and services for their clients.

www.aginganalytics.com/biomarkers-of-longevity

Introduction

The next edition of the [Longevity Biomarkers Ecosystem Q2 2021](#) report was published in May 2021, providing an enhanced overview of 85 companies, 160 investors, and 100 biomarker panels.

Deep Knowledge Group considers longevity biomarkers as a strategic core engine for its longevity activities and as a major catalyst for the development of the whole longevity industry. They represent the major key to transforming aging science theory into practical Human Longevity applications over the next several years. Moreover, biomarker panels can be used as tangible, validated tools to evaluate, benchmark, and compare longevity companies, conducting data-driven evidence-based due diligence.

Therefore, the question of access to the top expertise in longevity biomarkers is of a strategic importance for Deep Knowledge Group.

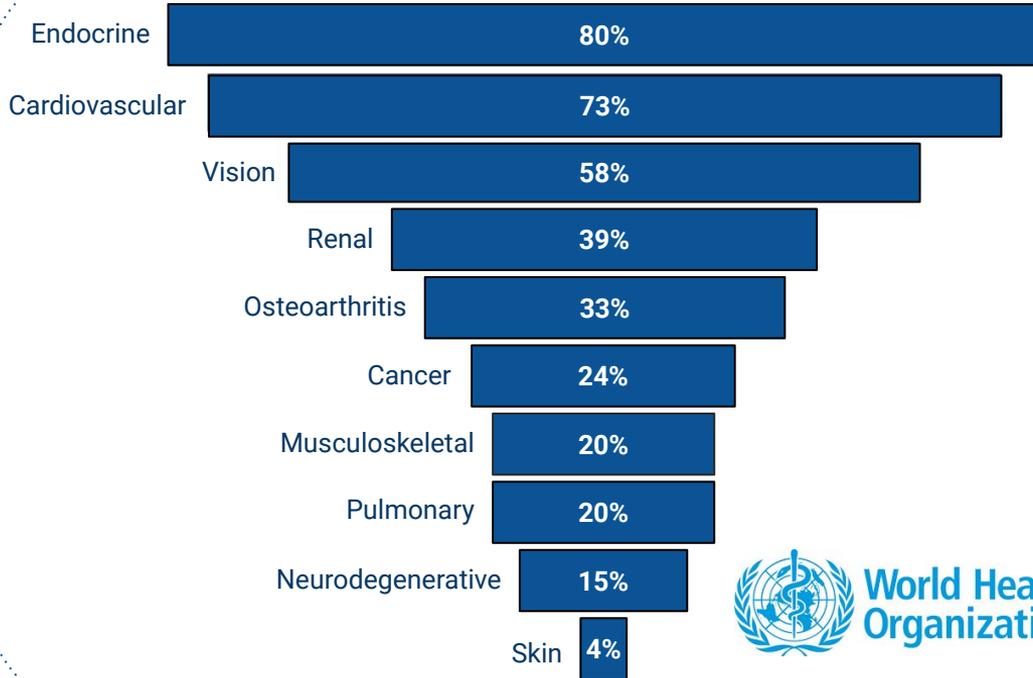
Further, longevity biomarker panels can be applied for financial products structuring, namely InsurTech and more complex financial products later on (such as for example HALE/QALE derivatives, biological age financial options and futures, and so on).



www.longevity.international/biomarkers

Health of Older Adults

Prevalence of Disorders in Patient Group in Age >60, %



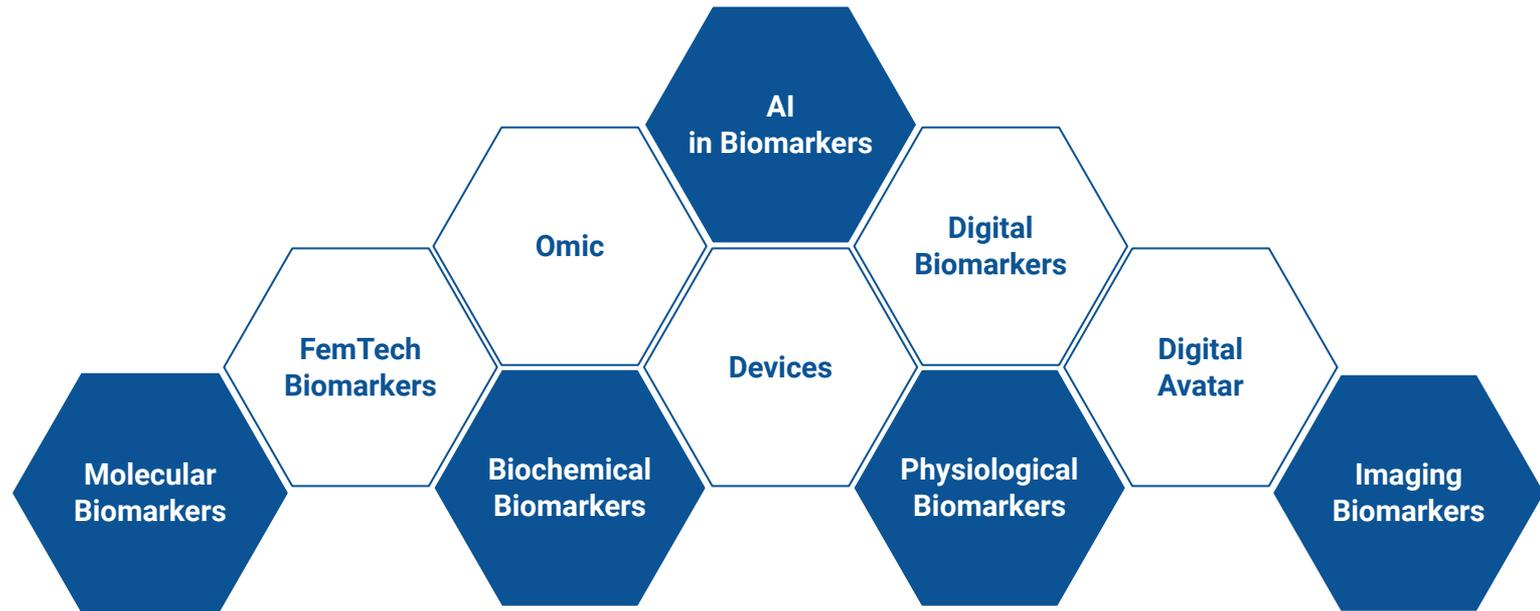
The world's **population is aging rapidly**. Between 2015 and 2050, the proportion of the world's older adults is estimated to almost double from about 12% to 22%. In absolute terms, this is an **expected increase** from 900 million to **2 billion people** over the age of 60. Older people face special health challenges which need to be recognized.

Multiple studies shown dramatic statistics in older cohort of patients. Approximately **80%** people develop **endocrine disorders** (**33%** of them have **diabetes**), **73%** - **cardiovascular disease** (**24%** have **coronary heart disease**), **58%** have problem with **eyes and vision** (**18%** seniors have **amblyopia**).

According to this prevalence of age-related disorders we have **selected biomarkers for our analysis**.

Longevity Biomarkers Framework

Ahead of database creation, we picked the **most significant types of biomarkers of aging**. The categorization of companies is based on the source of biomarkers, their focus level, practical outlook, and methodology. The framework not only brings a **comprehensive view of the market** but also **sustains relevance in advance to the development** of technologies and research approaches.



Longevity Biomarkers Landscape Q4 2021

AI Biomarkers

Companies - 300
Investors - 495
R&D Centres - 235
Non-Profits - 7

Digital Biomarkers

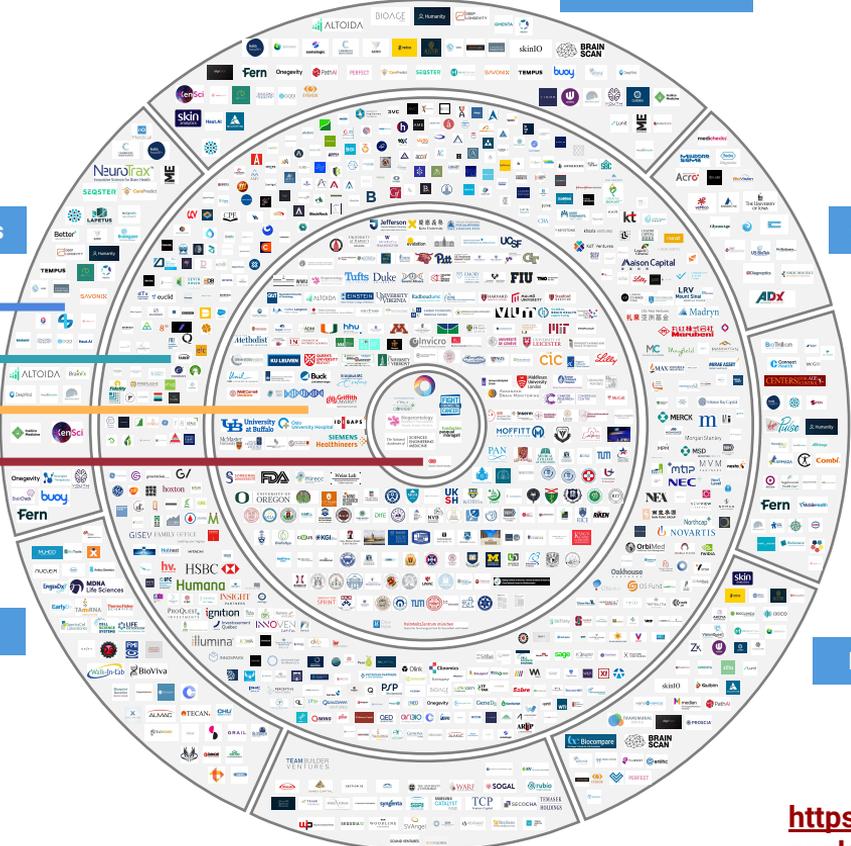
- Companies
- Investors
- R&D Centres
- Non-Profits

Systemic Biomarkers

Physiological Biomarkers

Molecular Biomarkers

Imaging Biomarkers



Omic-based Biomarkers



<https://mindmaps.longevityinternational/biomarkers-2021q4>

Biomarkers for Aging Evaluation

Systemic Approach for Aging Rate Assessment

Biomarkers of Aging (AFAR* Criteria)

- Predict the rate of aging;
- Monitor a basic process that underlies the aging process, not the effects of disease;
- Must be able to be tested repeatedly without harming the person;
- Work in humans and in laboratory animals

Biomarkers of Age-related diseases

- Minimally invasive
- Routinely used for Clinical Diagnostics
- Comprehensive
- Reliable

*AFAR - American Federation for Aging Research

Despite the growing interest to **Aging evaluation** there is still no gold standard of reliable biomarkers to predict and monitor Aging rate. Aging is a time-dependent multisystemic functional decline, and it is evaluated at different levels: molecular, systemic, physiological.

Several attempts to establish markers of aging have been made over the last 50 years, but the complexity of the **aging phenotype poses both conceptual and practical challenges**.

Despite previous efforts, **there is presently no commonly accepted definition of biomarkers of aging or either criteria for their selection**, resulting in an absence of reliable, verified methods for measuring healthy aging.

Biomarkers of healthy aging might be used as surrogate endpoints or outcome measures in trials of treatments aimed at extending life expectancy, and accurate, easily-measured indices of healthy aging could be used in public health-related population surveys.

However, there is **no standard reference for measuring healthy aging**, which makes conducting and assessing aging research across studies problematic.

Practical Application of Age-Related Biomarkers



01

Clinical Trials

- New pathways identification
- Age-adjusted clinical trial enrollment
- Clinical trial outcome prediction

02

Reproductive Longevity

- Reproductive longevity tracking
- Family-planning timelines

03

Preventive medicine

- Feature transfer from aging to disease
- Age-related disease screening and staging
- Immunosenescence analysis

04

Treatment & Diagnostics

- Age-personalized immuno-oncology treatment
- Mortality prediction
- Age-personalized vaccines

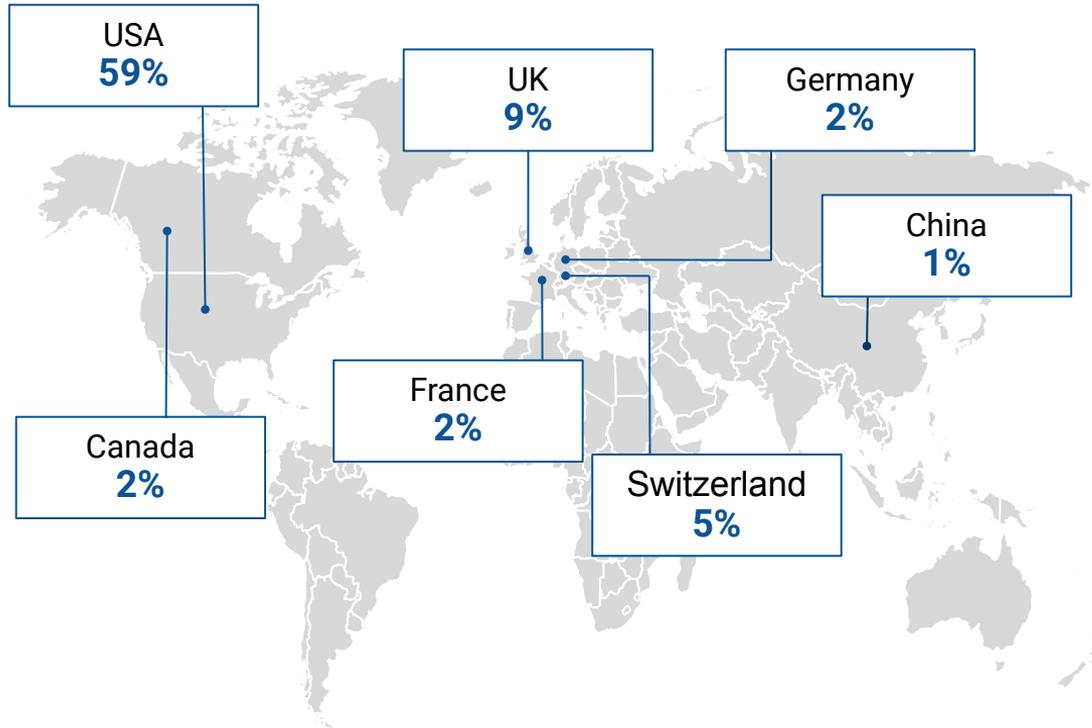
05

Healthy Living

- Wellness
- Sport
- Nutrition
- Life insurance

Biomarkers Market at a Glance

Distribution of Companies by Top Countries

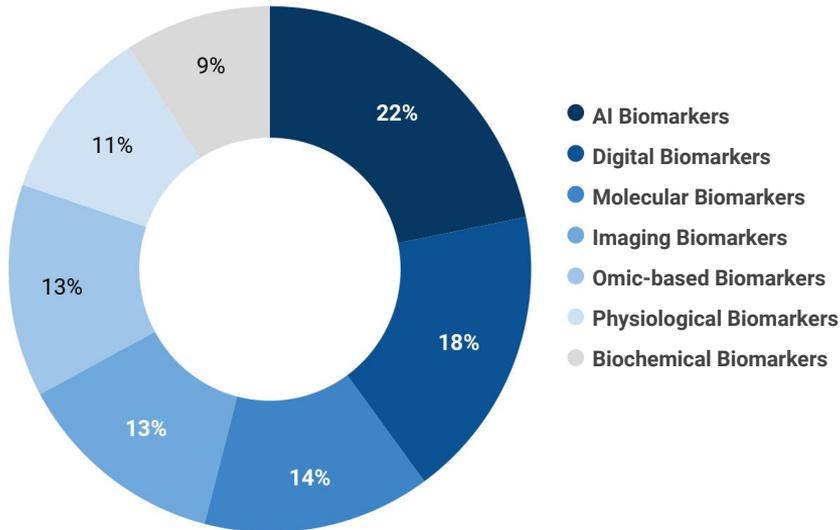


Overall companies involved in the Biomarkers development are distributed among **more than 25 countries** of the world. Nevertheless, **top 7 countries concentrate more than 80%** of all companies. The left graph illustrates how companies are distributed among these countries.

The USA is clear leader of the industry by the number of companies - **59%** of companies are allocated there. With great gap follows European region. **Europe** hosts over **17%** of all companies. The top European countries by number of companies are the **UK (9%)**, **Switzerland (5%)**, **France (2%)** and **Germany (2%)**. Switzerland are presented Big Pharma companies (such as Roche) as well as biomarkers specialized companies (eg. Scailyte, Centaura).

Biomarkers Market at a Glance

Distribution of Companies by Sectors



The clear trend is towards edge intelligence to sense precisely and **analyze relevant biomarkers explicitly**. In the future, all these applications will rely on systems supported by AI and innovative algorithms. Thus, distribution by fields of studies is presented on the left graph.

Companies are distributed equally among the specific types of Biomarkers. **AI Biomarkers Companies** constitute **22%** of all companies, other **18%** - **Digital Biomarkers** companies. A little less companies are engaged in the **Molecular Biomarkers** developing - **14%**. **Imaging Biomarkers** companies and **Omics-based Biomarkers** companies constitute **by 13%** of total amount of companies each. Despite **Biochemical Biomarkers** (i.e. biomarkers of functioning of cellular pathways) offer a broad spectrum of diagnostic capabilities, in this field the least companies are engaged - only **13%** of total amount.

Molecular Biomarkers

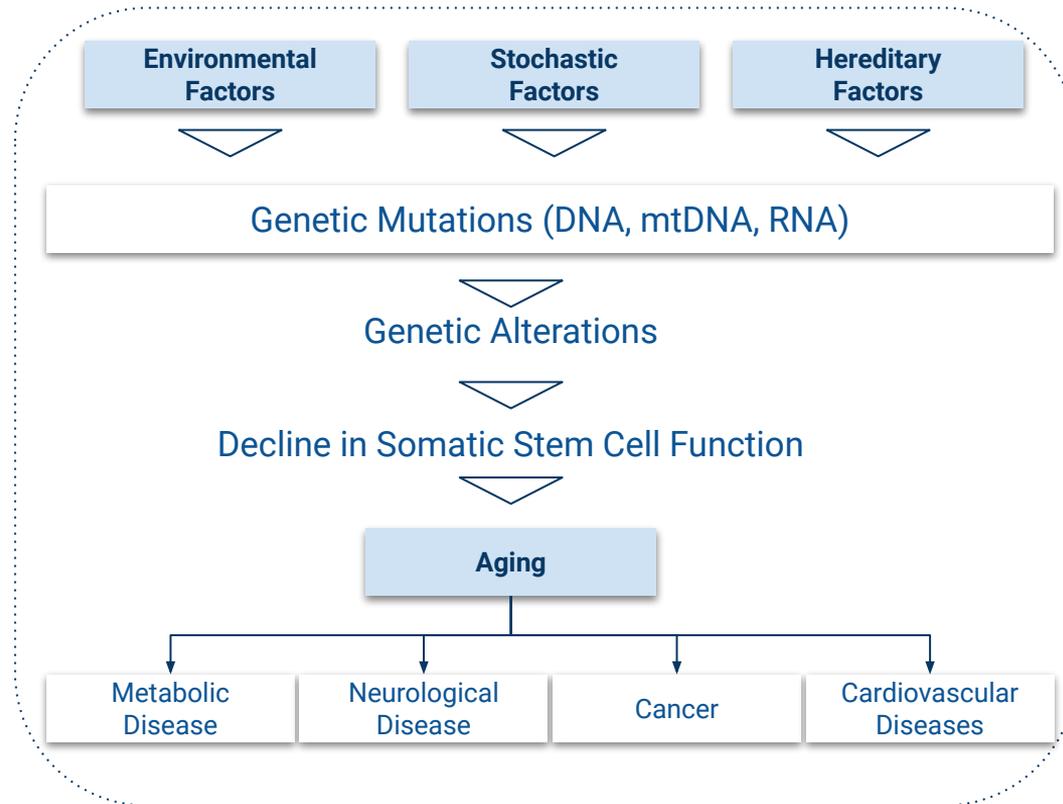
Category Characterization

The **environmental conditions** (stress, pesticides), **individual genotype** (genomic and mitochondrial DNA) and **stochastic factors** can induce **genetic and epigenetic alterations** that cause a decline in somatic stem cell function that can be the origin of metabolic, degenerative diseases, cancer and aging in the individuals.

In our report we have **analysed companies** which **offer Molecular Biomarkers for aging and age-related disease** that are clinically approved and have significant scientific evidence.

We include in our analysis **genes associated with age-related disease** as Endocrine disorders (Diabetes, hypothyroidism), Cardiovascular disorders (stroke, heart failure etc), Vision disorders (glaucoma, cataract), neurodegenerative (Alzheimer's, Parkinson, Sclerosis) etc. as well as **genes and mutations responsible for progeroid syndromes** (age-related monogenic hereditary disorders) and **populations of centenarians** whose lifespan is approximately twice the mean predicted for the population at the time of their birth will help to establish the function of a specific genotype in an individual's lifespan.

