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What direct-to-consumer medical technology to use in 2023 within the area of diagnosis to live for 150 years

A Master's Thesis submitted for the degree of
“Master of Science”

supervised by
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Affidavit

I, **STEFAN KRÄUTLER**, hereby declare

1. that I am the sole author of the present Master's Thesis, "WHAT DIRECT-TO-CONSUMER MEDICAL TECHNOLOGY TO USE IN 2023 WITHIN THE AREA OF DIAGNOSIS TO LIVE FOR 150 YEARS", 71 pages, bound, and that I have not used any source or tool other than those referenced or any other illicit aid or tool, and
2. that I have not prior to this date submitted the topic of this Master's Thesis or parts of it in any form for assessment as an examination paper, either in Austria or abroad.

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Signature

Preface and acknowledgements

I want to use this section to thank everyone who helped me to create this master thesis and overcome all the challenges I faced on the way.

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Special thanks to my mum and my dad. Since I know that no written or spoken can ever describe my deepest thankfulness for what they did for me all my life, I just want to say – Thank you for all!

Furthermore, I want to thank my brother Markus for representing someone who is and always will be by my side even though we do not hear from each other as often as I would like to. Thank you!

Special thanks to my love Hanna. For being not only my closest friend and the woman I love, but also the one I want to spend the rest of my life with. I am proud having her on my side, representing someone that I constantly can learn from. Someone I look up to and I am most proud of. Being the one next to whom I can enjoy the little things with, be myself and gives my life a deep meaning. Thank you!

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Abstract

This master thesis contributes to answer an essential and relevant question humankind tackles due to the drastic improvements and huge leaps in science and technology over the last decades within the area of longevity. Even though the life expectancy over the last years increased, still numerous people die due to age-related conditions which can be grouped into cardiovascular, respiratory, and neonatal diseases. Due to the unmanageable number of different methods and technologies out of which the latest ones get introduced within this work as well as products for consumers that suggest how to rejuvenate the human biology most successfully, this scientific work provides guidance and provides the most promising and impactful first step for an individual to take in order to live healthy 150 years already today.

Out of preselected direct-to-consumer genetic (DTC) tests as medical technologies within the area of diagnostics, which experts think of and represents the most impactful area to dig into, this master thesis provides an overview of advantages and disadvantages for selected products and services. Even though the comparison reveals only marginal differences between each product and service, one DTC genetic test establish itself as the preferred option with the most accurate results.

Nevertheless, when looking into the not-so-distant future, DTC medical technologies represent just the beginning of an era in which a lot of new innovations will change the biological immortality as known until today. Biologically speaking there is no rule given by nature that prevents immortality as it is shown by scientists all over the world based on their ground-breaking scientific discoveries. At some point in time technological advancement progresses at such a huge pace so that it does not matter how fast humans age or what kind of illness people get. This leads to the fact that scientific development will always be a step ahead. This phenomenon is also known as “longevity escape velocity”.

1. Introduction

Living up to 150 years might seem like a dream humankind long dreamed of. With the current available medical technology as well as being under 60 years old, humans nowadays easily reach 150 healthy years. Biological immortality is not a fantasy, but a not so far future anymore.

Over the last decades starting from 1950 up to 2021 the life expectancy of humans around the world tragically changed. If looked at the age of a newborn in Europe in 1950 it was estimated that it will reach around 63 years. In 2021 life expectancy increased to 77 years for the average European. This results in an increase of life expectancy of approximately 22%. The biggest changes of life expectancy can be seen in the developing countries (Figure 1).

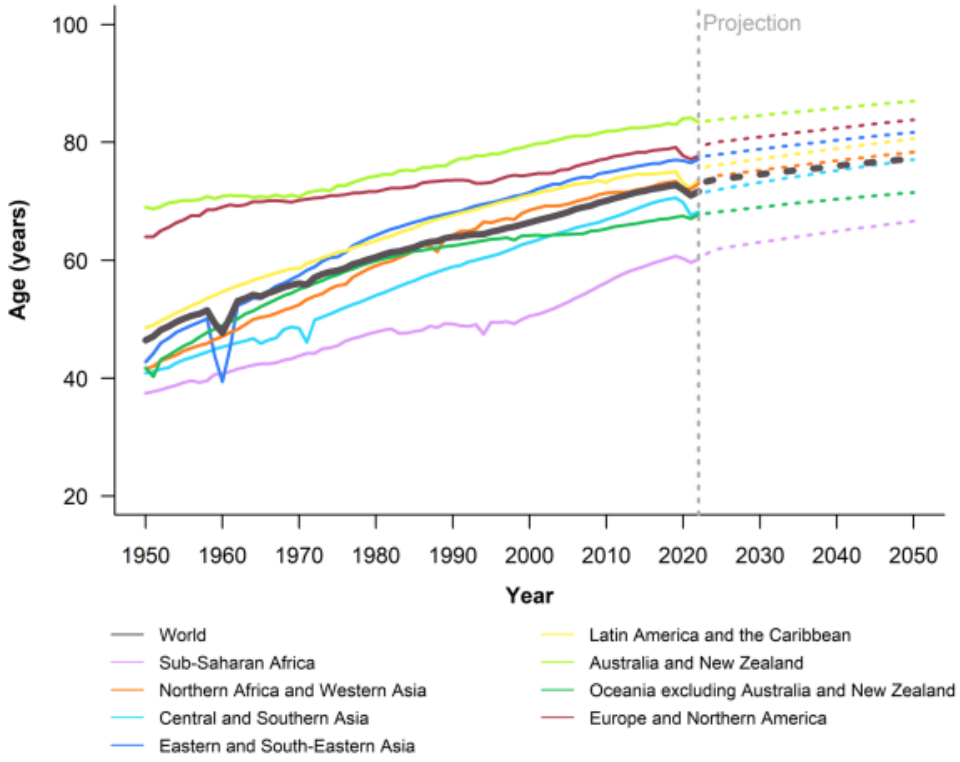

Figure 1 – Life expectancy at birth, from 1950-2021, and an outlook for 2022-2050, by region (United Nations Department of Economic and Social Affairs, Population Division, 2022)

These fundamental improvements during the last century are results thanks to following three key developments:

1) Discovery and development of vaccines and antibiotics for common disease,

2) Improved nutrition, agriculture, and civil organization,

3) Better care for mothers and babies during childbirth.

As it can be seen in Figure 1, the global average lifespan will reach eighty to ninety years by 2100 which is a huge achievement for humankind (Rosner, Ortiz-Ospina, & Hannah, 2019).

Besides the fact that our life expectancy increased during the last years, still 55% of the 55.4 million people die worldwide due to age-related diseases. The top global causes of death as it can be seen in Figure 2 can be grouped into following three areas of diseases:

1) Cardiovascular (ischaemic heart disease and stroke)

2) Respiratory (chronic obstructive pulmonary disease and lower respiratory infections)

3) Neonatal conditions (birth asphyxia and birth trauma, neonatal sepsis and infections, and preterm birth complications)

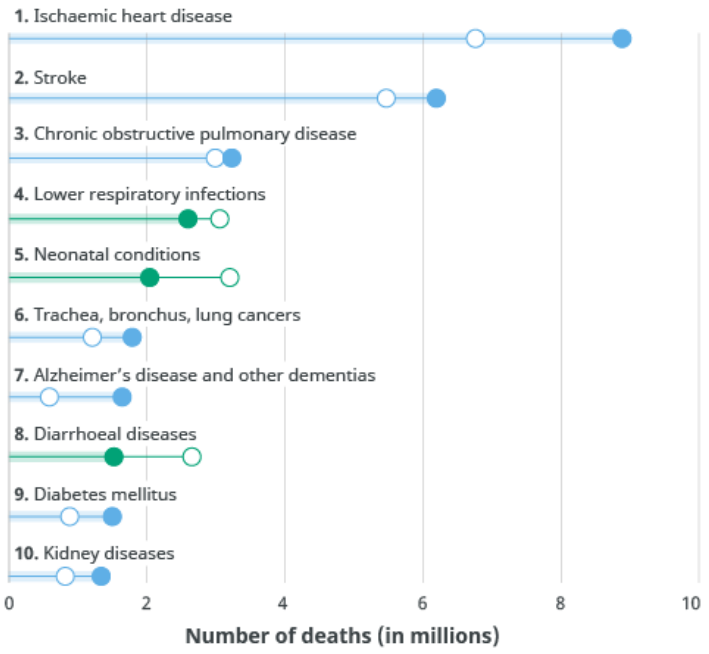

Figure 2 – Leading causes of death globally (World Health Organization, 2020)