Genetic Factors' Influence in Aging and Lifespan



Key Companies: Molecular Biomarkers

Genetic

Genetic Mutations

DNA



mtDNA



RNA

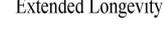
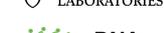


SNP Genotyping



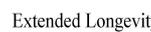
Epigenetic

DNA Methylation



Non-Epigenetic

Telomere Length

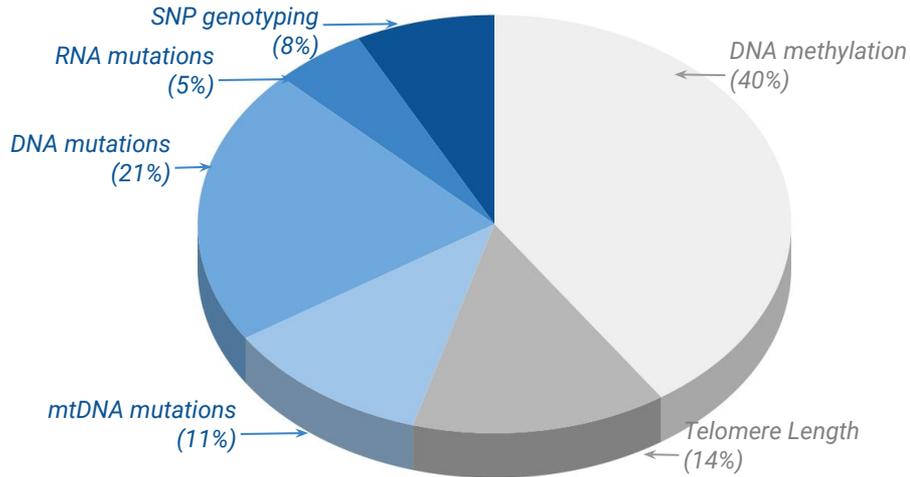


Market Overview of Molecular Biomarkers

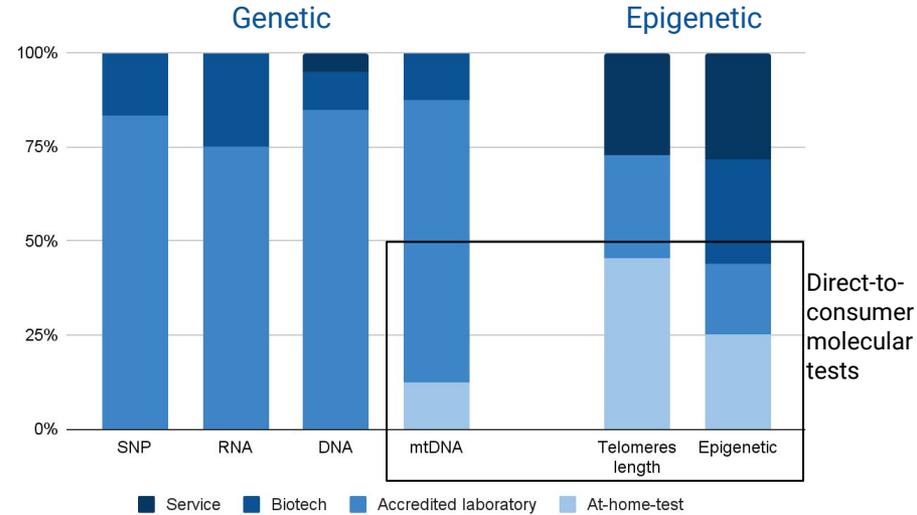
Distribution of Companies by Molecular Testing Approach

Genetic (blue):

Epigenetic (grey):

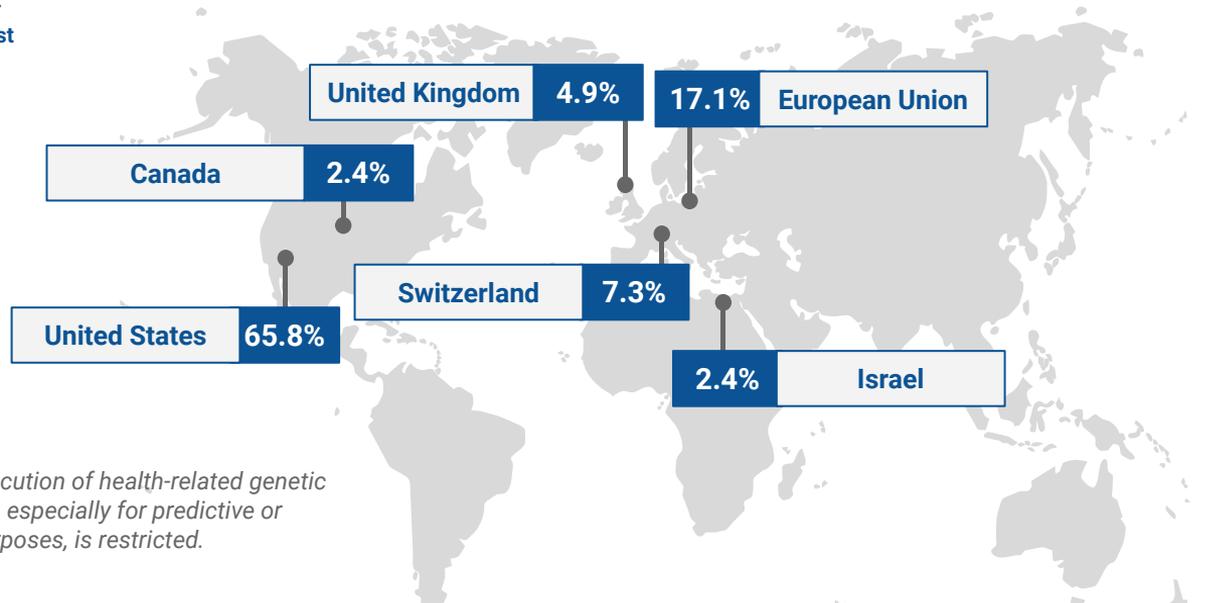
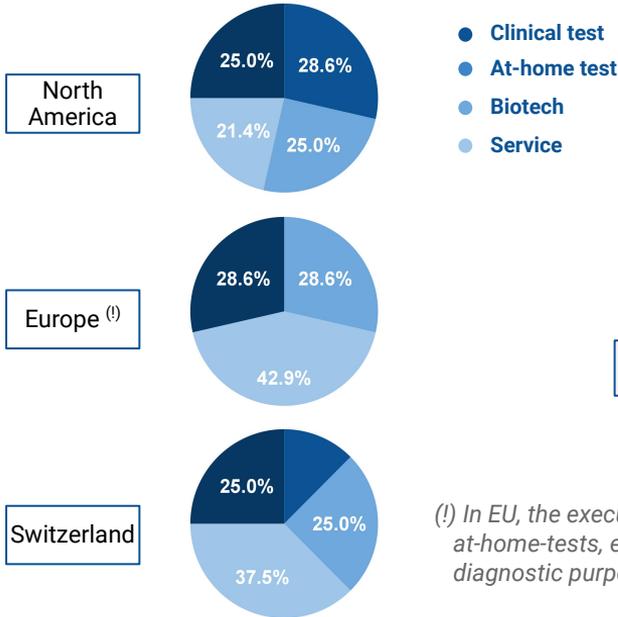


Approach vs Type of Company



Growing trends of **healthy lifestyle** and rising **health care awareness programs** have created the **demand for predictive and wellness molecular testing**. Genetic testing helps to predict future risk of disease and offers information and data about the genetic makeup of a child. In the market more than **50% share Epigenetic tests** for prediction **biological age** via measuring level of **methylated DNA** and **Telomere Length**. The **Direct To Consumer segment** is expected to **hold largest market share** over the forecast period due to growing awareness related to at-home genetic tests.

Genetic Diagnostic Market Geography

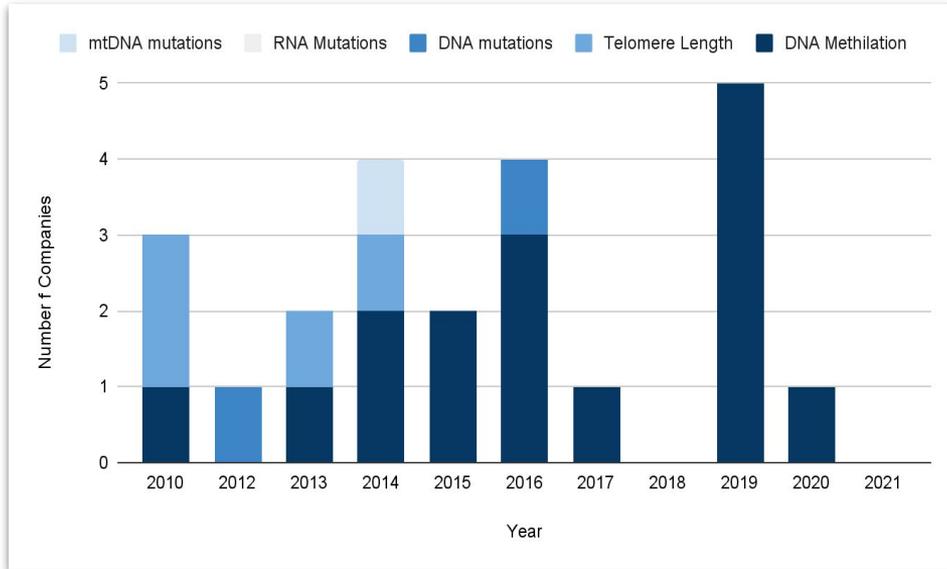


(!) In EU, the execution of health-related genetic at-home-tests, especially for predictive or diagnostic purposes, is restricted.

The global Aging Genetic Diagnostic market size is approximately **\$ 2.0 billion**. It is expected to expand at a **CAGR of 10.00%** from this period. The COVID-19 pandemic slowed up growth for this industry. The most companies (>65%) are located in **USA**, ~17% in Europe and 7% in Switzerland. This region characterized **rise in commercial interest** and **government support** for genomics and sequencing technologies, **high demand for personalized medicine**, and the presence of a substantial number of translational and academic research organizations. The increasing focus by governments of various countries, to regulate and create awareness regarding genetic tests, has successfully resulted in the faster adoption of these tests across the world. The increasing R&D funding, along with the strong market presence by major players in the market, has created a strong entry barrier for new entrants.

Genetic Market Trends for Aging Diagnostics

New Companies: Molecular Biomarkers



Key Market Trends

Development new biomarkers

Growth the number Epigenetic testing

Early diagnostics of age-related disorders

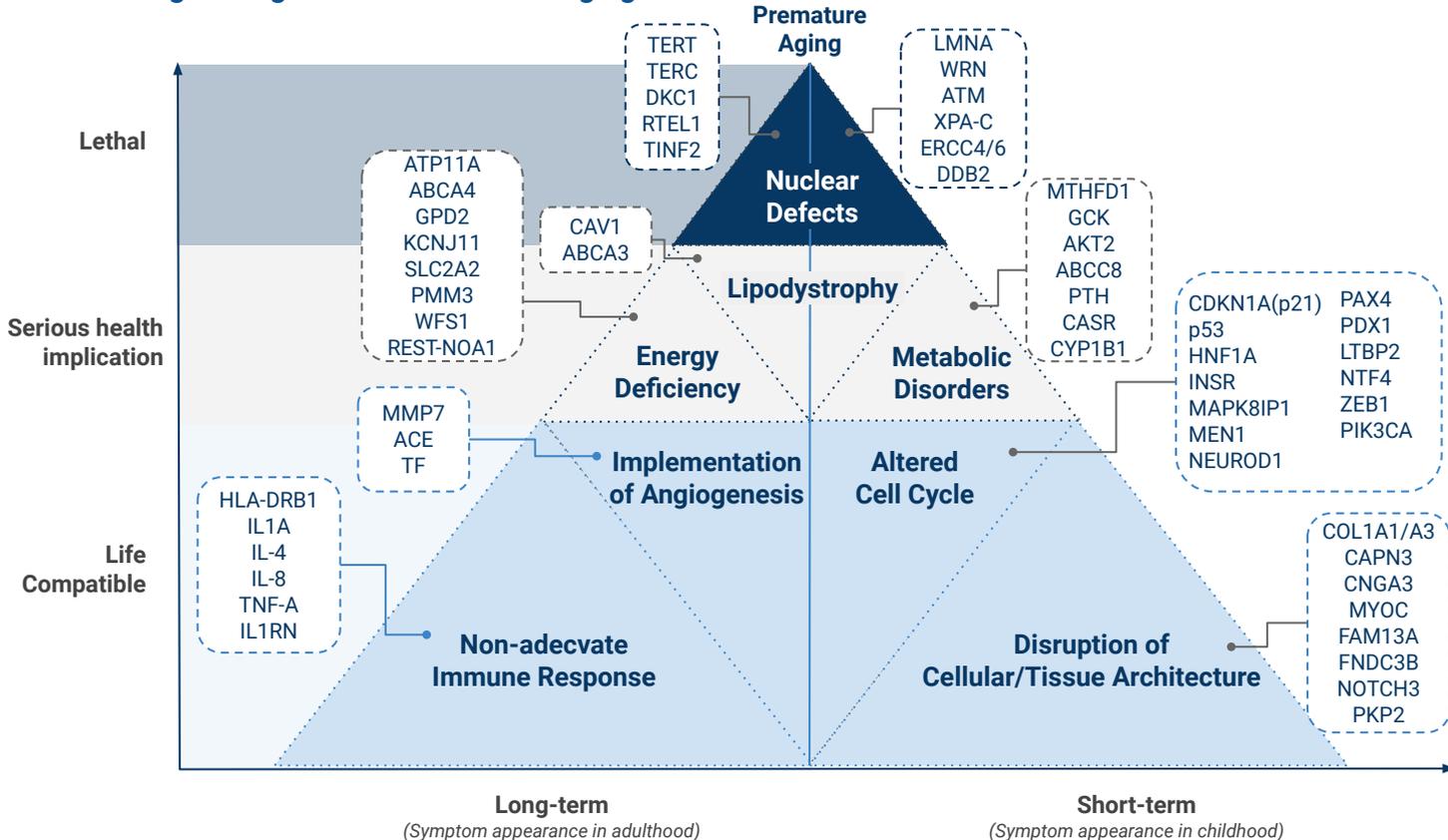
Growth of direct-to-customer market

Digitalization

How it is shown on graph for the last decade all new companies produce **Epigenetic tests**. This type of tests replaced other genetic tests even at-home-tests of Telomere Length which are sold directly to the customers. More than **50%** analyzed companies don't present detailed information about their founds, localization of head quarter and year of foundation. These companies often **don't have own product/test kit** and **do analysis in outsourcing laboratories**. High cost on genomic research equipment and complexity in predictive genetic testing are major factors that may restrain the market to a certain extent going ahead. Moreover, lack of trained professionals and inadequate funding are expected to create further challenges for market growth.

Aging Genetics and Aging

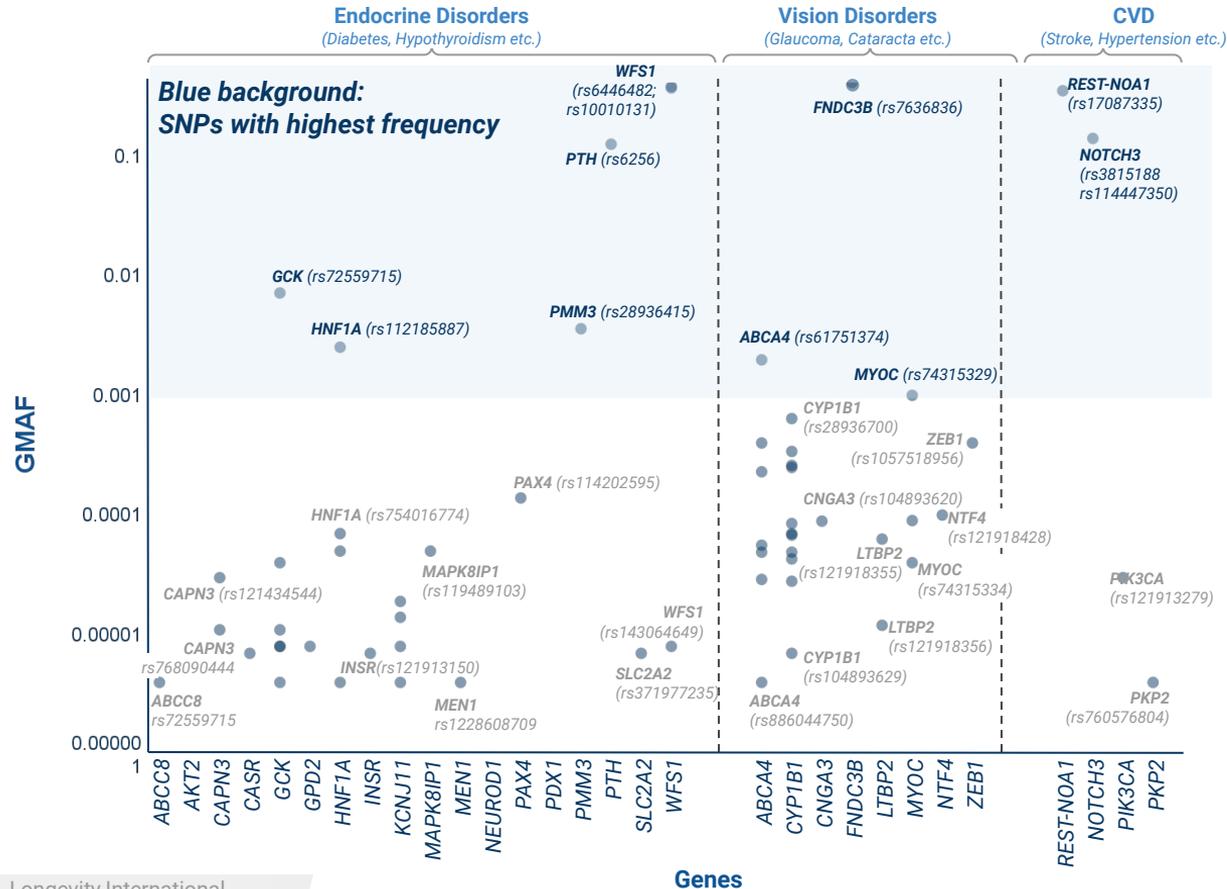
Ranking of Single Genes Involved in Aging Process



We have analysed the published genetic studies for two different populations: 1. **centenarians** whose lifespan is approximately twice the mean predicted for the population at the time of their birth; 2. **patients with extremely accelerated aging** as progeria, Werner syndrome etc. These data has helped us to **select the certain genetic factors** which act as modulators of the aging process. Presented **genes are associated with lifespan, resistance to diseases** that lead to early death.

In families whose members show **exceptional longevity**, in addition to other **environmental factors, family habits** (lifestyle, nutrition) are thought to influence survival, although data are limited on the contribution of these factors to greater resistance to disease.

Frequency for Clinical Approved SNPs Associated with Age-Related Diseases



The **single gene mutation** are used for diagnostic the risk of age-related disease such as **Diabetes, Glaucoma, Stroke** etc. Most of disease associated genes are rare with **GMAF** (**G**lobal **M**inor **A**llele **F**requency) less than 0.001. Another polymorphisms are more popular and make **significant impact** in disease development in elder patients (>60 years). Analysis of **ClinVar Database** and literature lets us select more **important genes** which can **implicate health in young people** and **accelerate their aging**: **GCK** (glucokinase), **HNF1A** (hepatocyte nuclear factor-1 alpha; HNF-1 α), **PMM3** (phosphohexomutase), **PTH** (parathyroid hormone), **ABCA4** (ATP-binding cassette), **FND3B** (fibronectin type III domain containing 3B), **MYOC** (myocilin), **REST-NOA1** (nitric oxide-associated protein 1), and **NOTCH3** (notch receptor 3). This is only a sample of genes selected for the most frequent disorder in old people.

Clinical Trials And R&D Examples of Practical Applications

XVIVOS is focused on developing novel algorithms and user-friendly interfaces for analyzing in vitro (or ex vivo) Big Data from high-throughput assays which are applicable to personalized medicine. In the process of achieving this, XVIVOS works with researchers and pharmaceutical companies to improve the analysis platform. The goal of XVIVOS is to integrate these data with pharmacogenomics, in order to discover the best drug for each patient. Further, XVIVOS also facilitates relationships between patients and researchers to assist with novel drug discovery when no current therapies exist.



Salimetrics' assay kits and CLIA-certified testing services are used to measure salivary analytes related to stress, behavior and development, inflammation, sleep, reproduction, health and immune function. Salimetrics continues to be a key partner in bringing best-in-class solutions to salivary bioscience research. By using Salimetrics, researchers can find and implement solutions where the full potential of salivary measures have yet to be realized.



Swiss DNalysis offers genetic tests developed by our experts in various fields. Laboratory analysis and storage exclusively performed in Switzerland accredited by Swiss Federal Office of Public Health following Swiss patient data protection rules, eligible for coverage by health insurance. Next-generation sequencing technology, confirmation of positive tests with Sanger sequencing, double-checking of negative results with MLPA, evaluation of mutation significance with several databases.



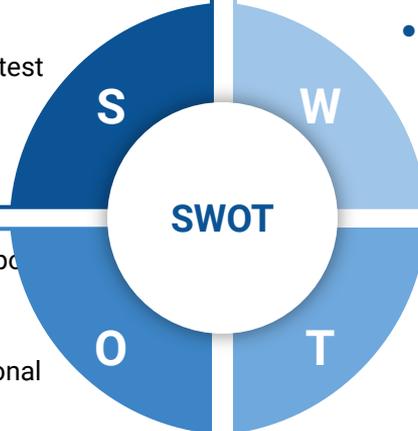
Molecular Biomarkers: SWOT Analysis

- Hereditary predisposition to disease can be diagnosed before manifestation of the disease.
- Molecular testing helps to predict future risk of disease and offers information and data about the genetic makeup of a child.
- Non-invasive technology for sample collection.
- Growth of number of companies that offer at-home test for self-diagnostic.

- The rise in commercial interest and government support for genomics and sequencing technologies
- The high demand for personalized medicine
- The presence of a substantial number of translational and academic research organizations.

- High cost of testing for customers.
- High cost on genomic research equipment and complexity in predictive genetic testing are major factors that may restrain the market to a certain extent going ahead.
- Lack of trained professionals.

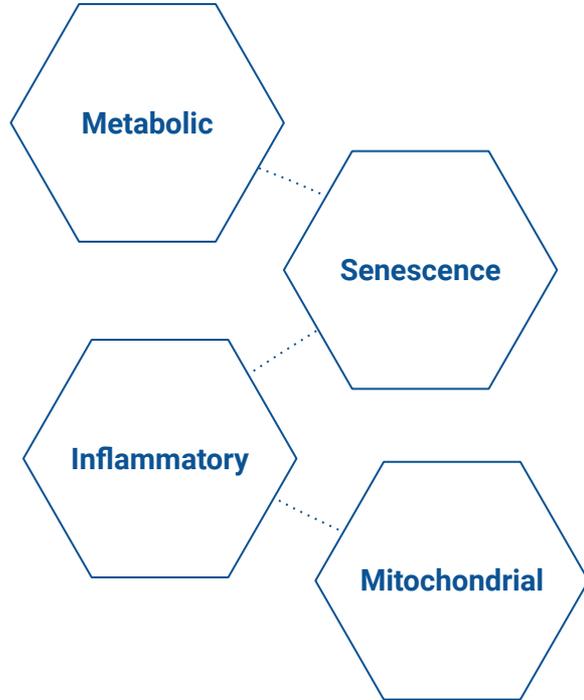
- The most of companies offered not-reliable biomarkers confirmed on a small group of patients.
- Currently no FDA approved at-home Molecular Test.
- Some European countries restrict using and sell at-home genetic tests directly to customers.
- The increasing R&D funding, along with the strong market presence by major players in the market, has created a strong entry barrier for new entrants.



Biochemical Biomarkers

Biochemical Biomarkers Framework

By Research Field



Selected companies offered **Biochemical Biomarkers** diagnostic has been splitted on four sub-categories by the **biological pathway** involved into **aging and age-related disease**. Also this market has been segmented by their **end-user of product**:

- accredited clinical laboratories,
- at-home tests,
- biotech companies (developing new biomarkers),
- service.

Also **invasivity of biomarker** as well as **sample types** (blood, urine, saliva etc.) are described as a main characteristics demanded for this category.

We have **evaluated companies** by the gradation of their clinical products **according to sensitivity of biomarkers to age-related disease** and **fold-change in older patients after 60 years**. The most reliable companies have been selected by this characteristics.

Besides, this analysis brings a **comprehensive view of the market structure** and **development**.

Scope of Companies with Biochemical Biomarkers Approaches

Metabolic

Senescence

Inflammation

Mitochondrial

Aging



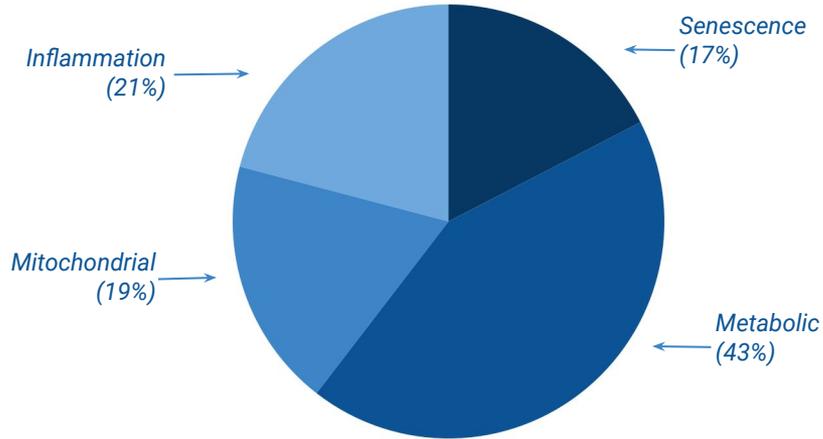
Age-Related Diseases



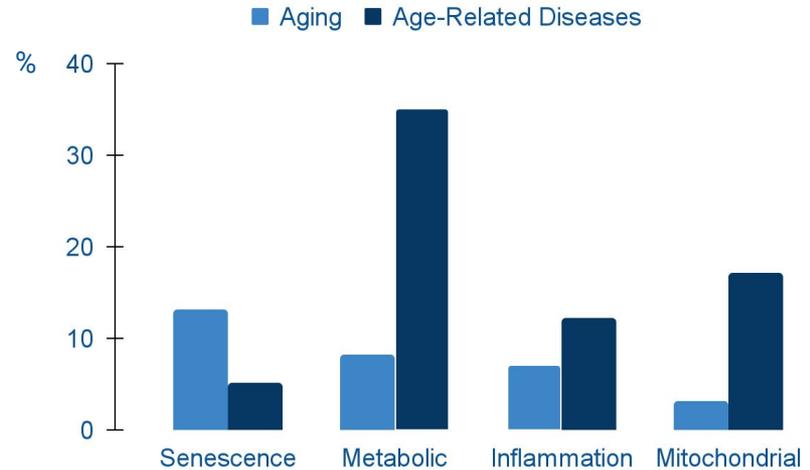
Biomarkers of **Metabolic state** are the most popular in the market as tool of assessment the **risks, detection** and **monitoring of Age-related diseases**. This fact may be explained by tests availability, low costs, reliability, good correlations between changes in organism state and biomarkers levels. Some companies provide **Senescence, Metabolic, Inflammation**, and **Mitochondrial** markers to evaluate **Aging**.

Market Overview

Distribution of Companies by Biomarker Type



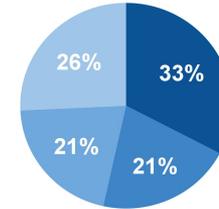
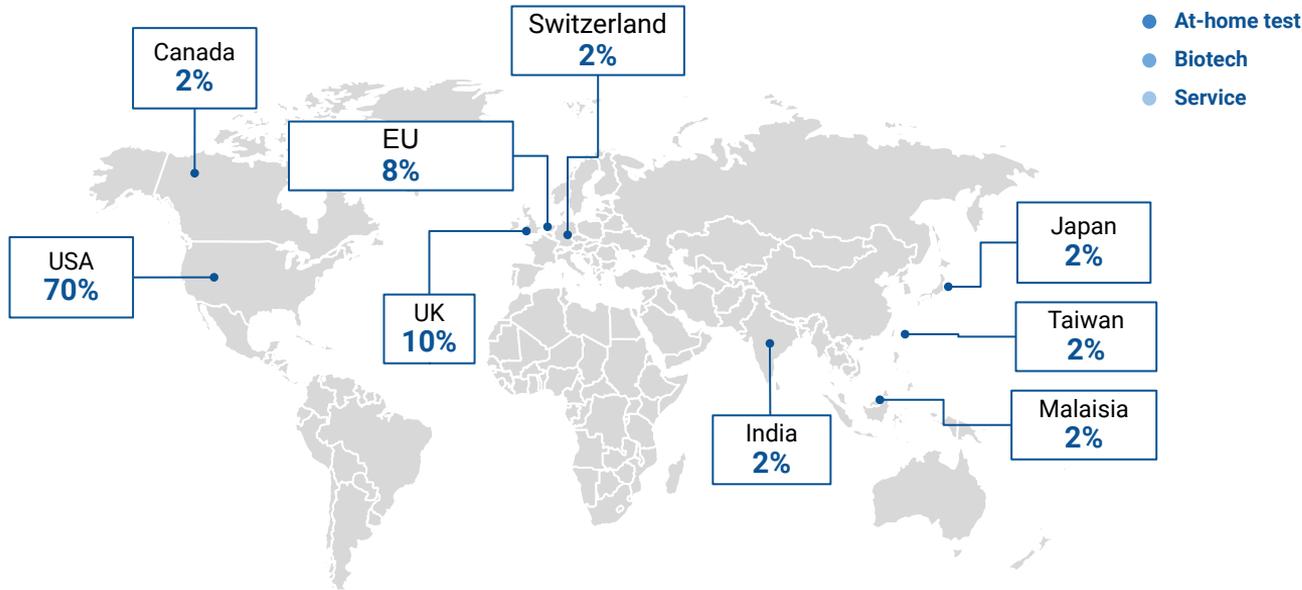
Distribution of Companies by Test Application



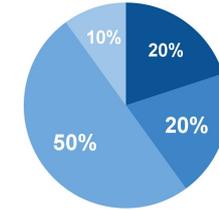
The most popular approach (**43%** of companies) for evaluation of **Age-related diseases** is **Metabolic** markers assessment. Such tests are routine and informative. Only several markers from this group are used for evaluation of **Aging**. **Inflammation** markers (**21%** of all companies) are used both for assessment of **General health state/Age-related disorders**, and for detection of **Inflammaging**. The **Senescence** markers testing is provided by **17%** of companies. **Mitochondrial** dysfunction markers (**19%** of companies) are used mainly as diagnostic tool to reveal **Age-related diseases**.

Geography of Biochemical Biomarkers Market

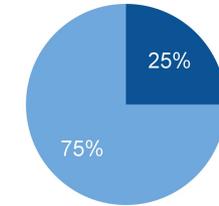
Distribution of Companies



North America



Europe



Asia

The **vast majority of Companies** that provide Biochemical Biomarkers testing is located in the **United States** and accounts for **70%** of the whole range of analyzed companies. Accredited laboratories with **Clinical tests** prevail and account for **33%** of the amount of analyzed companies in the **United States**. The **European region** follows with **20%** of companies, and the majority of companies are located in **UK**. **Biotech companies** developing innovative tests for further clinical use prevail both in the **European region** and in the **Asian region**.

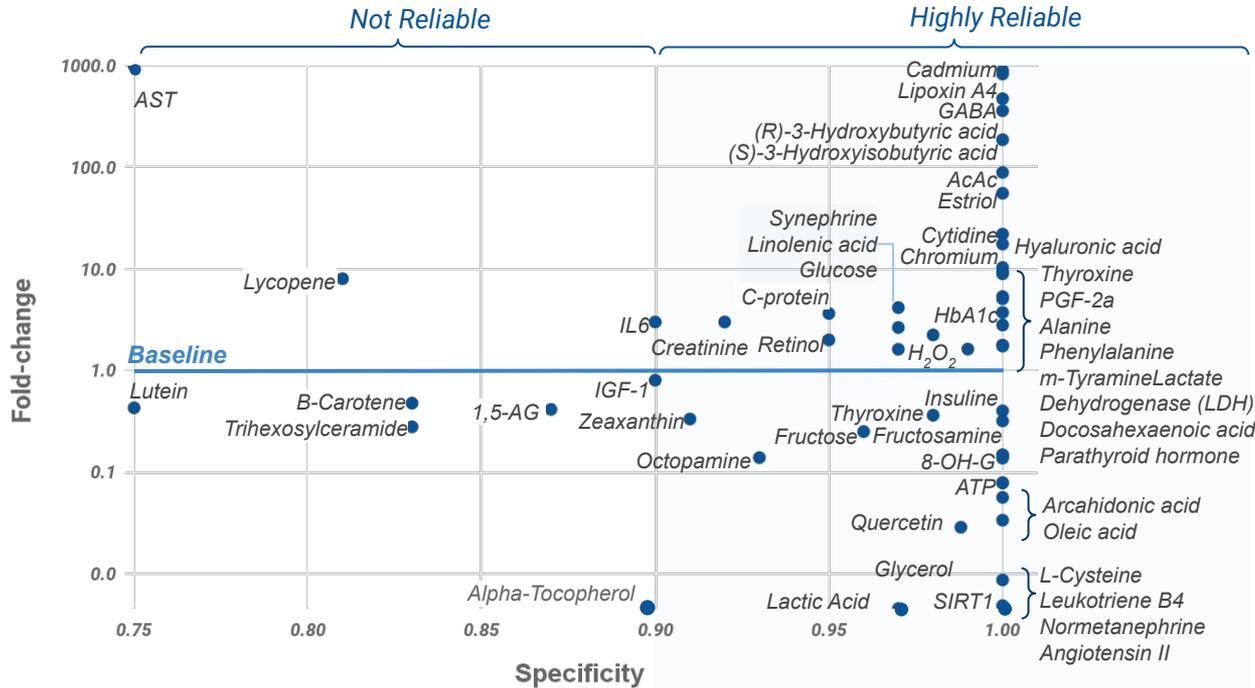
Gradation of Companies by End-User & Biomarker Type



The most of analyzed companies provides Metabolic biomarkers testing in form of **Clinical test** (performed in laboratory under healthcare worker assignment), or **At-home test** (at-home sample collection with subsequent shipping to the laboratory for analysis). At-home tests are expected to be more and more popular in future due to such advantages: possibility to evaluate health state with accurate & reliable lab results, easy to order test, easy to collect sample for biomarker assessment, results are delivered fast, there is ever no need for leaving the home. **Biotech** companies are developing new biomarkers to improve current evaluation of **Aging** as well as **Age-related disorders**, especially **Neurological diseases** and **Dementia**.

Reliability of Clinical Biomarkers for Diagnostic Aging and Age-Related Diseases

Clinical Biomarkers Reliability



AT-home tests

Jinfiniti Precision Medicine has developed lab tests to measure biomarkers of aging in patient's blood. It offers tests that measure NAD, senescence, inflammation, oxidative stress, or other hallmarks of aging, so patient can make better decisions directed at improving his healthspan. The **AgingSOS™** test contains 13 biomarkers that can be used to maximize patient's healthy longevity including circulating and intracellular NAD, SA-β-galactosidase, reactive oxygen metabolites, total antioxidant capacity, vitamin D, high sensitivity C-reactive protein and others.



Walk-in-Lab offers **Anti-Aging Tests**, including **Arthritis** (C-reactive protein, rheumatoid factor, antinuclear antibodies etc.), **Osteoporosis** (vitamin D, Calcium, phosphorus etc.), **Hair Loss (Alopecia)**, **Discount Panel** and **Anti-Aging Hormones Blood Tests** (testosterone, estradiol, prolactin, cortisol atc.) used to determine the main groups of biomarkers of aging reflecting and affecting the rate at which the body ages.



GlycanAge is the biological age test that measures patient's response to lifestyle change. **GlycanAge** determines patient's biological age by looking at the state of the immune system and inflammation. It analyses the glycans attached to IgG. The type of glycans attached to IgG are able to change the function of IgG from pro-inflammatory to anti-inflammatory and vice versa. The balance between them determines patient's general health status and biological age.



Clinical Tests

Life Extension offers **Healthy Aging Panel Test** of blood and urine for biomarkers of aging including thyroid hormones, vitamins (vitamin B12, folate, vitamin D, 25-hydroxy), cardiovascular risk markers (Apolipoprotein B, homocysteine, C-reactive protein), insulin resistance markers (Hemoglobin A1C, glucose, insulin, ferritin) and general health markers (complete metabolic panel with lipids, complete blood count and urinalysis)



Prodrome developed **ProdromeScan Blood Test** that measures hundreds of biomarkers and key biochemical systems critical for optimal health and longevity. The test panel involves markers of mitochondrial function, inflammation (gastrointestinal tract acids), C-reactive protein, metabolic markers and marker of DNA methylation (longevity).



SpectraCell designed the Micronutrient Test (MNT) which **measures 31 specific micronutrients** – vitamins, minerals, amino acids, antioxidants and metabolites—and how they affect cellular function in a person. The MNT uncovers deficiency so that it can be effectively treated, thus facilitating real prevention. Not only will correcting intracellular deficiencies slow aging and degenerative disease progression, but it can also prevent as well as repair cellular dysfunction, and by extension disease.



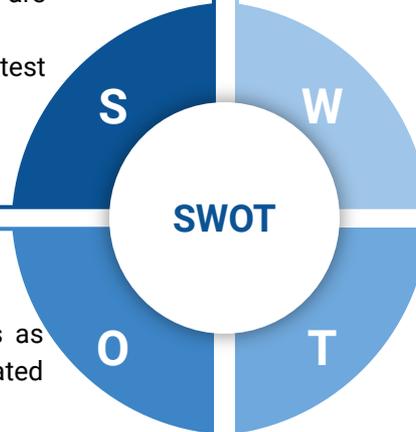
Biochemical Biomarkers: SWOT Analysis

- Easy to use for diagnostic of age-related disorders.
- Low cost of test kit and service.
- Variability of diagnostic markers.
- Enough trained professionals.
- The most of technologies for sample collection are non-invasive (urine, saliva, blood).
- Growth of number of companies that offer at-home test for self-diagnostic.

- High competition in the market.
- No clinically approved direct biomarkers for aging.
- No biomarkers that can evaluate risk of development and mirror of age-related diseases progression.

- Combination of biomarkers can improve prediction.
- CDEs and quality control examples are available.
- The development of the new blood-based markers as perspective for evaluation of aging and age-related diseases.

- The procedure of sample collection sometimes is invasive (for example CSF) and has risk for health.
- The most commercial tests for “healthy living” use non-specific biomarkers.

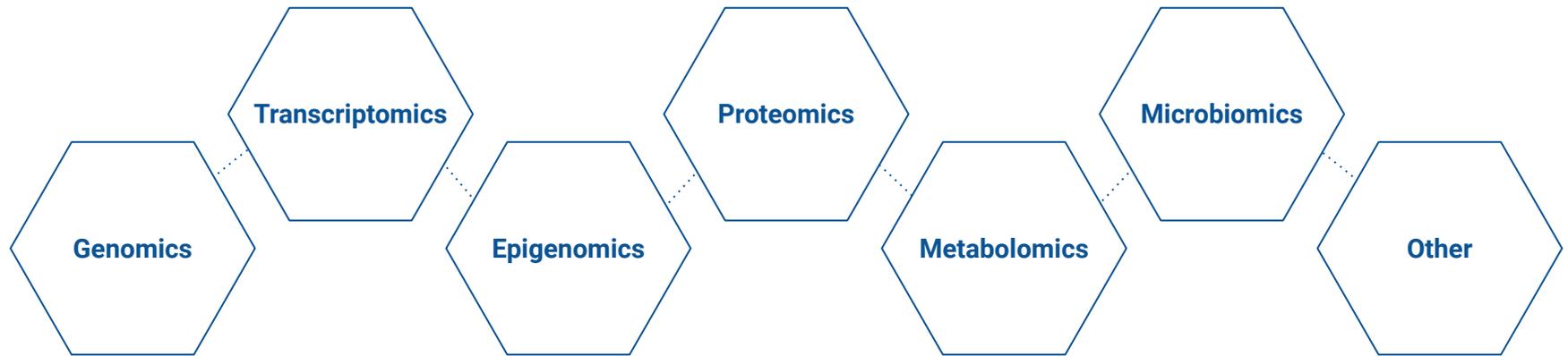


Omic Biomarkers

Omic Biomarkers Framework

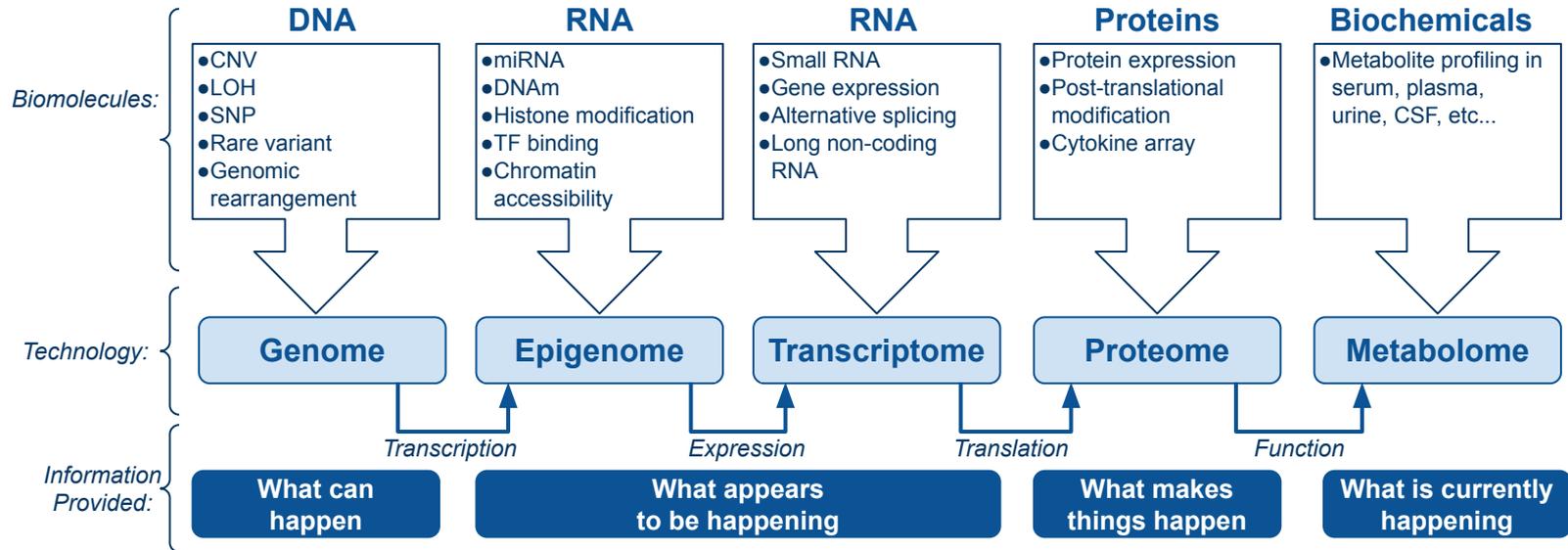
Ahead of database creation, we picked the **most significant fields of omics diagnostics for aging and age-related disease**. The categorization of companies is based on the main technologies applied for prediction of aging progression and **supported by the latest scientific evidence**. Also, companies were distinguished by their area in the market - accredited clinical laboratories, at-home tests, biotech companies (developing new biomarkers), service. Thus, the framework not only brings a **comprehensive view of the market**, but also **sustains relevance in advance to the development** of technologies and research approaches.