Various scientific papers like the one from (Yanagi, et al., 2017) which states that "age-associated, chronic low-grade inflammation augments the susceptibility and severity of pneumonia" or the journal article "The epidemiological link between ageing and respiratory diseases" from (Viegi, Maio, Simoni, Baldacci, & Annesi-Measano, 2009) show direct correlation between age-related causes and cardiovascular as well as respiratory diseases. Therefore, it is possible to state that the majority of global deaths represent diseases caused by age-related issues. Since there are so many of them, scientists and experts first had to group them and call them "The Hallmarks of Aging". These hallmarks consist of genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion and altered intercellular communication (López-Otín, Blasco, Partridge, Serrano, & Froemer, 2013) as well as protein crosslinking (Fedintsev & Moskalev, 2020).

It is apparent to wonder why so many people still pass away, notably from cardiovascular and respiratory diseases, given that those conditions have been well-known since 1950 and that fatalities have continued to rise in recent years despite an increase in life expectancy.

Arguing that there are no approaches out there how to avoid this premature death due to age-related diseases would not be correct. An increasing number of people nowadays actively participate in longevity friendly behaviors like doing frequent health check-ups, quit smoking as well as drinking alcohol, reduce sugar consumption, eat less, but more vegetables, supplement, be physical active, get enough sleep, meditate, and educate themself to name just a few. Together with these behaviors there is support by more than 500,000 (MedTech Europe, 2022) medical technologies to enable people to live to 150 years.

Out of the various approaches to avoid premature death and increase individual longevity that currently exist, researchers and experts in that field argue that early and accurate detection of age-related diseases is one of the biggest lever there is right now. People with an early diagnosis of cervix, colon, breast, and bladder cancer have an increased survival rate of factor 5.43, 6.3, 3.6 and 20.8 (World Health Organization, 2020) than their respective rate for late-stage diagnoses (National Cancer Institute,

2023). Hundreds of millions of people worldwide live with an undiagnosed disease (Marwaha, W. Knowles, & A. Ashley, 2022). More than thirty million lives of the nearly sixty million global deaths can be condensed down to conditions that are treatable if caught early (Young, Diagnosing Early, 2021). This leads to the statement that detecting age-related diseases early is one of the biggest levers when it comes to enable everyone to live to 150 years already today.

The following chapters will guide through necessary topics such as the fundamentals to better understand key terminology as well as technology that enable humans nowadays to live to a high age. It ends with a comparison of four promising direct-to-consumer (DTC) genetic tests and how they influence individual longevity. Following the introduction, there is chapter 2 Fundamentals, which provides a short overview over the most fundamental definitions in order to better understand DTC genetic tests as medical technologies and how they work. Furthermore, the basic biological processes like aging and what is causing it are getting introduced. With all the fundamentals it is easier to follow the comparison of DTC genetic test technologies and how they impact longevity. Chapter 3 State of the art provides a short introduction to what current available DTC medical technologies and options do nowadays exist as well as get used to diagnose age-related diseases. Within this chapter and previously mentioned technologies, products and services that are used to diagnose such diseases and turn out as the most promising ones get introduced. Having a solid foundation and a profound knowledge about DTC genetic tests, chapter 4 Problem description states the key question that is getting answered within this thesis and furthermore gives an glimpse into the methodology how necessary data was collected and formatted for the following comparison. After the research approach, the purpose of chapter 5 Results is comparing previously introduced genetic diagnostics based on the characteristic “type of sample”, “number of users”, “price”, included reports and/or services”, “number of times and percentage of genome or exome sequenced”, and “number of detected diseases”. Based on the results, within chapter 6 Discussion each of the given products and characteristics get compared to each other in order to identify similarities and differences. This finally leads to a recommended DTC genetic test. Lastly, chapter 7 Conclusion and outlook provides a recommendation for a DTC genetic test and

answers the key question of this thesis as well as provides an outlook what technologies and approaches will await humankind within the next 10 years from now.