By Research Field



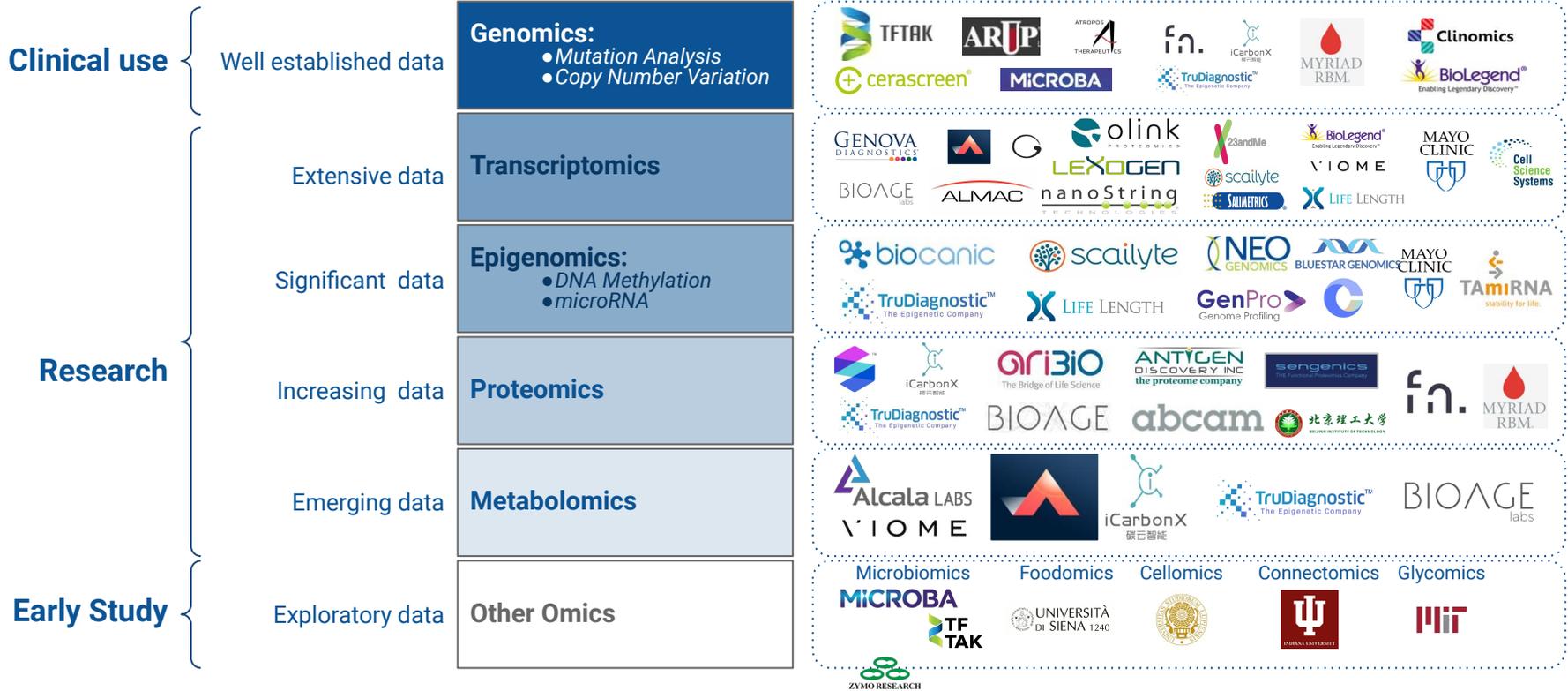
Omic Approaches in Clinical Diagnostic of Aging and Age-Related Disorders

Relationship between single and multi omics data analysis



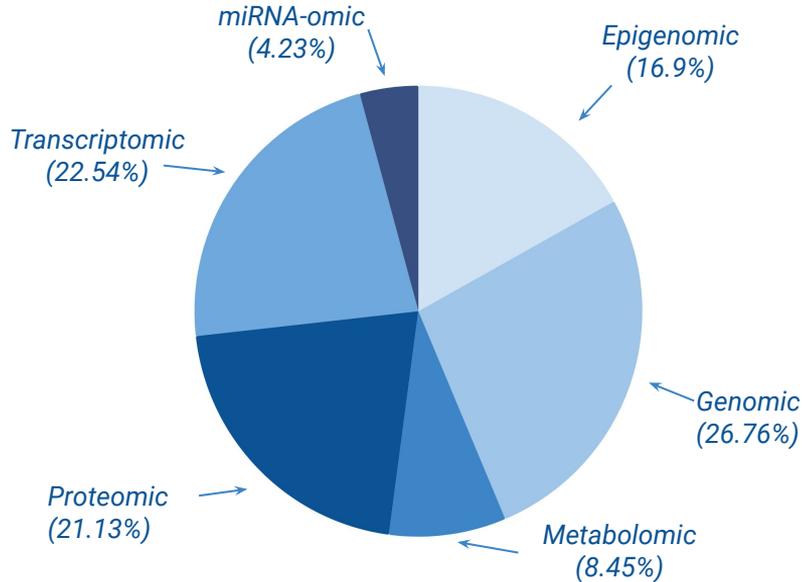
For **evaluation of aging and age related diseases** traditional diagnostic classifies patients into groups according to their clinical characteristics (ie, phenotypes). However, these classifications do not provide insight into the functional or pathobiological mechanisms of the disease within the individual (ie, endotype). **Omics is the comprehensive assessment** of the molecules that **constitute a cell, tissue, or organism**. Integration of multi-omics data, such as genomics, proteomics, and metabolomics, along with clinical data **allows for better understanding of age-related disease pathogenesis** and will be **important for prognosis of aging and predicting, diagnosing, and treating disorders**.

Gradation of Individual Omics Technologies for Studying of Aging

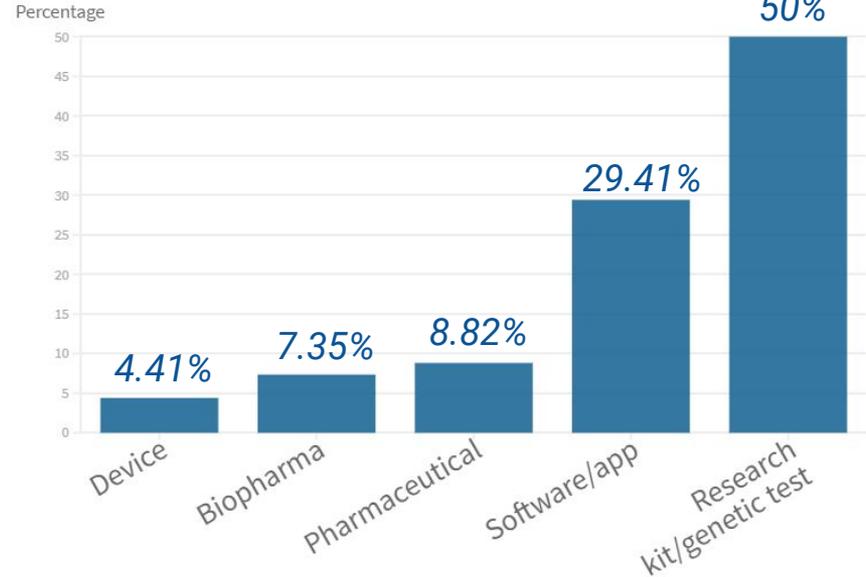


Market Overview

Distribution of Companies by biomarker type

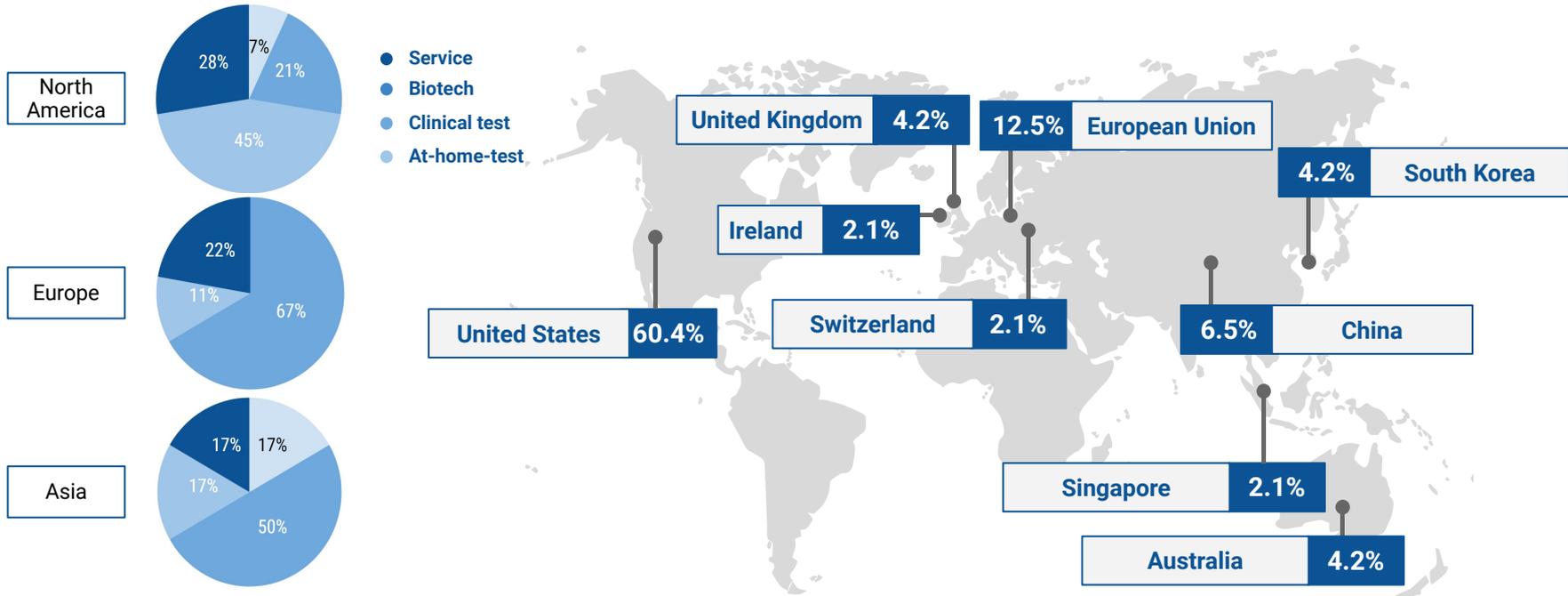


Distribution of companies by product type



The most popular biomarker type among companies is **genomic biomarker** - **26.76%** of all companies use it for analysis. Following are transcriptomic and proteomic biomarkers: they are used by **22.54%** and **21.13%** of companies. Then there are **epigenomic and metabolomic biomarkers**, which are utilized by **16.9%** and **8.45%** of companies respectively. Finally, the least share is occupied by miRNA, which is analyzed by **4.23%**. The most of the companies are involved in research kit/genetic test development. However, there is a promising number of companies building a software and applications.

Omic's Market Geography



The global spatial Omic's market size is expected to reach **\$ 500 million** by **2030**. It is expected to expand at a **CAGR of 10.00%** from this period. The COVID-19 pandemic slowed down many industries worldwide. However, this market did not face the extensive negative impact of the pandemic. **Startups** and **well-established players** continued their **product development** and launched novel solutions. The **USA is a leader** in this area and **share ~60.4%** of all companies on the market. This region characterized **rise in commercial interest** and **government support** for genomics and sequencing technologies, **high demand for personalized medicine**, and the presence of a substantial number of translational and academic research organizations.

Key Market Trends

Key Market Trends

Clinical application

From Omic to Multi-Omic assay

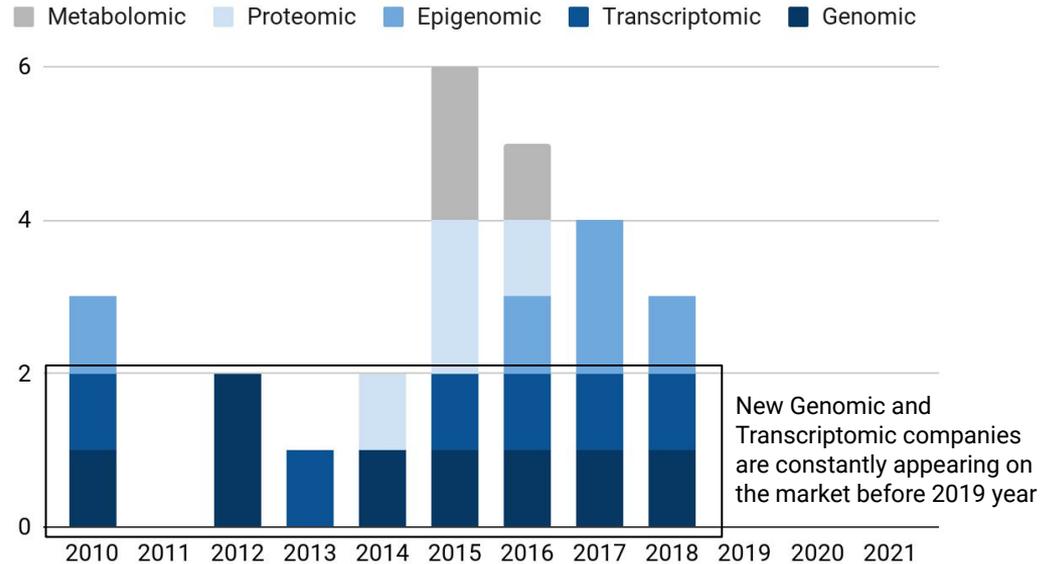
Early prediction of age-related disorders

Proteomic biomarkers quantification

Growth of direct-to-customer market

Digitalization

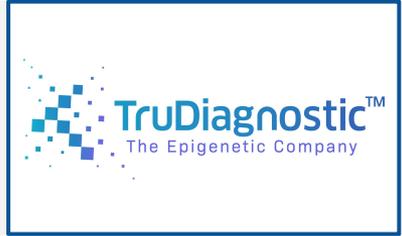
New Companies: Omic Biomarkers



First omic companies appears in the market after 2000. For the last decade the number of these companies grow slowly, **only 18 new companies** appeared on the market. More the all **no any development** of the new companies after 2019. The **Genomic** and **Transcriptomic** biomarker are the top categories in this development. Currently, **genomic tests are relatively niche market** with a number of services **available over the internet**. However, the commercialization of personal genome sequencing is set to grow and, in the future, it **could become a routine part of clinical practice**.

Clinical Trials And R&D Examples of Practical Applications

TruDiagnostic is a CLIA-certified and HIPAA-compliant lab which uses a multi-omic approach with the primary focus in DNA Methylation. TruDiagnostic began with TruAge – a test that measures Biological Age by looking at Methylation. Now this laboratory also provide a full suite of aging related metrics. This includes telomere length measurements, intrinsic and extrinsic age calculations, immune cell subset deconvolution, current pace of aging, and more.



Clinomics is a leading company for early diagnosis of cancer/diseases based on genome and pursues to overcome aging and diseases through liquid biopsy and Multi-Omics technology. Clinomics specializes in offering a genome-based, early cancer diagnostic service through the technology of Multi-Omics analysis and simultaneous detection of CTC and cfDNA in the blood with our internationally renowned biomedical information processing abilities.



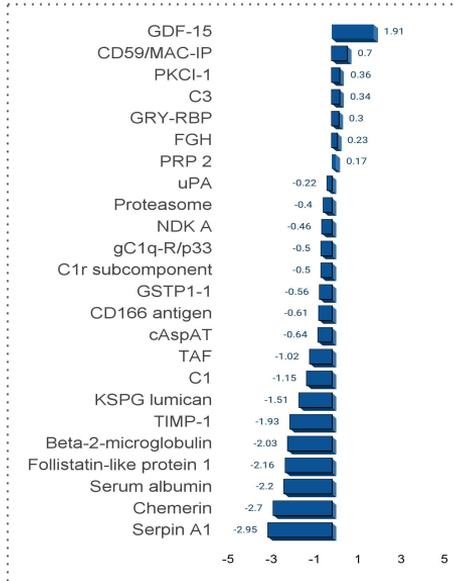
BioAge is biotech companies developing mapping human aging from the ground up. BioAge utilizes broad anti-aging pathways to target specific age-related diseases. BioAge has a unique proprietary biobank of longitudinal data and AI platform for identifying longevity targets. The company is building deep molecular profiles of these samples, incorporating proteomics, metabolomics, and transcriptomics to identify the best drug targets for healthy aging.



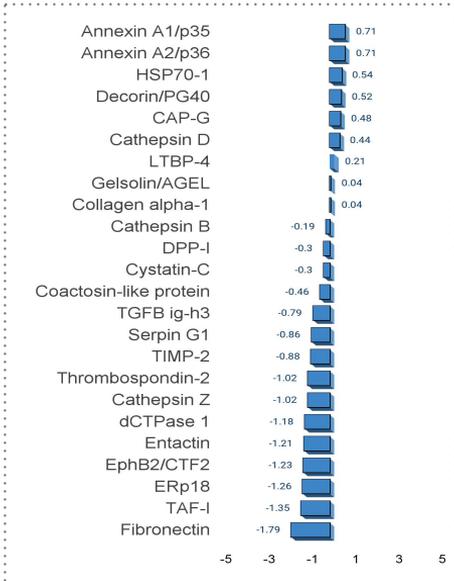
Plasma Proteomic Assay in Older Adults

Changes of Biomarkers Level in Plasma in Older Patient (>60 years) vs Young, Log2(Old/Young)

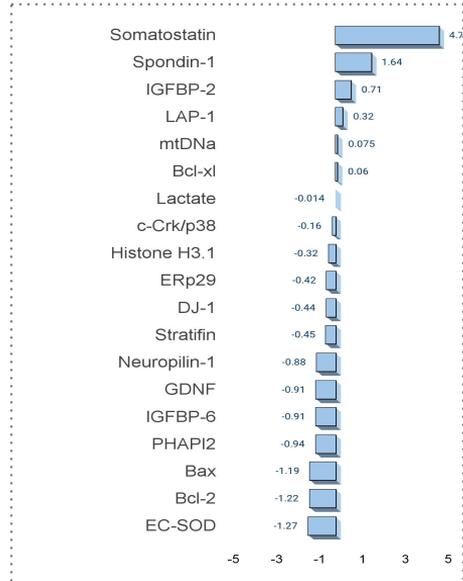
Inflammation & Immune Response



Extracellular Matrix & Proteostasis



Mitochondrial Function & Cell Survival



While unbiased transcriptome and in vitro proteome analyses are valuable, they do not directly assess the presence of secreted proteins in human body. Thus, proteomic studies are needed to accurately and quantitatively identify SASP factors as they are present in the secretomes of senescent cells. BLSA's (Baltimore Longitudinal Study of Aging) analyses identify several **candidate biomarkers of cellular senescence** that overlap with aging markers in human plasma, including **GDF15, Somatostatin, SOD, Fibronectin, and SERPINs**, which **significantly correlated with age in plasma from a human cohort**, and facilitate the identification of potential senescence biomarkers to assess the burden, originating stimulus, and tissue of origin of senescent cells in vivo.

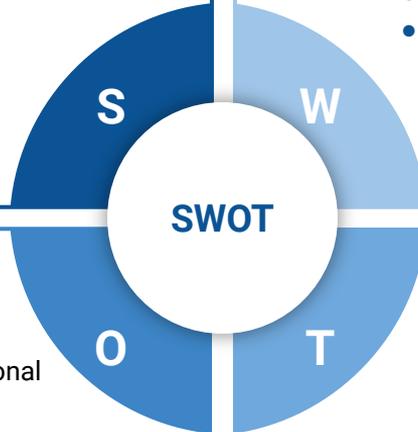
Omic Biomarkers: SWOT Analysis

- Represents net results of transcriptional and translational regulation.
- Non-invasive procedure of sample collection.
- Good method for prognosis of aging, predicting, diagnosing, and treating disorders.

- High cost of testing for customers.
- High cost on research equipment and complexity in predictive genetic testing are major factors that may restrain the market to a certain extent going ahead.
- Lack of trained professionals.
- No standards for data interpretation.

- The rise in commercial interest and government support for genomics and sequencing technologies
- The high demand for personalized medicine
- The presence of a substantial number of translational and academic research organizations.

- Not all omic approaches have established protocols.
- Time consuming analysis.
- Need special software for data processing.



Physiological Biomarkers

Physiological Biomarkers Overview

Physiological biomarkers refer to measurements of physical capability and physiological function. It is a person's ability to perform the physical tasks of everyday living, are useful markers of current and future health. These anthropometric measurements and noninvasive tests are one of the clearest ways to assess age-related changes. The main advantages of physiological biomarkers are their simplicity and public accessibility.

The most common physiological biomarkers are **handgrip strength and gait speed**. These biomarkers assist in the evaluation of generalized weakness and frailty in middle-aged and older adults. Another example is physiological function biomarkers such as **pulmonary function tests, blood pressure, and pulse-wave velocity**, which might show specific organs' functional decline.

The physical capability and physiological function biomarkers are mostly implemented in clinics for the **overall health assessment of middle-aged and older adults**. However, such biomarkers are detectable only in the late stage of aging, so they are not helpful for early diagnostics.

Additionally, physical capability test are used in **population-based studies**. These objective measures complement self-reports, improve validity and reproducibility.



Physiological Biomarkers Examples

- Handgrip strength
- Gait speed
- Chair rise time
- Standing balance
- Pulmonary function tests
- Pulse-wave velocity

Practical Applications of Physiological Biomarkers in Longevity

Handgrip strength and gait speed indicate the generalized weakness and frailty caused by the progressive loss in skeletal muscle mass and strength, known as sarcopenia.

Poor performance in tests of grip strength, walking speed, chair rise time and standing balance, and so on, are associated with **higher mortality rates**.

The skin strength, elasticity and diminution of subdermal fat can define the person's **biological age** with high accuracy by 3D facial imaging.

The risk of osteoporosis can be assessed by altered body composition and bone health measurements with dual-energy X-ray absorptiometry (DEXA).

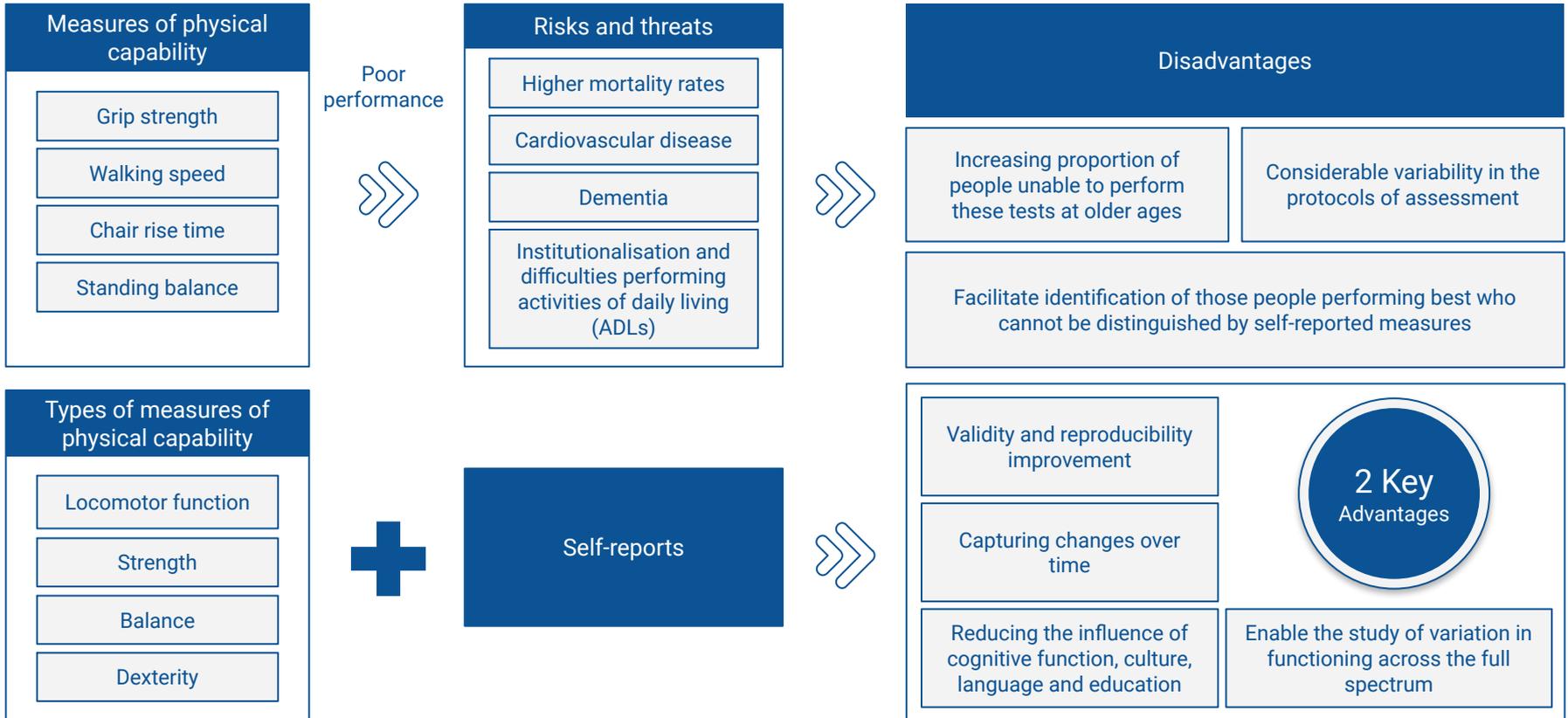
Lower levels of physical capability are associated with **higher risk of cardiovascular disease (CVD), dementia, institutionalisation and difficulties performing activities of daily living (ADLs)**.