1.1. Summary

Living 150 years as a human is no story for the future anymore. Out of the various approaches currently existing, researchers and experts in that field argue that early and accurate detection of age-related diseases is one of the biggest lever. Life expectancy has risen globally in the past decades with a significant increase in older adults and centenarians. Longevity research is a growing area of interest in the scientific community, with gaps in life expectancy at birth between countries remaining wide. In 2021 the difference between countries with the highest and lowest life expectancy was around 33.4 years. Longevity is connected to aging, but its root cause is not yet defined. There are several scientific papers that show a direct correlation between age-related causes and cardiovascular as well as respiratory diseases. Therefore, it is possible to state that the majority of global deaths can be condensed down to age-related causes, also known as "The Hallmarks of Aging". These hallmarks consist of genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion and altered intercellular communication. Arguing that there are no approaches out there how to avoid this premature death caused by age-related diseases would not be correct. People nowadays actively participate in longevity friendly behaviors like doing frequent health check-ups, quit smoking and drinking alcohol, reduce sugar consumption, eat less and more vegetables, supplement, be physical active, get enough sleep, meditate, and educate themself. Additionally, people get supported by more than 500,000 medical technologies to live to 150 years. The following chapters provide a guide through the necessary fundamentals, state-of-the-art technologies, and methods as well as a comparison of preselected DTC genetic tests and how they impact longevity.

2. Fundamentals

This chapter provides a short overview over the most fundamental definitions in order to better understand already existing DTC genetic tests as medical technologies and how they work so that people nowadays live to 150 years. The reader gets to know first, what is the genome and exome before getting introduced into the topic longevity and how it is connected to aging and therefore humans die before reaching healthy 150 years as well as the causes of aging.

2.1. Genome

The genome is the complete set of genetic information for an organism. It is made up of DNA, which is a long chain of building blocks called nucleotides. There are four types of nucleotides in DNA: adenine (A), thymine (T), cytosine (C), and guanine (G). These nucleotides are arranged in a specific order to form genes, which are the instructions for making proteins. Proteins are the building blocks of cells, and they perform a wide range of functions, such as catalyzing metabolic reactions, replicating DNA, responding to stimuli, and transporting molecules across cell membranes.

Humans have a genome that is made up of 23 pairs of chromosomes, which are long strands of DNA. Each chromosome contains many genes, and the total number of genes in the human genome is estimated to be around 20,000-25,000. The genome also contains non-coding regions of DNA, which do not code for proteins but may have other roles, such as regulating gene expression.

The genome is inherited from our parents, with half of the genome coming from the mother and half from the father. This means that each person's genome is unique, and variations in the genome can lead to differences in traits, such as eye color and susceptibility to certain diseases.

Scientists have been able to map the human genome, which has provided a wealth of information about genetic disorders, disease susceptibility, and drug development. It has also led to many ethical and societal questions, such as issues of privacy, discrimination, and informed consent (Watson, 1990).

2.2. Exome

The exome is a subset of the genome that contains the exons, which are the coding regions of genes. Exons are the regions of DNA that contain the instructions for making proteins, while introns are the non-coding regions that are transcribed into RNA, but are later removed before the final protein is formed. The exome represents around 1-2% of the total genome, but it includes more than 85% of disease-causing mutations.

Exome sequencing is a technology that allows scientists to sequence the exons of a genome, rather than the entire genome. This can be more cost-effective and efficient than sequencing the entire genome and can still provide a wealth of information about genetic disorders, disease susceptibility, and drug development.