Physiological Biomarkers Applications

- **Sarcopenia diagnostics**
- **Risk of osteoporosis evaluation**
- **Risk of CVD evaluation**
- **Risk of dementia evaluation**
- **Biological age estimation**

Biomarkers of Physical Function Domain Overview



Physiological Biomarkers: Examples of Practical Applications

Babylon is a company that makes healthcare affordable and accessible all over the world. They deliver it through the devices people already own, e.g. smartphones. Babylon is combining AI and technology with human expertise, and their areas of expertise are **24/7 access to doctors, Dedicated Care Advisor, Personalized Care Plans, Seamless referrals to specialists, Digital health tools, Chronic disease management.**



Mediage is a company that provides digital healthcare services targeted at promoting the healthy life of people. It is connecting digital healthcare data globally based on innovative health information analytics. They provide **genetics check-ups, analysis on major disease, cancer, and mortality risks based on the biological age health index, nutrition recommendations, mobile check-ups and counseling, and big health data platform.**



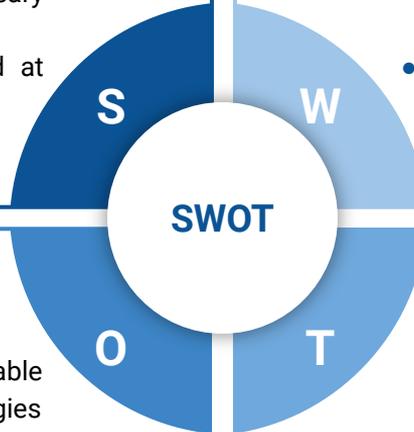
Sonde is detecting changes in your health from changes in your voice. With a short voice sample Sonde, symptom detection technology can tell if you are at **risk for leading health conditions, including asthma, COPD, COVID-19, depression, and anxiety.** Organizations use Sonde's respiratory vocal biomarker platform to enable non-invasive and accessible biomarkers in their programs.



Physiological Biomarkers: SWOT Analysis

- The complex analysis of many physiological biomarkers will give information onto accurate health states.
- The physiological biomarkers also analyze both early-stage and predisposition to certain diseases, which helps individuals to understand necessary preventive measures and treatment.
- Some physiological biomarkers can be measured at home surroundings as well as at clinics.

- The development of cutting-edge AI and ML technologies will simplify the biomarkers data analyzes and improve the accuracy.
- The spread of novel biotechnologies as portable analyzers, wearable devices, and digital technologies will increase quality and decrease costs.
- The study of the molecular mechanism underlying physiological biomarkers is a key way for understanding and eliminating numerous diseases via the development of new screening procedures and treatment.



- The physiological biomarkers can define a few pathogenic states at the same time, so it can be hard to define the real problem.
- The accurate result can be received by a complex approach that includes many physiological biomarkers, which can be expensive and public inaccessible.
- Their research is needed because the list of physiological biomarkers is incomplete

- The environmental and lifestyle factors can influence the biomarker quantity and quality, which may affect the accuracy of the test.
- Existing data repositories have a lot of controversial information, so more investments in research are needed
- The biomarker data is not full (lacking in the data from all ages, sexes, races, etc.), which may cause inaccurate results for certain population groups.

Digital Biomarkers

Practical Applications of Digital Biomarkers in Longevity

Cardiovascular health disorders, such as heart stroke, coronary artery disease, heart attack are associated with high mortality rate. Some of them can be even “silent” - the damage is done, but the person is not aware of it. Monitoring and evaluating **cardiovascular health biomarkers**, obtained from smart devices, helps to predict and control cardiovascular disorders

Neurocognitive digital biomarkers are used to identify and predict such neurocognitive disorders as Alzheimer's disease, amyotrophic lateral sclerosis (ALS), brain tumours, epilepsy, Parkinson's, autism spectrum disorders, dyslexia, etc. Many of them are associated with aging. Furthermore, analyzing neurocognitive biomarkers can significantly improve life quality among the elderly.

Aging-clocks are established with the help of ML technologies. Huge massive of data obtained from digital biomarkers are used to develop aging models and predict life expectancy. Aging clocks have proven to be an indispensable tool in aging research, letting scientists understand its mechanisms and develop longevity interventions.



Digital Biomarkers Applications

- Several types of cancer prediction
- Control of drug release
- Give information about cardiovascular health
- Predict aging-related neurocognitive disorders
- Implementation in aging-clocks

Digital Biomarkers from Smart Devices

Digital biomarkers from smart devices are parameters collected and processed by such devices as portables, wearables, implantables or ingestibles. A number of different portable devices can be utilised for the collection of digital biomarkers including smartphones and tablets.

Most commonly, these biomarkers are accounting such physiological conditioning as the temperature of human skin (by digital thermometer), blood pressure (by digital sphygmomanometer), body motion (by gyroscope, accelerometer, and magnetometer), heart rhythms (by wearable electrocardiograph), heart rate (by photoplethysmography device), and blood oxygen levels (by noninvasive pulse oximeter). These measurements complement and can even **replace traditional physiological tests**.

Additionally, some devices can measure biochemical parameters in body fluids. These biochemical parameters are pH, blood oxygen saturation, protein concentration, amino acids, lipids, electrolytes and metabolites, hormones, and pathogenic bacteria. Moreover, such devices can control the not only concentration of biomarkers but also automatically controlled drug release.



Digital Biomarkers from Smart Devices Examples

- **Human Skin Temperature**
- **Blood Pressure**
- **Body Motion**
- **Heart Rhythms**
- **Blood Oxygen Saturation**
- **Drug Concentration**

Digital Biomarkers Trends



AI technologies

Currently, AI technologies are used for deep analysis of aging-biomarkers, mortality risk score, aging-clocks development. Researchers are working on the metabolic profile of all-cause mortality risk.



Smart devices

Challenges in smart device manufacturing and data analysis relate to measurement accuracy, non-invasiveness and comprehensive research approaches. Digital biomarkers obtained from smart devices are also proceed using AI/ML technologies



Personalized medicine

AI and ML approaches in analyzing biomarkers data allow to predict individual health status as well as aging pattern. Specific database development will help to implement individual approaches in personalized medicine.

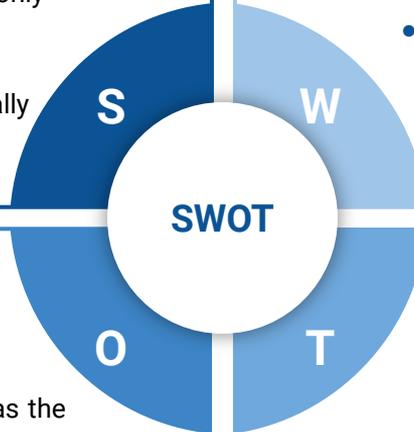


Due to the huge amount of data, obtained from different types of biomarkers the leading trend is related to deep and precise analysis. Most of companies in digital biomarkers field collect data from smart devices and/or online and proceed them using modern AI technologies.

Smart Devices Biomarkers: SWOT Analysis

- Measurements are complement and could even replace traditional physiological tests, which is simple and useful for customers
- There are a number of aging-related biomarkers. Thus, the analysis of smart devices biomarkers can not only predict overall health status, but also longevity.
- Some devices can define circulating biochemical parameters, measure concentrations and automatically control drug release .

- The obtained biomarkers data can be analyzed with the cutting-edge AI and ML technologies which will improve aging analytics and provide personalized medicine.
- A wide range of wearable smart-devices can serve as the source of longevity biomarkers
- Innovative devices manufacturing can provide high quality health/longevity monitoring for all segments of customers
- The score/causal longevity models development using AI/ML technologies



- There is no single biomarker (or a single set of biomarkers) that enables the reliable and accurate measurement of aging progression in humans.
- There are always limits of detection and limits of quantitation in biomarkers measuring.
- The analyzes of some biomarkers requires complex computational methods which can be definitely expensive.

- The environmental and lifestyle factors can influence the biomarker quantity and quality, which may affect the accuracy of the test.
- There is no single approach how to analyze biomarkers data.
- The biomarker data is not inclusive and equitable (lacking in the data from all ages, sexes, races, etc.), which may cause inaccurate results for certain population groups.

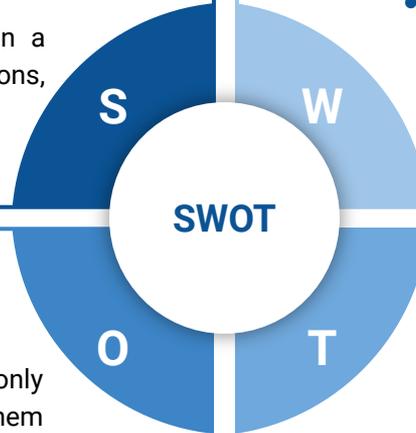
Digital Neurocognitive Biomarkers: SWOT Analysis

- Several studies indicate the link between neurocognitive biomarkers and aging.
- Digital neurocognitive biomarkers analysis can provide precision and individual approach in diagnostic/treatment of neurocognitive disorders
- Some mental tests would have a similar value in a variety of different health-related implementations, including measurements of functional age in panels.

- There are always limits of detection and limits of quantitation in biomarkers measuring.
- Some of technologies must be further approved by FDA, etc.
- There is not single neurocognitive biomarker for precise prediction of several complex diseases

- The development of unique statistical model which will present the link between neurocognitive biomarkers and aging.
- Development of innovative devices which will not only detect neurocognitive biomarkers but also analyze them and treat several neurocognitive diseases
- Manufacturing of low-cost, modular touch screen device for integrating multiple cognitive and biometric assessment technologies.

- The environmental and lifestyle factors can influence the biomarker quantity and quality, which may affect the accuracy of the test.
- There is no single approach how to analyze biomarkers data.
- Some mental/writing tests have their accuracy limit

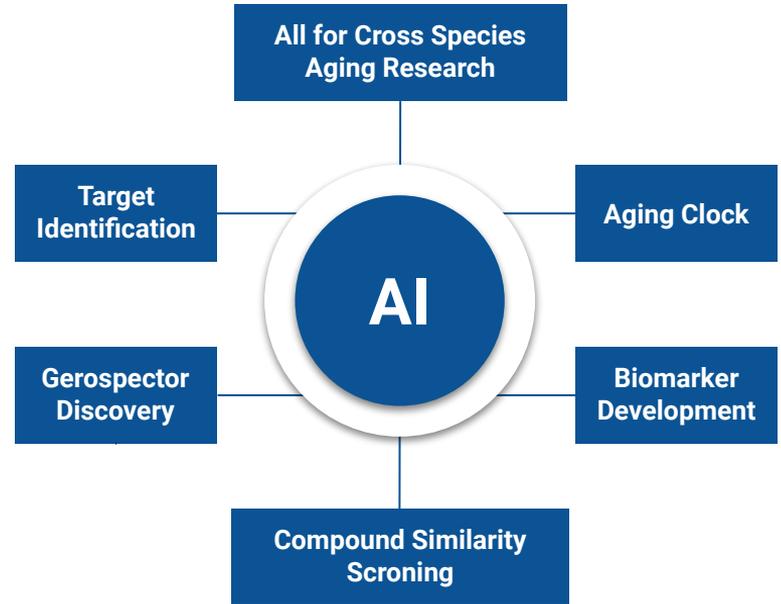


AI in Biomarkers

Increasing Necessity Role of AI in Longevity Research

Currently, there is a necessitating paradigm shift toward more excellent prevention, personalization, precision and patient participation, utilizing all available tools and technologies that are market-ready today to optimize healthy longevity. **Artificial Intelligence is considered a significant engine and driver of future Longevity science and industry.**

The unique role of **AI in longevity lies in P4 medicine.** P4 medicine is a medical model that separates people into different groups—with medical decisions, practices, interventions and products being tailored to the individual patient based on their predicted response or risk of disease. The main difference between P4 medicine and the traditional medical approach is that P4 is directed to the individual patients' wellness, while the conventional approach is directed to population wellness. P4 is defined by the fact that its constituent leading-edge technologies have already achieved a state of market-readiness and clinical implementation, consists of those Longevity-relevant technologies and techniques that are in practice today, what remains to be done in terms of actually applying them for the extension of Healthy Longevity is primarily a matter of data mining, analysis and management, driven by **advances in biomedicine, data science and Artificial Intelligence.**



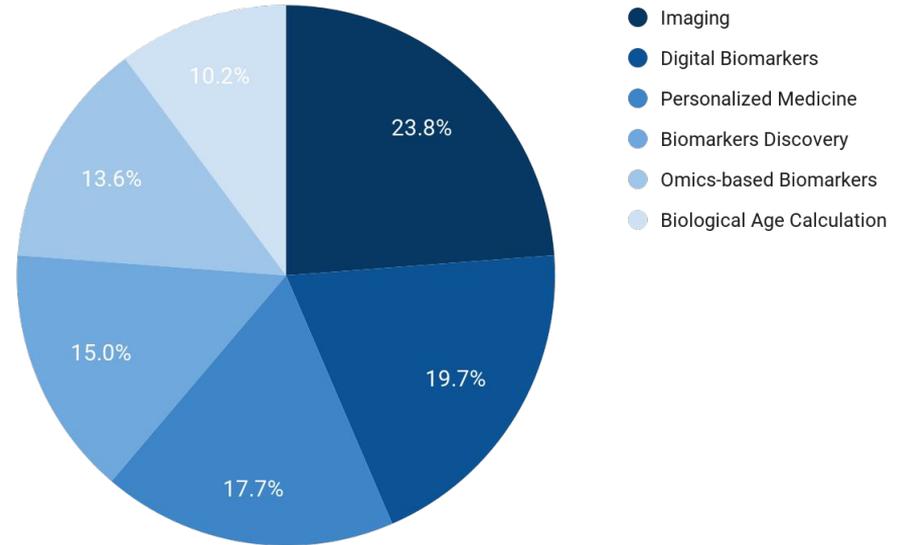
AI in Biomarkers Overview

Artificial intelligence (AI) is a broad discipline of computer science concerned with creating intelligent machines that can accomplish activities that would normally need human intelligence. It is widely embedded in our everyday life and its implementation in clinical researchers and the pharmaceutical industry.

Artificial intelligence-enabled algorithms develop impartial hypotheses for prospective biomarkers or combinations, exploring all feasible scenarios, and **provide better analysis and decisions for precise diagnostics and treatment.**

AI-based biomarkers are divided into subgroups such as imaging, digital biomarkers, personalized medicine biomarkers, omics-based biomarkers, new biomarkers discovery, and biological age calculations via different biomarkers of aging measurement. They are preferably used in imaging, digital biomarkers and in personalized medicine. However, this technology is new and quickly spreads in other fields of study which means that these are **not all possible implementations of AI-based biomarkers.**

Distribution by Subcategories, %



Aging Clocks: Description and Comparison

DNAm Aging Clocks

Horvath Clock
353 CpG sites

MedAE = 3.6

Hannum Clock
71 CpG sites

RMSE = 3.9

Weidner Clock
3 CpG sites

MAE = 3.3

DeepMAge
1000 CpG sites

MedAE = 2.8

Second Generation DNAm Clocks

GrimAge
1030 CpG sites +

MAE - N/A

PhenoAge
513 CpG sites +

MAE - N/A

Blood-based Aging Clocks

Aging.AI
41 blood parameters

MAE = 5.5

Phenotypic Age
9 blood parameters

AUC = 0.88

Transcriptomic Aging Clocks

Transcriptomic Age
Prediction (TRAP)
Blood RNA profiles

MAE = 7.8

Fleischer Clock
RNA-seq profiles

MAE = 7.7

To determine biological age and predict life expectancy, a set of similar or dissimilar biomarkers is most often used. **The DNA methylation (DNAm) clocks** are currently the most popular biological clocks and predictive algorithms for biological age. They're the most precise, with a **median absolute error (MedAE)** of less than 4 years.

DeepMAge clock, which was created using feed-forward neural networks, stands out among this bunch. They are the most precise (**MedE = 2.8**).

Other clocks based on **gene expression** and **biochemistry profiles** provide a different perspective on aging, but they have yet to surpass the **MAE 5 year mark**. Proteomic, genomic, and other aging metrics may develop in the coming years, but high-throughput solutions will necessitate major breakthroughs in the accompanying quantification methodologies.

Deep Aging Clocks

Types of Deep Aging Clocks

Methylation aging clocks

Actually the first developed aging clocks(2013). Methylation aging clocks predict aging and associate it with DNA methylation

Hematological aging clock

Hematological aging clocks are developed from blood biomarkers data. Blood biomarkers data can be obtained from simple and universal blood tests.

Imaging aging clocks

Imaging aging clocks can be developed using only photographic data. Furthermore, many genetic and phenotypic disorders can be diagnosed from a picture.

Transcriptomic aging clocks

Transcriptomic aging clocks are based on gene expression data from several tissues. Transcriptomic data enable the identification of the genes most implicated in specific diseases, such as cancer.



Multiple data types can be used to predict aging and explain the link between aging and mortality, disease, general wellbeing, or other biological processes such as methylation, gene expression, microbiome, and imaging data. Processing the huge amount of data using ML/DL technologies provide different types of deep aging clocks which represent specific aging-models.

The Different Aging Clocks Quantify the Different Features of the Aging Process

All modern aging clocks are proven to be invaluable tools for biogerontology since they offer a unique opportunity to quantify the aging process. This ability is essential for testing geroprotective interventions and studying age-related diseases. Further research has shown significant differences in the Telomeres, Clinical Biomarker and DNAm clocks operate, more specifically the low correlation between their predictions and their unequal sensitivity to certain age-related diseases.

Epigenetic clocks were correlated with each other in the $r = 0.3-0.5$ range ($P < 0.001$ for all). Clinical biomarker algorithm measures were correlated with one another in the $r = 0.4-0.6$ range ($P < 0.001$ for all). However, telomere length was not significantly correlated with estimates from epigenetic clocks or clinical-biomarker algorithms ($r = -0.05-0.03$; $P > 0.05$ for all), and correlations of epigenetic clock measures with clinical-biomarker-algorithm measures were generally low.

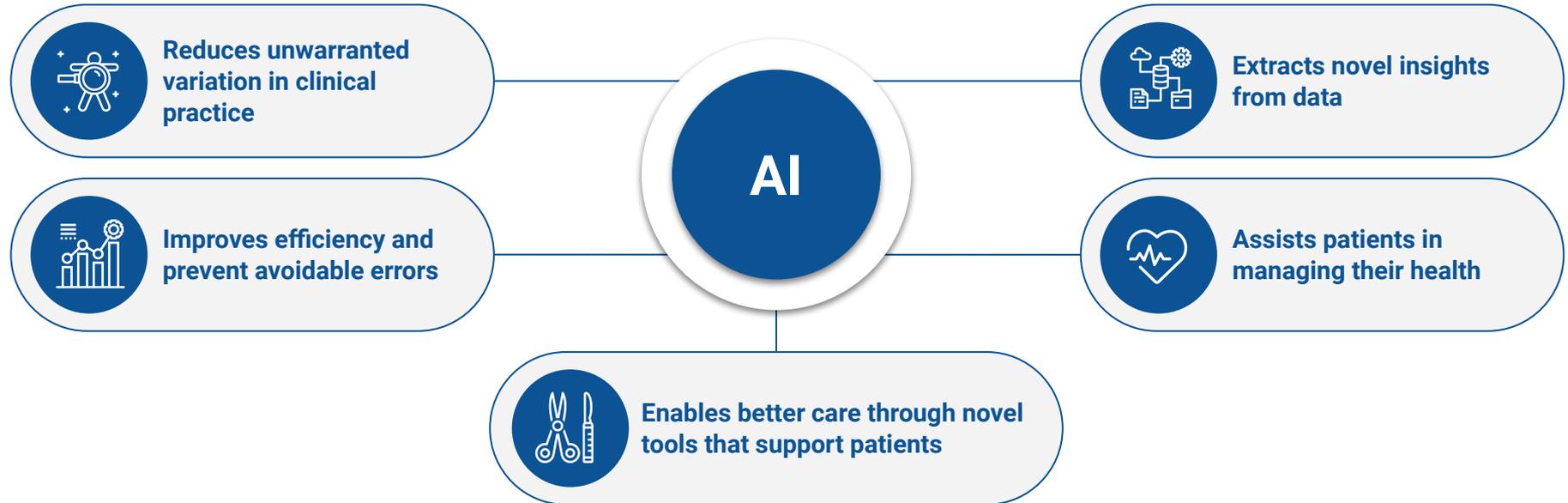
Correlations of Different Age-Clocks (shown above the diagonal)

Telomeres	Telomere Length	-0.03	-0.02	-0.03	n/a	-0.05	0.03	-0.04	Cellular Level of Measures Assayed in Blood
	DNA methylation	353-CpG Clock	0.52	0.37	0.96	0.08	0.02	-0.01	
		99-CpG Clock	0.32	n/a	0.07	0.01	-0.02		
		71-CpG Clock	n/a	0.15	0.10	0.12			
Clinical Biomarkers	DNAm Aging Clock	n/a	n/a	n/a	Patient Level of Measures Assayed in Multiple Organs				
	KDM Biological Age	0.43	0.39						
	Age-Related Homeostatic Dysregulation	0.56							
	Pace of Age								

KDM - Klemera-Douba method

Benefits of AI in Healthcare

Artificial Intelligence holds enormous potential for improving the health of millions of people around the world. It can be used to improve the speed and accuracy of diagnosis and screening for diseases; to assist with clinical care; strengthen health research and drug development, and support diverse public health interventions, such as disease surveillance, outbreak response, and health systems management. Besides, these amazing, but already well-known benefits of AI application, there are a few potentials of AI for healthcare that are mainly unknown for public. **AI has the potential to solve challenges such as:**



AI in Biomarkers: Examples of Practical Applications

Scailyte is a company that is using AI for **biomarkers discovery**. On a multiomics level, ScaiVision (patented analytical machinery) allows them to evaluate and recognize unusual events from single-cell data. They have the ability to quickly turn around big data cohorts obtained from clinical trials and pinpoint exact biological targets.