Exome sequencing is particularly useful for identifying genetic causes of rare diseases, as it can help to pinpoint the specific gene or mutation responsible. It can also be used to identify genetic risks for common diseases, such as cancer, heart disease, and diabetes. Additionally, researchers can use exome sequencing to identify new genes associated with certain diseases or traits.

Exome sequencing can also be useful for identifying novel drug targets for certain diseases. By identifying the genetic mutations that cause disease, researchers can better understand the underlying biology of the disease and develop new drugs that target specific mutations.

It is important to note that exome sequencing does not capture all genetic variation and therefore a complete genome sequencing is needed in certain cases. Also, not all genetic variations that occur in the genome are located in the exons, therefore some mutations may be missed with exome sequencing. More on the technology of whole exome sequencing (WES) follows.

2.3. Longevity

Over the last decades life expectancy played a big part in human progression. When looking back at 1950 global life expectancy was almost 9 years lower than 72.8 years in 2019 (United Nations Department of Economic and Social Affairs, Population Division, 2022). Due to the facts of a large increase in older humans (85 years and

older) (Waite, 2004), continuous recordings of maximum lived years within a lifespan (Wilmoth, 2000) as well as an increasing number of living centenarians (Robine & Paccaud, 2005) the area of longevity raised interests in the scientific community. Longevity is defined as the capability to survive past the average age of death (De Benedictis & Franceschi, 2006). Even though life expectancy at birth between countries was reduced, existing gaps remain wide. As it can also be seen in Figure 1, in 2021 the difference between countries with the lowest and the countries with the highest life expectancy was around 33.4 years. Life expectancy at birth in 2021 in Australia, regions of China, and Japan, as representative countries for a population with a high life expectancy, was close to 85 years. When compared to the opposite side of the graph, in Central African Republic, Lesotho, Nigeria, and Chad the life expectancy at birth were below 54 years (United Nations Department of Economic and Social Affairs, Population Division, 2022).

2.4. Aging

When research and experts talk about longevity it is always directly connected to aging. Aging is the key process that determines or influences the longevity of a human or animal being. Furthermore, there needs to be a distinction between chronological, psychological, and biological age.

Even Denham Harman, a former shell Oil biochemist developed a radical theory, which proved that free radicals (free radicals are atoms with a single and unpaired electron, like oxygen, which like to steal another electron from other atoms or molecules) damage human cells already in the 1950s. Anyhow, a common consensus or a single and unified theory of aging as well as its root cause is still not clear (Young, What is Aging, Anyway?, 2021). Although various researcher and experts tried to find a definition for aging like Dr. David Sinclair with his theory about “the loss of epigenetic information (the epigenome is a system of chemicals and proteins that modify genes in such a way that it starts or stops protein synthesis)” (Sinclair, 2019), Dr. Aubrey de Grey who sees aging as “an accumulation of molecular damage” or Alex Comfort who refers to aging as “a decrease in viability and an increase in vulnerability” (Comfort, 1956) to just name a few, an “universal theory of aging” is

not yet defined. Meanwhile Dr. Eric Verdin and his team at the Buck Institute are working on such a definition of an “universal theory of aging”.

In order to provide the community consisting out of researchers and enthusiastic longevity experts a common understand for aging without agreeing on its root cause, a group of European scientists lead by Carlos Lopéz-Otín published a paper in 2013 which deals about “The Hallmarks of Aging”. These so-called hallmarks try to do create a common understanding even though they do not represent a single root cause. They furthermore meet three essential criteria: they occur during normal aging; they speed up aging processes, if researchers want to do so; and if acted against these, slow down aging. In Carlos Lopéz-Otín published paper the hallmarks which impact aging were defined as follows (also seen in Figure 3):

1) Genomic instability (occurrence of mutations during cell division due to natural errors, radiation, or toxic influences)

2) Telomere attrition (reduction and loss of “protective caps” at the end of each chromosome due to replication, which leads to genomic instability)

3) Epigenetic alterations (incorrect expression of genes due to changes of methyl groups assembled around the genes, which are part of the epigenome, a system of chemical and protein interaction)

4) Loss of proteostasis (imbalance of extra proteins in and around the cell with necessary instructions for genes)

5) Deregulated nutrient sensing (malfunction of cell mechanisms to detect scarcity of essential nutrients and therefore misinterpret need of build up or break down of proteins to generate resources)

6) Mitochondrial dysfunction (mitochondria refuse to produce energy due to shortage of nicotinamide adenine dinucleotide (NAD+) which leads to dying cells)

7) Cellular senescence (natural death state of an individual cell after multiple cell divisions which causes inflammation and other problems)

8) Stem cell exhaustion (depleted or damaged reserve stem cells and slower generation of new stem cells)

9) Altered intercellular communication (senescent cells that secrete substances and infect neighboring cells to become inflamed or senescent as well)

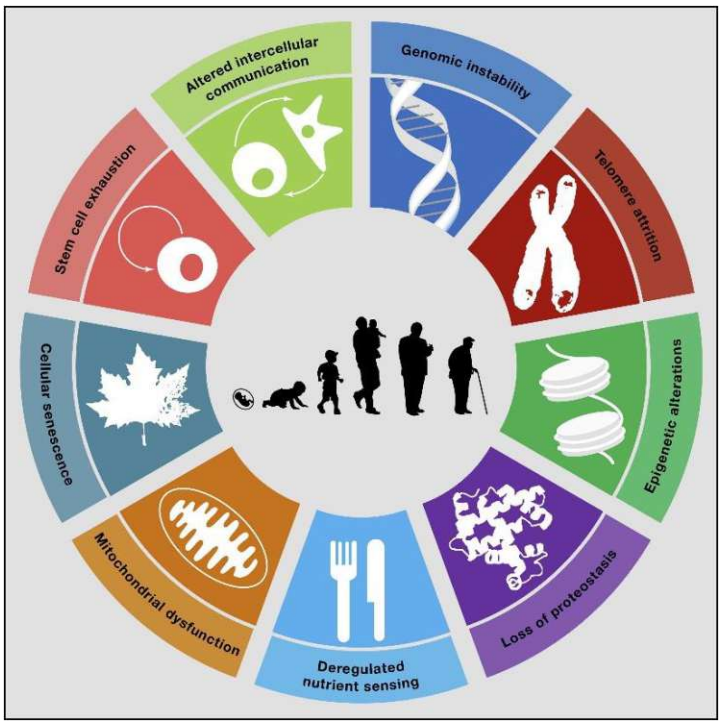

Figure 3 – The Hallmarks of Aging (López-Otín, Blasco, Partridge, Serrano, & Froemer, 2013)

During the last years since the hallmarks were published another 10th hallmark was added to the list – protein crosslinking (individual proteins bind together through a sugar molecule in a process called glycation) (Fedintsev & Moskalev, 2020).

2.5. Medical technology

Medical technology is defined as services (i.e., medical, and surgical as well as organizational and supportive), products (i.e., equipment, drugs), facilities and solutions intended for use in the diagnosis, prevention, treatment or mitigation of diseases or other conditions to save and improve people's lives (A. Gaev, 2020) (Davida, M. Juddb, & Zambutoc Raymond, 2020) (MedTech Europe, 2022). Medical technologies accompany humans starting from prevention up to diagnosis and cure. They are divided into three main categories (MedTech Europe, 2022):

1) Medical devices (MDs) are services or products that prevent, diagnose, monitor, treat and care for people.

2) Digital health are all services or products that use information and communication technologies (ICTs) to cover the whole spectrum from prevention up to care for people.

3) In vitro diagnostics (IVDs) are non-invasive tests that use biological samples (i.e., blood, urine) to determine persons health.

2.5.1. In vitro diagnostics (IVDs)

According to article 1 (2)b from European Union (European Union, 1998) an in vitro diagnostic medical device is defined as "any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment, or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information:

1) concerning a physiological or pathological state, or

2) concerning a congenital abnormality, or

3) to determine the safety and compatibility with potential recipients, or

4) to monitor therapeutic measures."