Cogenica is a company that uses **omic-based biomarkers** for precision medicine. It has advanced automated Clinical Decision Support tool for genetic analysis, allowing them to quickly understand next-generation sequencing data, increase case throughput, and improve health outcomes, which makes a significant difference in people's lives.



Centaura is a company that involves AI in **age calculators** work. Centaura's mission is to explore the biological foundations of aging-related processes and create tailored medicines to tackle their core causes in order to **prevent and reverse aging**, keeping individuals healthy and effective both mentally and physically.



AI in Biomarkers: Examples of Practical Applications

Proscia is a company that uses AI for **imaging biomarkers assessment**. With its Concentriq® digital pathology platform and pipeline of computational applications, Proscia is pushing labs beyond the limits of traditional tools. These technologies are revolutionizing pathology's economics and practice, putting the power of modern, data-centric medicine to work in the fight against cancer.



Savonics is a digital based biomarker platform. Their **digital mobile platform** was designed by a team of leading data neuropsychologists, engineers, and scientists based on hundreds of years of test history. This digital neuropsychologist is used by many researchers, providers, and consumers. They provide solutions and tools to engage better understanding of cognitive health and make progress in the fight against dementia.



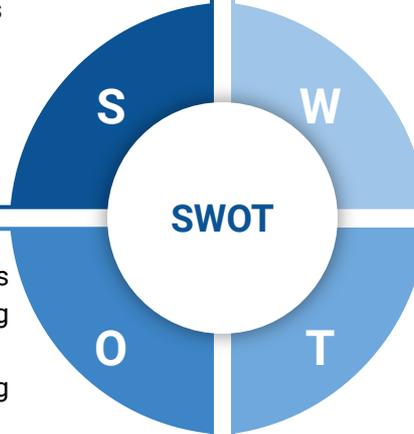
Tempus is a company that aims on making **precision medicine** a reality through the power of data and artificial intelligence application. They enable physicians to make real-time, data-driven decisions to deliver personalized patient care, while facilitating the discovery, development, and delivery of optimized therapeutic options for patients through distinct solution sets.



AI Biomarkers: SWOT Analysis

- Collecting vast amounts of data from the daily lives of people not in a hospital and provide continuous monitoring of health state
- Use powerful statistical algorithms for multi-omics data operating.
- Individual patient level approach which provides solutions for both preventive and personalized medicine decisions
- Increasing percentage of deep diagnostic and preventive medicine.
- Advanced Biomarker-based Prognostics
- Non-invasive

- Possibility to create new apps, mobile and wireless devices or human chips for collecting and integrating data and using Big data.
- AI biomarkers can be used to improve drug development and treatment.
- Continuous monitoring powered by Big Data Analytics.
- Advanced Biomarker-based prognostics.
- AI-driven in silico personalized treatment optimization.
- AI-driven personalized in vivo drug optimization.
- Treatment optimization based on patient genetics.



- Use only the data from mobile apps, or devices, not medical equipment.
- A lack of digital biomarkers popularization.
- Lack of accurate measurement of some physical biomarkers by mobile devices.

- Possibility to hack collected data or use in criminal cases or in geopolitical migration processes.
- Risks associated with the microchips technologies.
- The problem of tests standardization.
- The problem of the data storage technologies.
- The productivity of machine and computer analysis.
- The problem of integrating data from molecules, cells, organs, the individual, families, communities, and the natural and man-made environment.

Imaging Biomarkers

Imaging Biomarkers: Executive Summary

Key definition 1: Medical Imaging - refer to the imaging techniques that assist with identification of disease/condition based on imaging biomarkers patterns, or to determine pharmacological response to the treatment by changes in characteristic imaging biomarkers.

Key definition 2: Imaging biomarkers - biological characteristic or features that is measured from biological image. Imaging biomarkers serve as an indicator of the health status, disease or condition progression.

Imaging application can be applied to probe various pathological conditions- it is a versatile approach. Moreover, imaging may help to find details that might be not available for measuring by other approaches. It may include determination of: tumor size shrinkage / increase, reduction / expanding of the metastatic sites, improvement / assess of the brain activity during functional tests, choosing an appropriate patient group while applying MRI or CT to distinguishing ischemic stroke from cerebral hemorrhage. All of those data would be unavailable without imaging approaches.

Main Features of the Chapter

Database of Selected Companies, R&Ds and Investors focused on Medical Imaging platforms, softs, devices, ect.

Overview of Main Sectors of Medical Imaging companies

Role of AI in Medical Imaging

Review of Notable Medical Imaging Companies

Medical Imaging Market trends overview

Medical Imaging Sector Overview

1

Medical Imaging platforms, software or devices that can be related to digital health systems used to process images of various body parts for diagnostic, treatment - monitoring or research purposes.

2

In the Medical Imaging market, AI-based medical imaging represent fast-growing sector. AI-processing allows for automated, accurate and faster way of clinical data analysis.

3

AI-based medical imaging do not represent a ready-to-use product until it's algorithms trained on vast clinical case data to be able to recognise patterns of disease or to predict disease risk.

4

The access to large, high-quality datasets of clinical case data represent a bottleneck for Medical Imaging. Yet, a plenty of such images sets already exist - in particularly for Radiology sector.

Why Medical Imaging Sector is Becoming More Important Now?

According to recent reports, the global medical imaging market size was valued at USD 15.9 billion in 2020 and is expected to grow further.

The **trends driving** the development of **Medical Imaging sector** are arising of **an aging population** and the increasing **need for early-stage diagnostic** among elderly and youths. The high-yield niche in preventive and personalized diagnostics will be occupied by AI medical imaging due to the nature of its algorithms - neuronal networks, deep-learning able to identify patterns that clinicians may not be thought to look for or even to detect an initial disease trays more accurately than clinicians.

The main limit for the wide application of such AI technologies - clinical data that is used for their training - then vaster it is - then more precise AI prognostic and diagnostic.

Considering these facts, there is a demand for autonomous, quality accurate and predictive imaging-processing tools. To facilitate the creation of such, there is a need in access to clinical case imaging data.

Imaging Biomarkers Categorization

The system below describes the most common application areas of the digital Imaging software, devices and platforms that used in in the clinical and R&D. As such, we distinguished 5 sectors and categorized companies accordingly. It worth to highlight that over 80% of our selected companies is applying Artificial Intelligence, Deep Learning, and Neural Networks algorithms for the processing of the imaging data in order to develop autonomous, precise diagnostic tool that will help clinicians, researchers, clinical trails organizations for more accurate and faster diagnostics.

1

Neuroimaging - large profilization of Medical Imaging software, devices and platforms - that focused on MRI, fMRA, CT, angiography scans, etc. scans analysis for finding a signs and characteristic patterns of pathological conditions or to trace a treatment progress in the brain

2

Ophthalmic Imaging - (microvasculature and optic nerve)to identify ocular-related diseases as diabetic retinopathy, age-related macular degeneration, glaucoma ect.)

3

Radiological imaging - the category include various software, platforms for radiological imaging for various body parts. The imaging produced is based on X-rays, positron emission tomography, and other

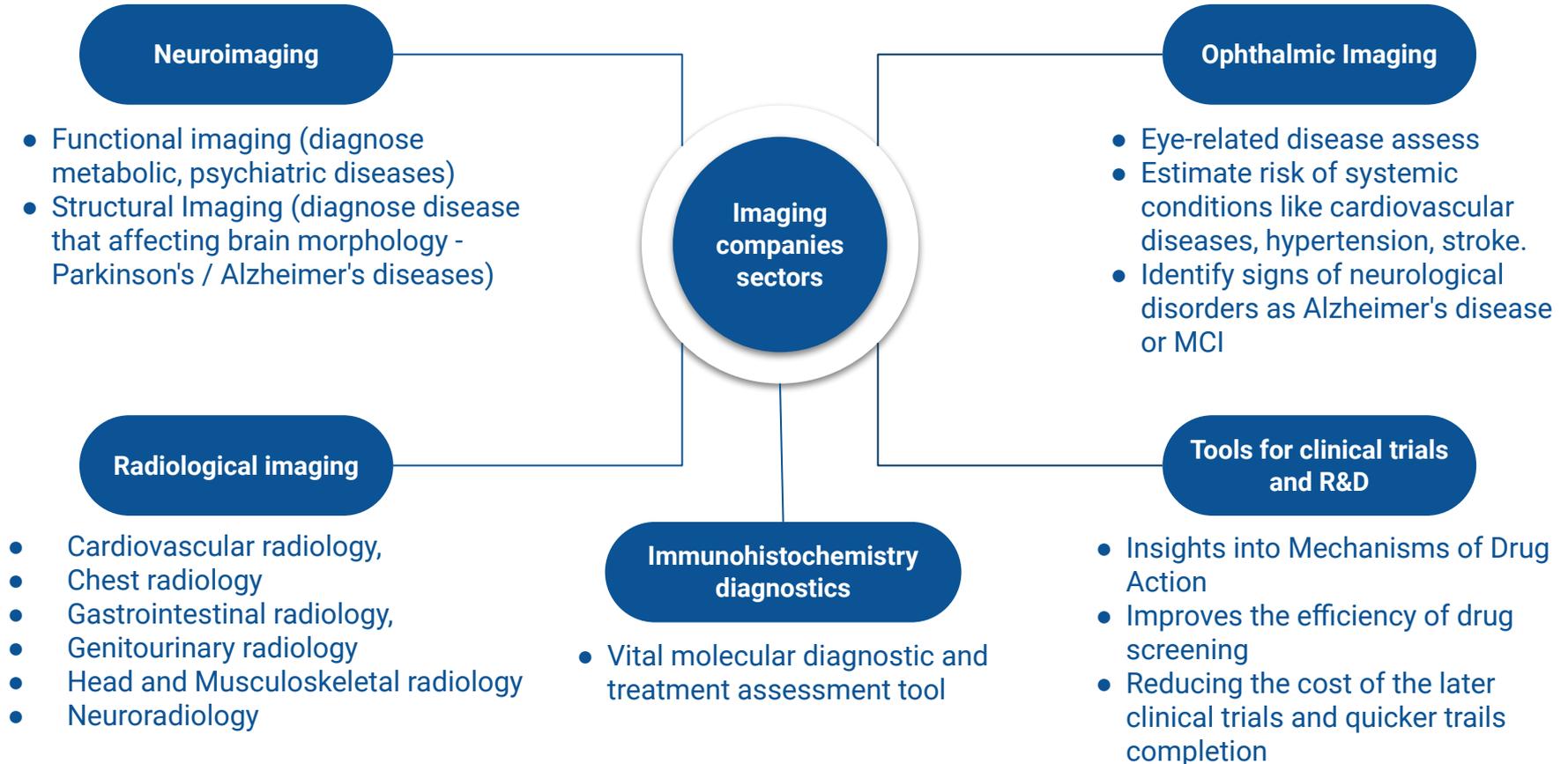
4

Immunohistochemistry diagnostics sector is aiming to assist pathologists in accurate diagnoses and speed up the sample processing

5

Tools for clinical trials and R&D - Forster processing of big data of imaging samples that producing through clinical trials.

Imaging Biomarkers Categorization



Imaging Biomarkers: Examples of Practical Applications

Median brings together imaging specialists and advanced imaging technologies to simplify and improve the quality of clinical trials. The **software platform iSee®** extracts biomarkers using multiple imaging criteria as well as carries out expert oversight of images, automating and standardizing lesion identification, selection, and assessment. In addition, Median's **AI-powered diagnostic software, iBopsy®**, supports doctors with end-to-end technology by providing accuracy, well-timed diagnosis, and avoiding invasive procedures for patients.



IXICO is a well-known neuroimaging provider, collaborating with pharma and biotech companies to improve the outcomes of CNS clinical trials. Using advanced data-driven technology, the company develops and implements innovative neuroimaging biomarkers and image processing techniques that give accurate, rich structural and functional information. IXICO's AI neuroimaging algorithms for Alzheimer's, Parkinson's, and Huntington's disease detecting are based on over 100,000 MRI and PET brain scans from CNS clinical trials.



MedQIA provides an automated AI-powered technology platform to manage imaging for oncology, lung, innovative, and post-market trials. Their **cloud platform and self-improving AI algorithms** allow them to automate complex procedures, control quality, and maintain transparent metrics for each step in the imaging workflow. This contributes to increased efficiency and lower-cost investigations with a shorter turnaround time. The mission is to modernize imaging trial and radiology decision support management by leveraging artificial intelligence automation platforms.



FemTech Biomarkers

FemTech Overview

1

FemTech can be related to software, products and services, and diagnostics that use technology to support women's health.

2

In the FemTech market, Reproductive Health is the largest focus but FemTech is not entirely limited to this category.

3

Other popular and widespread areas in FemTech include Pregnancy & Nursing, General Healthcare, Diagnostics, and Periods.

4

Metrics are tackled via platforms (apps, telehealth, etc.), deep tech (AI, ML and big data), and devices (wearables, sensors, remote patient monitoring.)

5

The FemTech industry can be understood as a continuum process – pre-care → during care → post-care.

Why FemTech is Becoming More Important Now?

The contribution of a woman's health potential throughout pregnancy is enormous. Moreover, the health of the reproductive system, overall health, and controlled pregnancy all play a significant role in the birth of a healthy kid. Specialized medical attention should be given to maximize pregnancy success for both the baby and the mother.

Women are standing up for their rights in all aspects of life, like workplace, health, and equality now more than ever. With the rise of more women dedicating themselves to career, women are deciding to have children later in life and thus require more medical intervention.

More women start thinking about themselves as an individual with own necessities and want to take care of their health in every sphere, including general healthcare, sexual healthcare, emotional wellbeing, pregnancy, period, etc.

Considering these facts, there is a demand for improvement and efficiency of women's healthcare to meet these demands.

FemTech Biomarkers

The term **biomarker** (biological marker) refers to a broad range of measures that capture what is happening in a cell or organism at a given moment. Biomarkers are objective medical signs (as opposed to symptoms reported by the patient) used to measure the presence or progress of disease or treatment effects. The **female biomarkers** are specific to a woman's body and oriented on events that may happen only in a woman's organism. In this report, the female biomarkers are divided into five subcategories: **biomarkers of female cancers, fertility biomarkers, pregnancy biomarkers, biomarkers of female reproductive health, biomarkers of general women's health**. All these categories connect with each other, and most companies belong to few categories.



Biomarkers of female cancers refer to biomarkers that diagnose or predict women cancers (breast, ovarian, endometrial cancers, etc.).



Fertility biomarkers refer to biomarkers that assess women capability of getting pregnant and giving birth.



Biomarkers of general women's health refer to biomarkers of any women body system except reproductive. It can be cardiovascular, gastrointestinal, skin etc.

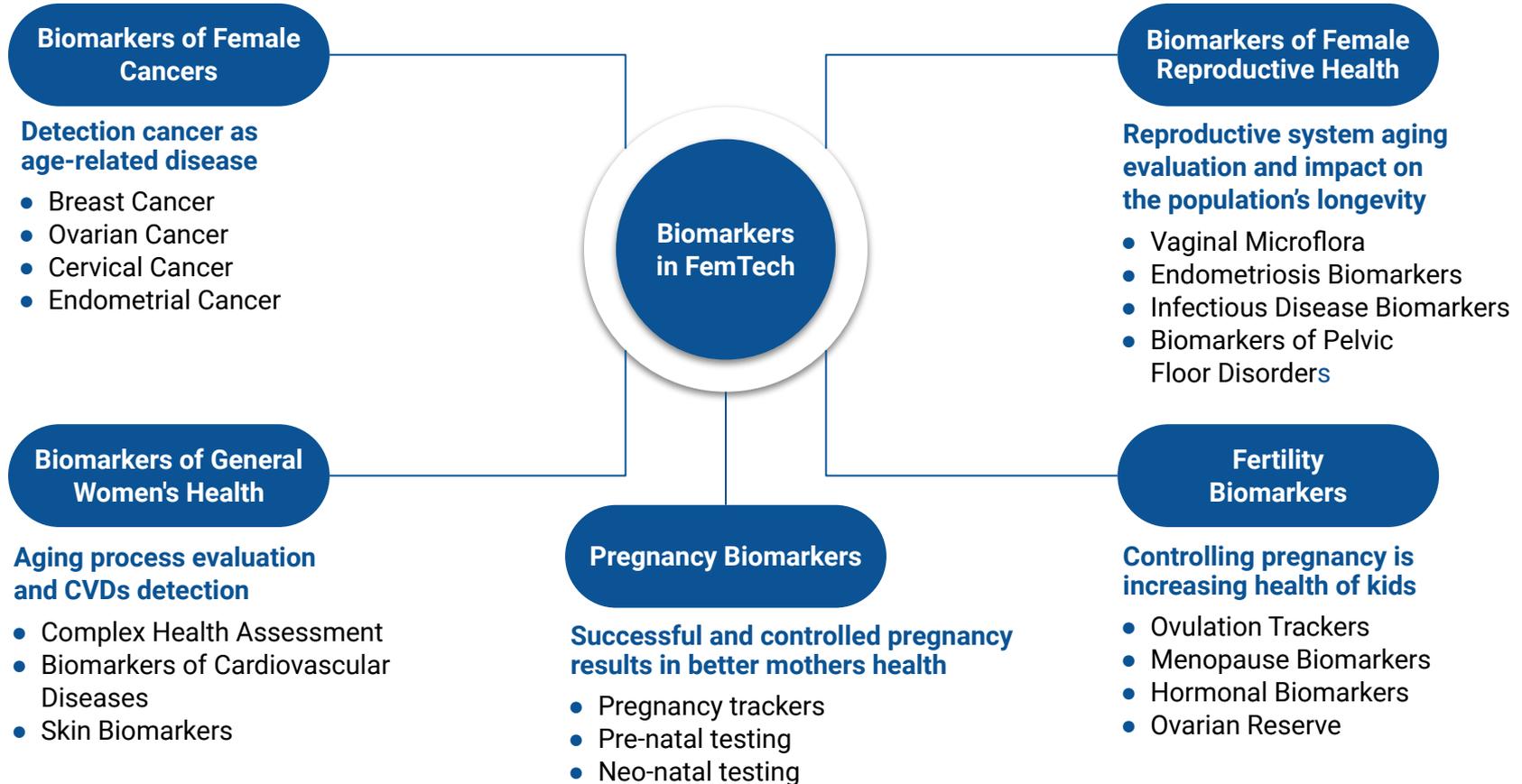


Pregnancy biomarkers refer to companies that develop or implement biomarkers to monitor various events during pregnancy.



Biomarkers of female reproductive health category refers to biomarkers that diagnose or predict various conditions in women reproductive system that can affect life quality.

FemTech Biomarkers



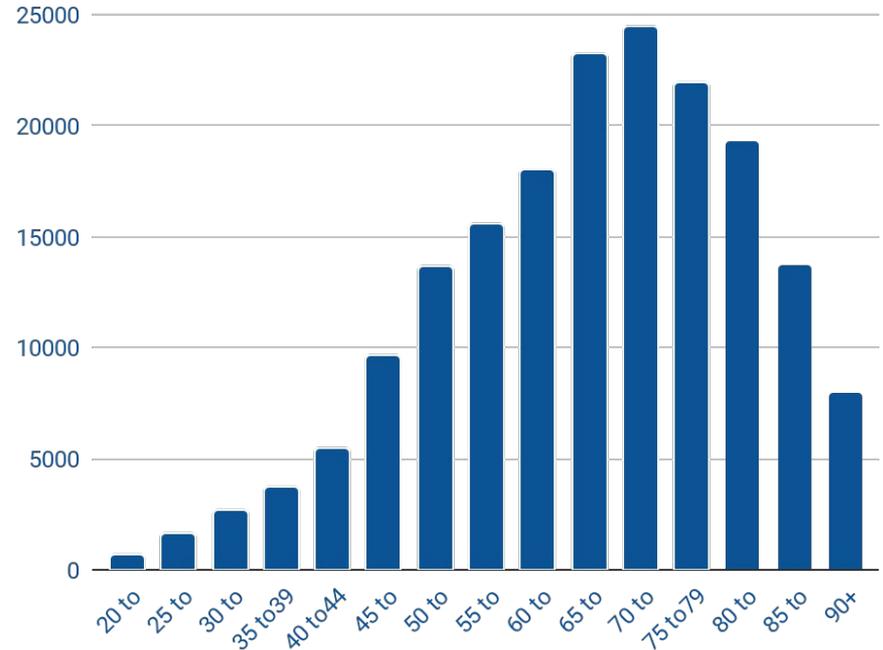
Biomarkers of Female Cancers in Longevity

Cancer is a great threat to female longevity. Usually, the presence of cancer positively correlates with aging due to metabolic, genetic, and physiological dysregulation. Female cancer is not an exception. Statistics say that the number of cancer cases gradually increases and reaches its peak at 70-74 years. However, after this, it declines. The reason for that is simple, not that many people survive to the age of 75-100.

If we talk about female cancers, the highest risk of developing **breast cancer** is women aged 25-49 (about 43%). In older adults, it declines to 21%. Survival rates of women diagnosed with breast cancer are 76%, reflecting the efficiency of new treatment technologies.

Assessment of female cancer biomarkers can not only predict suitable treatment but also **prevent the onset of cancer and promote longevity**. Biomarkers show the key pathways of cancer development, so prevention might include changes in lifestyle, nutrition, quitting bad habits, regular health assessments to monitor not only whole-body functioning but separate systems as well (reproductive).

Age and a Number of Cancer Cases in Female Population per 100,000 People, UK



Pregnancy and Fertility Biomarkers in Longevity

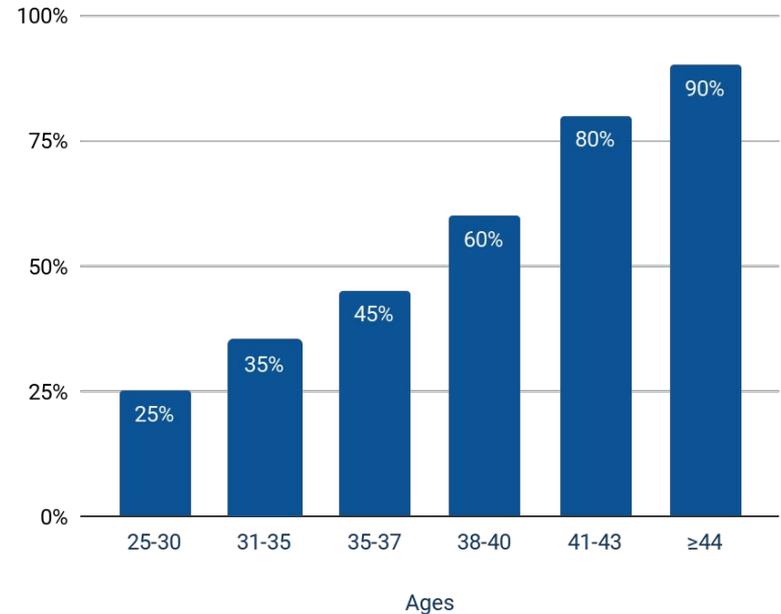
Pregnancy and fertility biomarkers measure reproductive capabilities and the general health of women at any age. On the other hand, **infertility** is a harbinger of various health risks in women, such as early mortality. Infertility status presented in a woman's reproductive years is an early biomarker of risk stratification later in life, which includes not only absence of pregnancy but also adverse health events that underlying reasons of infertility.

In general, infertility increases with age due to the accumulation of **genetic mistakes** in oocytes. It can be caused by different environmental factors such as radiation, chemicals, smoke, free radicals, and toxins. But these mistakes can be a reason for female infertility as well.

Another reason for infertility can be ovarian reserve depletion. The biomarker that clinicians use to estimate the number of oocytes is the **Anti-Müllerian hormone**. The overall levels of AMH decline accelerated after 40 years of age, so it is considered to be a biomarker of reproductive aging.

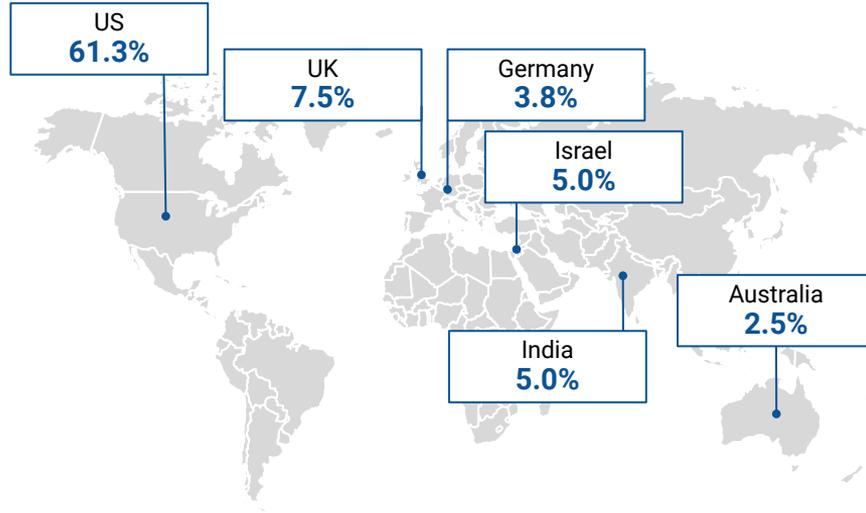
Overall, even though the percentage of infertility cases increases with age, there are various ways to cure it, **eliminating its causes**.

Percentage of Genetically Abnormal Embryos in Different Age Groups, %

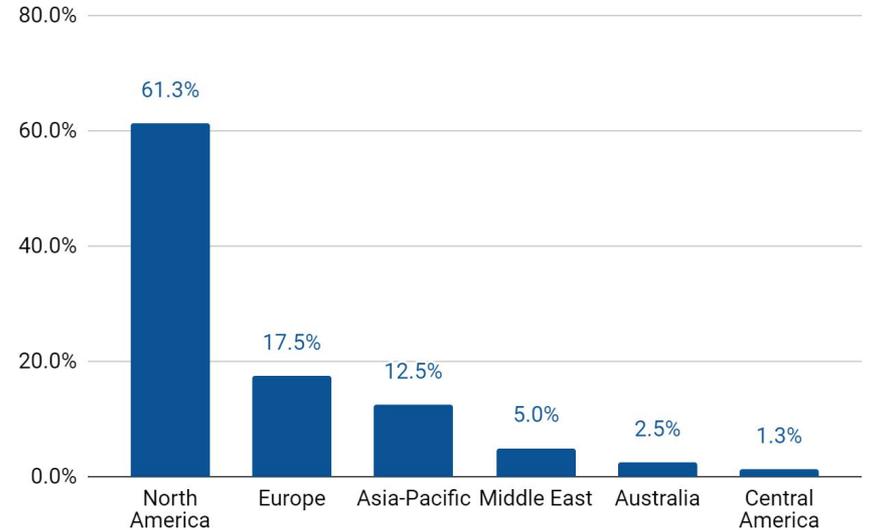


Market at a Glance: FemTech Companies

Distribution of Companies by Country, %



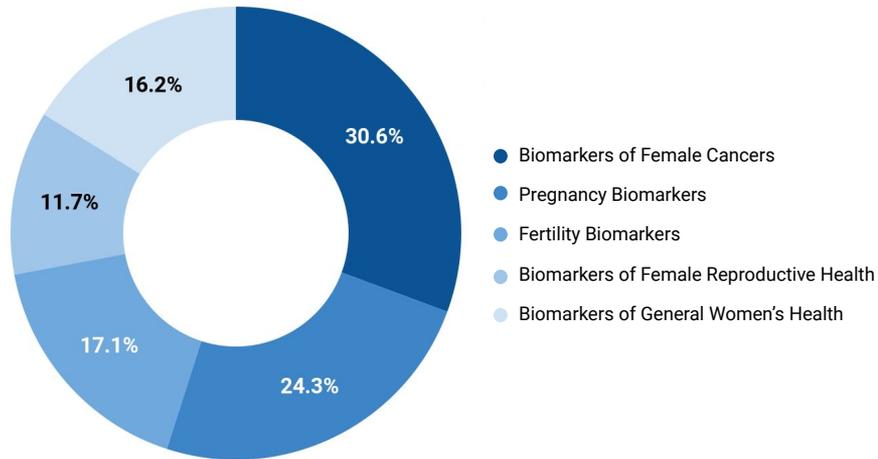
Regions with the Largest Number of Companies



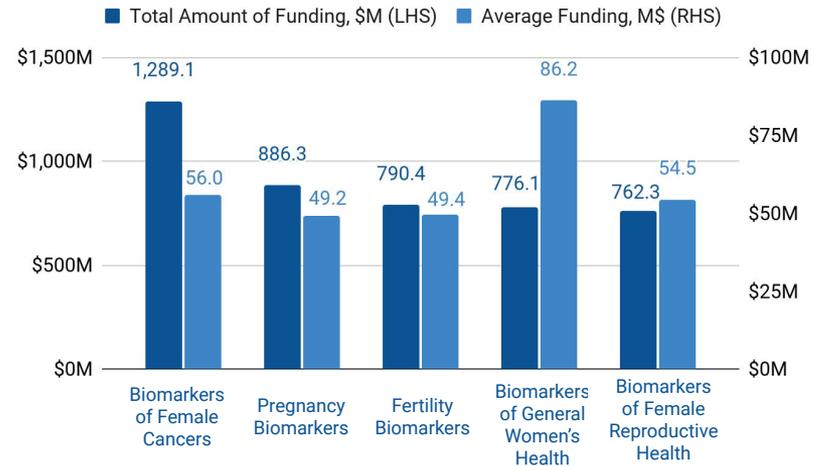
Most of the companies involved in the developing biomarkers of female health are allocated in the North America region (**in the US particularly 61.3%**). Top second region is **Europe** where located **17.5% of companies**. Most of European companies are situated in the UK and Germany - business and research centres of the European region. Almost 13% of companies are from Asia-Pacific region. **Around 5% of all companies are located in India** - main center of pharmaceutical production and bioscience research activity in the South Asia region.

Market at a Glance: FemTech Companies

Distribution of Companies by Category, %



Funding Amount by Category, \$M

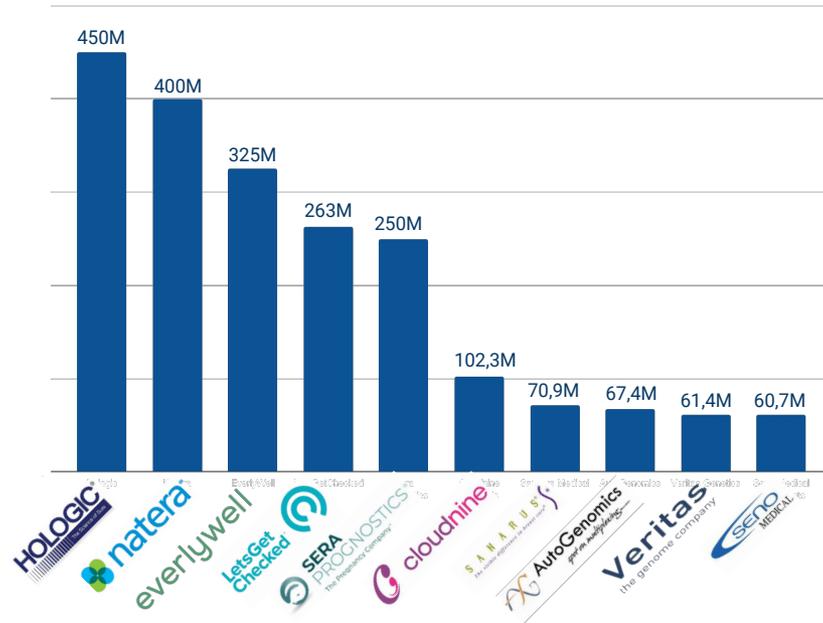


The **one third** of companies are involved in the field of Women Cancers Biomarkers - close to 31% of total number of companies. Companies involved in the development **Biomarkers of Female Cancers receive around \$1.3B investments**, however, this field is only the second by average amount of investments.

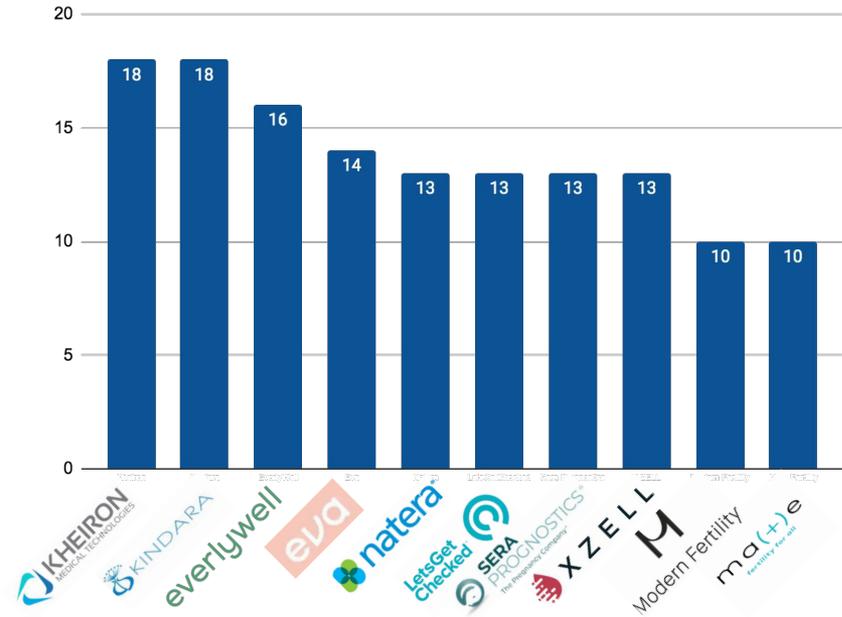
Around 24% of all companies are operates in the Pregnancy Biomarkers field. This area receives around \$886M of investments. **Around 17% and 16%** of companies are doing **Fertility Biomarkers and Biomarkers of Female Reproductive Health respectively**. Being the last area by total amount of funding, Health of Reproductive System Biomarkers is the third by average amount.

Market at a Glance: FemTech Companies

Top Companies by Funding, \$M



Top Companies by Investors Number

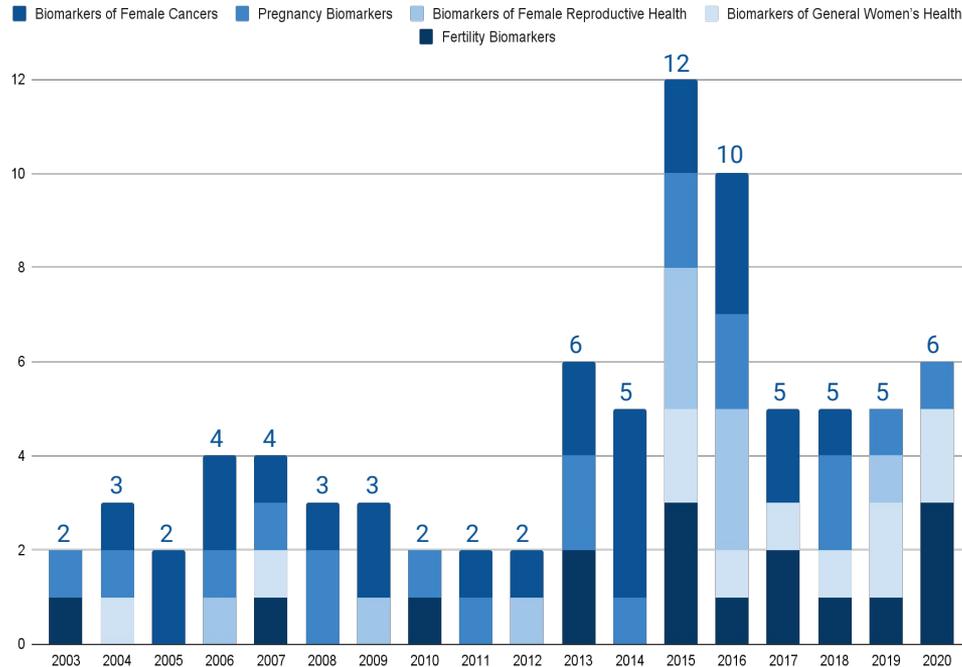


The company with the most significant funding is **HOLOGIC**, and its financing constitutes ~**450M\$**. The second place is taken by **Natera** (**400M\$**). Notably, both companies belong to the female cancers biomarkers category.

The companies with the most significant number of investors are **Kheiron** and **Kindara** (**18 investors**).

Market Trends

New Companies: FemTech Biomarkers



The graph illustrates **the growth in the number of companies on the market** since 2003.

There has been a **rapid development** of companies that research/develop/implement FemTech biomarkers **since 2013**. The biomarker of **female cancers** is a top category in this development. Due to the FDA approval of new efficient breast cancer therapy, the investments in this area increased.

Due to the improvement of general awareness of women general and reproductive health biomarkers **after 2015 year** evolved, many new companies focused on **fertility, reproductive and general health, and cancer**.

The upward trend is also noticeable for the area of **fertility/infertility biomarkers**. The reason for that might be an increase in the number of women trying to conceive at the age of 30-40. Such factor is mainly associated with the overall increase of lifespan.

Biomarkers of Female Cancers Examples of Practical Applications

IsonoHealth provides the world's first portable and automated 3D-breast ultrasound scanner called ATUSA. It combines a patented 3D ultrasound scanner and AI technology to **make whole breast scans and localize breast lesions** with consistent accuracy matching the best operators using traditional ultrasound equipment. Using Artificial Intelligence and proprietary radial scan method, IsonoHealth creates precise 3D visualizations of lesions as well as sagittal, transverse and coronal views.



Ovation Diagnostics is a cancer diagnostics company focused on improving the detection of ovarian cancer. **Using a novel biomarker present in urine samples of ovarian cancer patients, they are establishing a laboratory assay and a rapid lateral flow test which will offer women an efficient, non-invasive and accessible technique of detecting ovarian cancer.** The novel test will show higher specificity and sensitivity for ovarian cancer in comparison to existing methods of detection.



MobileODT is an AI-based health-tech company that establishes medical device technologies for cervical cancer screening. It supports the World Health Organization strategic mission to eliminate cervical cancer by 2050. **"Eva System" is an innovative product that provides next-level cervical examination, complete digital solution for magnified cervical visualization, documentation and teleconsultation.**



Fertility Biomarkers: Examples of Practical Applications

MiraCare markets the first FDA and CE registered comprehensive women's health monitoring platform with 99% of accuracy in clinical trials. It provides a palm-sized device for personalized ovulation tracking, fetal health monitoring, measuring ovarian reserve and detecting menopause at home, with expandability into chronic disease monitoring. The data automatically syncs to the Mira app. Using AI technology, it learns personal health patterns. Telemedicine connects users with doctors.

The logo for MiraCare, featuring the word "mira" in a lowercase, rounded, green sans-serif font.

NOWDiagnostics develops and manufactures diagnostic tests that utilize a single drop of blood, serum or plasma and deliver results within minutes. One of the products is **the ADEXUSDx® hCG Test** - an immunoassay used for the qualitative detection of human chorionic gonadotropin in blood, plasma, or serum. Indeed, human chorionic gonadotropin detection helps health care professionals in the diagnosis of early pregnancy.

The logo for NOWdiagnostics, featuring a blue checkmark icon inside a circle, followed by the text "NOWdiagnostics" in a blue sans-serif font.

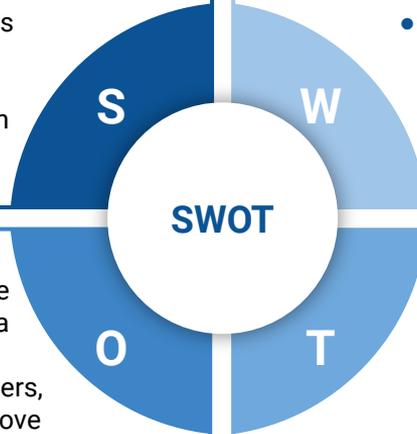
EverlyWell is a digital health company that establishes consumer testing, virtual care, at-home collection tests, and digital results. It provides a number of women's health tests, including ovarian reserve test, perimenopause test, postmenopause test and women's fertility test. All of these tests utilize finger prick sample collection to quickly and accurately measure the levels of specific hormones in the blood.

The logo for EverlyWell, featuring a green circular icon with a leaf-like shape inside, above the text "Everly Well" in a green sans-serif font.

FemTech Biomarkers: SWOT Analysis

- The comprehensive analysis of FemTech biomarkers will provide precise health status information of women.
- FemTech biomarkers can also be used to assess the early stages of a female disease as well as an individual's predisposition to it, which can assist people understand what preventive measures and treatments are required.
- Some FemTech biomarkers can be tested in both the home and the clinic, so women can monitor her health state in comfortable surroundings.

- The advancement of cutting-edge AI and machine learning technologies will make biomarker data analysis easier and more accurate.
- New biotechnologies such as portable analyzers, wearable devices, and digital technologies will improve quality of check-ups while lowering prices.
- The creation of new tests and treatments based on the study of the molecular mechanisms using FemTech biomarkers is a critical step toward eliminating of numerous female related diseases.



- In case FemTech Biomarkers usually are concerned on female health they can not identify disease states at other organ systems, and it can be difficult to pinpoint the true issue without usage of other biomarkers panels.
- A complicated approach using several FemTech biomarkers, which can be costly and inaccessible to the general public, can yield an accurate result.
- Because the list of FemTech biomarkers is short, more research is required.

- The quantity and quality of biomarkers can be influenced by menstruation cycles which can impair the test's accuracy.
- There is a lot of disputed material in existing data archives, thus more investigation is needed.
- The biomarker data is incomplete, which could lead to erroneous conclusions for some demographic groups.

The Next Frontier: Towards a “Digital Avatar”

Progress in Artificial Intelligence Enables Creation of “Digital Avatars”



Digital Avatar is a graphic representation that is associated with a user to serve as their identification. Avatars can be a picture, artistic drawing, or a three dimensional representation. With the advent of the digital revolution, its use has spread to many fields including medicine. Currently, the digital avatar is being used in medical education such as for training models using augmented reality in order to explain anatomy to students with a three-dimensional human body. The digital avatar in health allows plan a path and observe the body of a patient in alternate scenarios.

A virtual profile of all health data can be generated through collection of multiple types of data, some of which are visualized also in 3D through devices or augmented reality. Biomarkers serve to diagnose issues and evaluate the overall health status and predict the aging rates of each individual. Gathering more of this type of data e.g. periodic blood tests, will enable a complex, highly personal picture of each person, whose predictive power will be proportional to the quantities of input classes and the intrinsic capabilities of the AI-driven analysis aimed at recreating biomarker networks.

With the technologies of healthcare advancing, the digital avatar will evolve from a data collection and disease focused tool to a truly longevity focused tool. Instead of looking at unidimensional, disease-linked biomarkers, it will be able to look at the whole organism in an overarching health point of view, and focus mainly on prevention and extending patient healthspan.

The Evolution of Digital Human Avatar

Envisaged a **five-stage evolution of Digital Human Avatars** from 0.5 (the current state of Avatars available on the market) to 1.0, 2.0, 3.0, and 4.0. This classification framework is based on a number of specific factors including:

- their technological sophistication;
- their use of AI for assessment, predictive analytics, and personalized recommendations;

- the frequency with which they measure the biomarkers that they encompass;
- the overall scope of markers impacting health, Longevity, performance, and QALY across the full human lifecycle, from biology to behavior, technology, and environment that they are capable of measuring, integrating and predictively analyzing.

Digital Avatar 1.0



2022

Digital Avatar 2.0



2023

Digital Avatar 3.0



2024

Digital Avatar 4.0



2025-2027

AI and Digital Platforms: Towards a “Digital Avatar”



Longevity Biomarkers and Financial Industry

Biomarkers for Financial Market

The value of the information derived from the biomarkers cannot be reduced to the scientific only. Many financial instruments can be optimized using biomarkers-based longevity and/or mortality indices. Such instruments shows great value for a whole variety of entities, both governmental and privately held, providing optimized hedging solutions.

Besides different types of financial instruments, biomarkers assessment can become a crucial part of the valuation and due diligence processes for Longevity- and Pharma-related companies. It is well known that companies participating in drug development are highly exposed to the risks related to the human validation (i.e. clinical trials). It is often hard to predict and assess whether a solution provided by a given company is relevant to the market. In this case, biomarkers-derived information might play a crucial role in the assessment of the company's performance, allowing to evaluate how its services affecting human Longevity.

These two different approaches suggest great improvements in the financial market enabling optimized risk management both in terms of Longevity risks hedging, and investment risks reduction.

Who can benefit?	
Independent Financial Advisors	Private Equity Funds
Private Banks & Wealth Managers	Corporations
Asset Management Companies	Venture Capital Funds
Challenger Banks	Retail Banks
Pension Funds	Insurance Companies

Reverse Mortgage

A reverse mortgage is a type of loan that is used by homeowners at least 62 years old who have considerable equity in their homes. By borrowing against their equity (at rates starting at less than 3.5% per year), seniors get access to cash to pay for cost-of-living expenses late in life, often after they've run out of other savings or sources of income. In comparison with traditional asset-backed loans, **reverse mortgage loans provide the elderly with a means of hedging longevity risk by helping to maintain a sustainable level of retirement income**, while retaining tenure in the home.

From the borrower's perspective, the most notable merit of a reverse mortgage is clearly that the borrower is not required to repay the loan until he or she dies or leaves the home. Another favorable feature is the "non recourse" clause. When the loan is terminated, the borrower (or his or her estate) only needs to repay the loan amount or proceeds from the sale of the house price: whichever is the lesser sum.

There are some challenges for the Longevity economy which drive the popularity of reverse mortgages for retirees: **a low-interest financial environment** that provides insufficient returns on pension savings, **generous retirement age** and **early withdrawal rules**, **a great fluctuation in the labor market**, **an erosion of traditional family support systems** and a **significant proportion of one-person households**

How Does a Reverse Mortgage Work?



You're 62 or older and have equity invested in your home



You need to access to that equity to pay your daily expenses



A reverse mortgage allows you to borrow against your home's equity with no monthly payment required as long as you stay in your home



The loan is repaid once the house is sold

Crossover Risk for Reverse Mortgage Lender

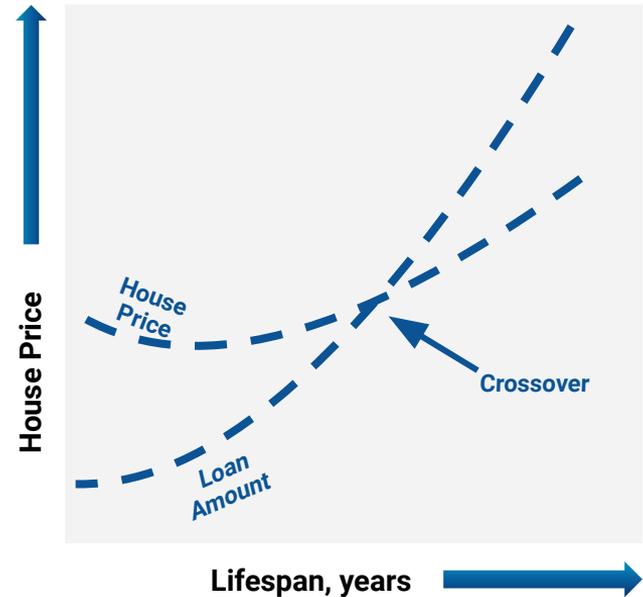
Although reverse mortgage loans provide many attractive benefits to retirees, they also involve many risks from the lender's perspective. The risk in reverse mortgage loans can be summarized as the "crossover risk".

If the loan value exceeds the collateral house value at any point of contact time, the lender is limited to recover only the proceeds of the sale of the house equity when a reverse mortgage loan is terminated. Any excess is therefore considered a loss to the lender. Since the interest rate is usually higher than the house price value increasing, the loan value will undoubtedly exceed the house value at some future point.

On the other hand, however, if the loan is terminated before the crossover, any excess of the proceeds from the sale will revert to the borrower rather than becoming the lender's gain. This feature of reverse mortgages is reminiscent of options contracts.

Due to the dramatic improvement in the mortality rate since the 1970's, longevity risk has become the most crucial risk in a reverse mortgage product, as a result, banks and other lenders should form reserve capital to cover the longevity risk or it to capital markets via insurance contracts, longevity derivatives etc. In both cases the effective measure of longevity risk, such as biomarkers-based biological age prediction models is a key aspect of the lender policy.

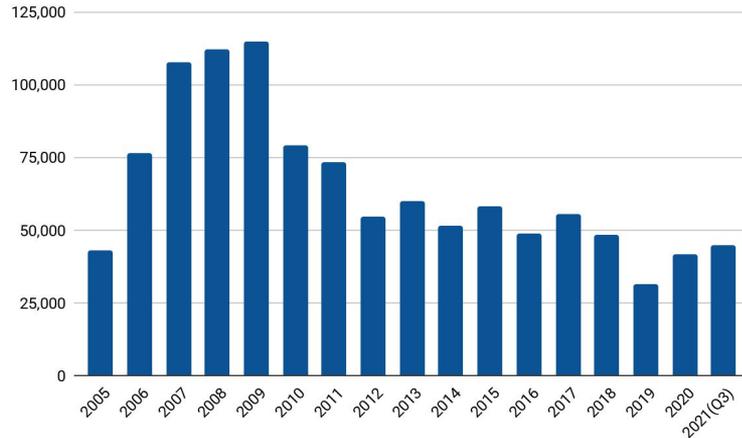
Crossover Risk Scheme



The USA Market of Reverse Mortgages

The Home Equity Conversion Mortgage, or HECM, is the federally insured reverse mortgage product. It is insured by the Federal Housing Administration (FHA), a branch of the U.S. Department of Housing and Urban Development (HUD). HECMs account for nearly all reverse mortgages made today in the U.S. On the left graph there is the number of HECMs made in each year since the program began. Due to the bubble on the American real estate market and the World Financial crisis 2008, the big banks and other financial institutions became indifferent to this financial instrument, as they couldn't find an efficient way to deal with some specific idiosyncratic risks. However, increasing demand for reverse mortgages due to drives described early and more efficient risk-management algorithms will undoubtedly increase the volume of loans and their market value soon. Over the past two years, the decline in market size is due to weakened demand due to the pandemic and the completion of transactions (sales of mortgaged real estate), concluded more than ten years ago.

Annual HECM Endorsement, Number of Deals



Total U.S. Market Volume and Home Price Index



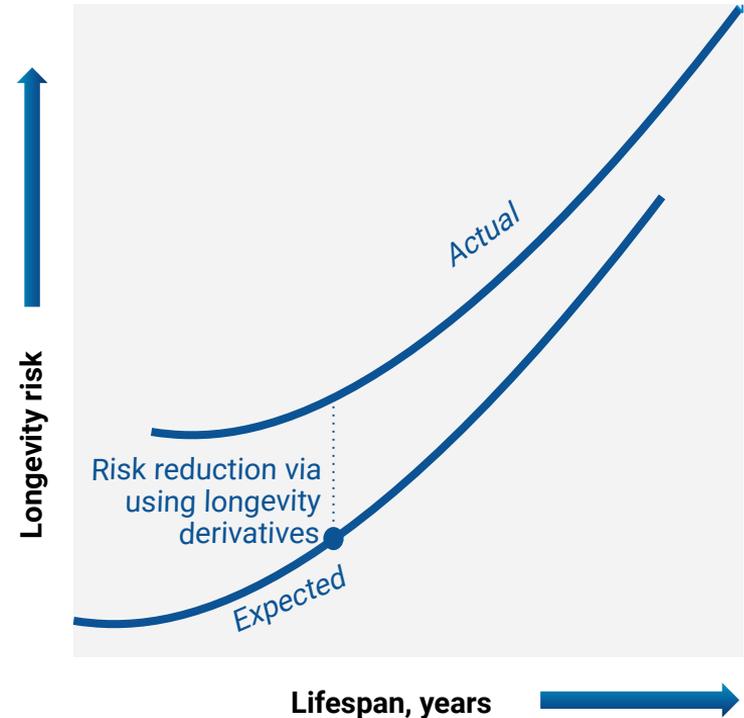
Longevity Risk / Longevity-derived Financial Instruments

A new global capital market, the Life Market, is developing and “longevity pools” are on their way to becoming the first major asset class of the twenty-first century. Longevity risks arrive due to inaccurate predictions of the level of mortality rate and numbers of retirees.

Thus, Longevity-derived financial instruments are used in order to hedge such risks. In general, these derivatives are designed to generate income for investors due to increased Longevity, as well as reduce the negative impact for companies suffering from Longevity risks. Longevity risks have a weak correlation with other financial risks. Although the Longevity Derivatives Market has a large number of economic agents, the main ones are hedgers (pension funds and insurance companies, have an incentive to transfer Longevity risk off their books), speculators, and arbitrageurs (investment banks and hedge funds are interested in acquiring exposure to longevity risk since it has a low correlation with classic market risk factors, therefore small beta coefficient attracts investors a lot.

New opportunities are opening up for all these agents because of the increased accuracy of risk assessment and forecasting and selection of the correct risk management tool.

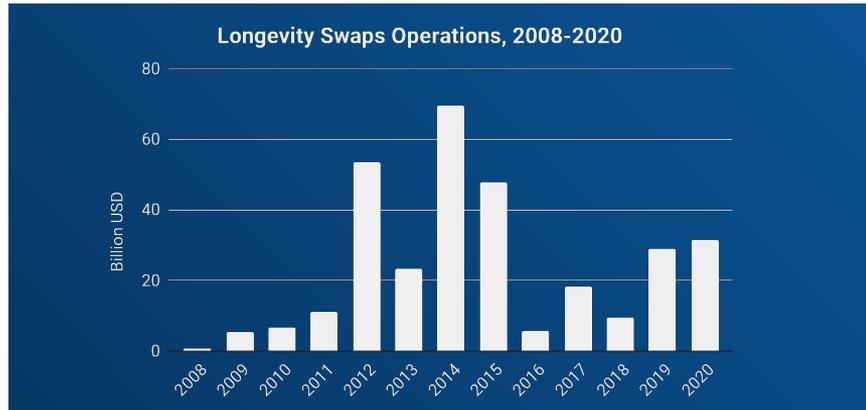
Hedging with Longevity Derivatives



Longevity Risks for Companies and Governments

Longevity risks are of great interest for both governmental and private institutions

The graph below depicts the dynamics of longevity swaps' operations in the period of 2008-2020 years. During this period, deals for the amount of \$ 313 billion had been struck. The amount of new operations correlates with life insurance market size. For example, the insurance market size in the US also significantly dropped after the 2015 year and slightly recovers during the 2016-2020 years (IBISWorld, 2020).



Source: Artemis, Longevity Derivatives

Governments tend to have a two-dimensional interest in Longevity securities. First, for hedging financial institutions sensitive to such risks, second, for securing its own exposure, as it is a significant holder of the Longevity risks: via the pay-as-you-go state pension system; via its obligations to provide health care for the elderly and for many other similar reasons.

Ensuring an efficient annuity market and efficient capital market for Longevity risk transfers means that government can affect and reduce concentration risk and provide construction of national longevity indices.

Government helps to share Longevity risk fairly across generations and provides a fair risk premium. When issuing longevity derivatives based on biological age, the government could insure age-related diseases and implement more advanced and actionable metrics for government pension programs.

Government = Insuring age-related diseases + Minimising of spended resources + Using accurate and realistic health indicators

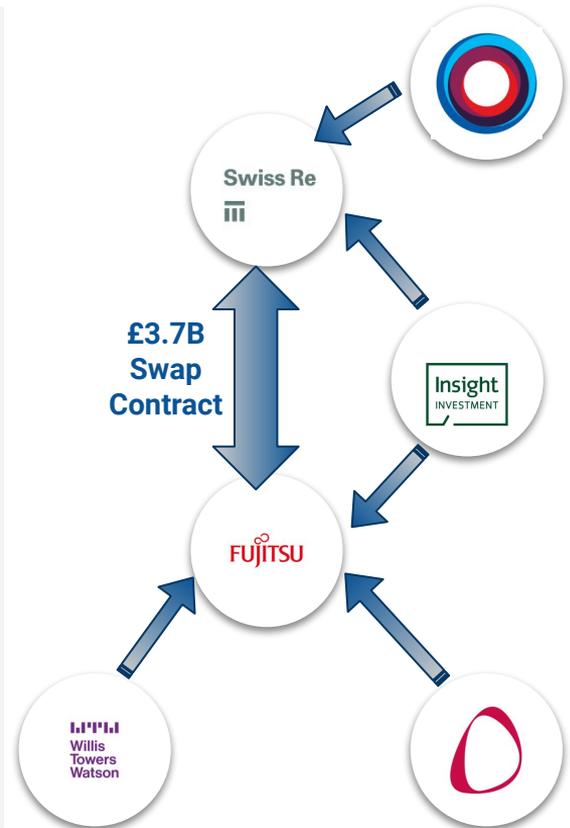
Examples of Longevity Derivatives Users' Activities

Financial institutions which wanted to make a profit from arbitrageurs fees have started to issue longevity derivatives in 2003. Global reinsurer **Swiss Re** offered a three-year mortality bond whose principal payment was tied to an international mortality index. During all these years Swiss Re continues making big deals on the longevity derivatives market.

The last deal using longevity swap was signed in May 2021 between **Swiss Re as an arbitrageur** and **The Trustee of the ICL Group Pension Plan, a Fujitsu pension scheme, as a hedger**. This longevity risk transfer insured **£ 3.7 billion of hedgers' liabilities** and covers pensions in payment for approximately 9,000 members. **Other institutions** of the swap deal infrastructure include:

- **Willis Towers Watson** as actuarial and transaction adviser to the hedger
- **Gowling WLG LLP and Momentum Investment Solutions and Consulting** as legal and investment adviser to the hedger
- **Pinsent Masons LLP** as legal adviser to the hedger
- **Insight Investment** as calculation agent, collateral manager, and collateral valuation agent.

Daniel Harrison, Global Head of Longevity Solutions at Swiss Re says: "There is a compelling rationale for pension plans and insurers to transfer their longevity risk to reinsurers. We have a natural offset with our mortality business, the capacity to write the business onto our balance sheet, and the expertise to tailor the transaction to meet our client's needs."



Longevity Biomarkers and Financial Industry: Conclusions

Longevity biomarkers shows a great value for financial market, allowing engineering of optimized financial instruments and implementation of the biomarkers-based due diligence and valuation.

As was shown, many financial instruments can be formulated in terms of the Longevity. This implies the importance of the development different quantifiable biomarkers assessment approaches. As a result, such approaches can be used for:



It is important, that use of biomarkers in financial areas will positively affect not only institutional or other “big” players. Biomarkers can become a feasible solution for personal risk management too. Additionally, the active implementation of the biomarker-derived data will provide sufficient means for investment risks management which will optimize the effectiveness of the allocation process. This, in turn, can provide better and more efficient Longevity solutions for general public.

When time is money, biomarkers are the means for wealth management.

Possibilities for Further Improvements

The number of biomarkers of aging and their association with various diseases increases each year but a critical review of each of them is needed. Understanding that biomarkers of aging Industry development is an ongoing process means that the project needs to be further improved and monitored. For instance, new analytical reports need to be done for creating new accurate and current databases.

The database of firms, investors, and R&D facilities will be enlarged to accommodate new startups and established companies looking to increase their longevity products rollout efforts.

New techs like AI, Omics, and Digital monitoring gadgets assessment in biomarkers of aging Industry will be done to understand their impact on Biomarker Industry advances in general.

An extensive study on products and treatment methods to promote longevity or decrease rates of development of age-related diseases will be undertaken as well.

Multiple forecasts concerning biomarkers of aging Market trends are required to identify all aspects and further development of companies in longevity field. They are also needed to understand which forecasts were proven to be true in order to optimize the our analyzing strategy.

Avenues for Further Improvement in the Second Iteration of the Project

Database Expansion

Further Integration of Biomarkers of Longevity

Updates on the Most Notable Longevity Companies

Follow-up on Predictions Made in the Previous Iteration

Increase Number of Deeply Studied Cases

Separate Research on Longevity Biomarkers Development

Deep Analysis of AI and Omics-tech Implementation

Broad Assessment of New Longevity Startups

Current Monitoring of Longevity Biomarkers Trends

Conclusions

Key Takeaways



High demand for personalized medicine leads to rise in commercial interest and government support for Age-related Biomarkers and AI-technologies for Longevity. That trend accelerates strong funding of Longevity sector thus promoting faster innovation.



The amount of **clinical and biological data** in the world is steadily rising, with a projected **CAGR** of more than **30%**. The **number of datapoints** for clinical usage is **rapidly increasing**, and the only option to optimize their utilization is to create **digital avatars**. A **digital avatar is a forerunner in the field of personalized medicine**, which is still in its early stages. Because of the massive amounts of data, clear **analysis of such avatars is only feasible with the help of AI**.



The ability to monitor health status with accurate and trustworthy lab findings explains the market's significant appeal for the **at-home tests**. This **trend emerges** as a result of the **simplified procedure of ordering tests, collecting samples, and obtaining results**. Typically, such solutions arise as a result of the probable **removal of the need for hospital/lab visits**, making such tests an ideal solution for modern people. **This tendency is about to take off on a massive scale, and traces of it can already be observed**.



The **increasing popularity of Artificial Intelligence** leads to the creation of innovative techniques and the digitization of healthcare services. The **use of Artificial Intelligence** possibilities in both **preventative and therapeutic medicine** is a **major trend in the industry**. It is now evident that **AI can be used to augment many operations** in order to **save costs and enhance overall results**.

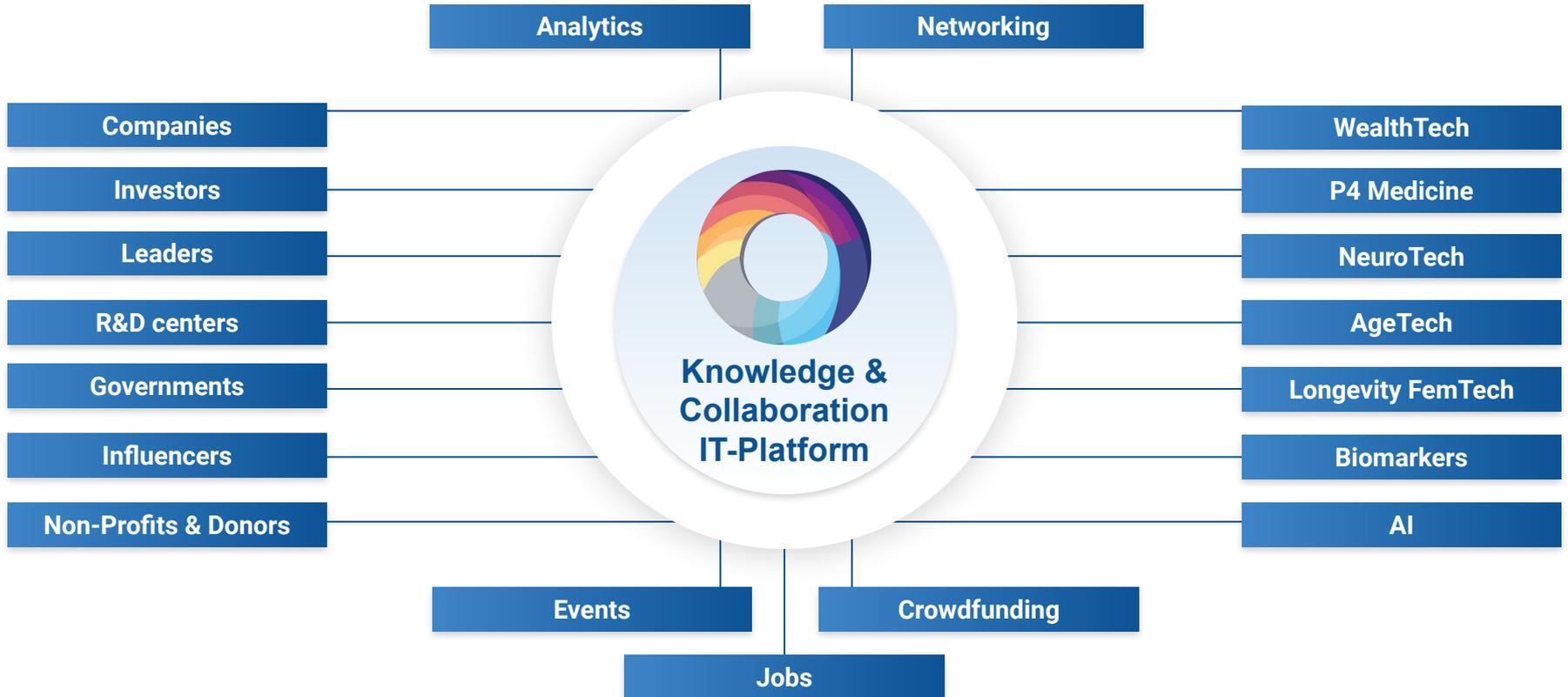


AI for Longevity will become one of the most impactful sectors within the industry in the next several years, and make its potential to accelerate the continued development of the industry in almost every sector, such as **Longevity R&D, therapeutic development, P4 Medicine, biomarker discovery**, and even non-biomedical sectors such as the **Longevity Financial Industry**.



Longevity risks are an important component of the **financial sector**, and as the **population ages**, their prevalence grows larger and more impactful. Because of the progression of the longevity industry, a lot of **innovation is altering the paradigm of longevity risk assessment**, which might possibly **lead to significant changes in the longevity financial sector**. As a first sign of such transformation, new derivatives and risk assessment approaches are developing.

Longevity.International: One-Stop Platform for Longevity Industry Knowledge





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