As it can be seen in Figure 4, each IVD is classified from A to D. Class A represents the medical devices with the lowest and Class D those with the highest risk. Under the IVD regulation, all IVDs have to be classified under a risk-based classification system. According to this classification each device poses a certain risk to the health of the individual and the public, if the diagnosis results in an incorrect test result. The number of devices commonly used by professionals working in the healthcare sector and people working outside this sector that are curious about their health can be seen in Table 1Table 1 – Risk-based classification system which represents risk the device poses to the health of the public and or an individual as result of an incorrect test result. Table based on . IVDs with risk-based classification B are the most used diagnostics. Reasons for that are receiving fast results from testing, high cost-effectiveness, high

accuracy, high reliability, high validity, and most important assist clinicians in diagnose, if the patient does or does not have a certain condition.

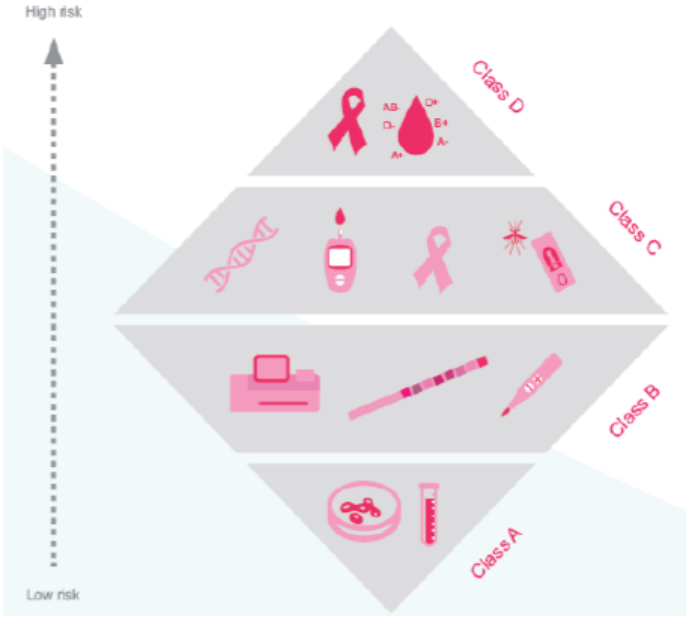

Figure 4 – Overview of IVDs and risk classification (Zauner, 2022)

IVD regulation classification system		Percentage of devices by class
D	High public health risk (e.g., blood safety / high risk infectious diseases)	4%
C	High risk for individual patients (e.g., cancer markers, dangerous infectious diseases, etc.)	26%
B	Medium risk for individual patients (e.g., blood chemistry, pregnancy tests, etc.)	49%
A	Low risk for individual patients (e.g., instruments, accessories, specimen collection systems, etc.)	21%

Table 1 – Risk-based classification system which represents risk the device poses to the health of the public and or an individual as result of an incorrect test result. Table based on (MedTech Europe, 2022)

2.6. Direct-to-consumer (DTC) genetic testing

Direct-to-consumer (DTC) genetic testing is a type of genetic testing that allows individuals to purchase genetic testing kits and receive their results directly without the need for a doctor's prescription or genetic counseling (Su, 2015). These tests are often marketed as a way to learn more about one's ancestry, health risks, or potential for certain traits.

DTC genetic testing companies typically use a small sample of saliva, blood, or cheek swab to analyze a person's DNA. The results are analyzed using various algorithms and are provided to the customer through an online portal. The results can vary in their level of detail and accuracy, and may include information about ancestry, carrier status for certain genetic conditions as well as risk for certain diseases.

While DTC genetic testing can be a convenient and accessible way for individuals to learn more about their genetics, it also has some limitations and potential drawbacks. One concern is that the results may not be as accurate or reliable as tests provided by a healthcare professional, and that the customer may not have the expertise to interpret the results properly. Additionally, there can be privacy concerns with DTC genetic testing, as the customer's genetic information may be stored and used by the company for research or other purposes.

Another important aspect to consider is that DTC genetic testing can only provide information about certain specific genetic variations and diseases and cannot provide a comprehensive analysis of all genetic variations that can affect health. Furthermore, DTC genetic tests may not be covered by insurance and the cost can be high.

2.7. Summary

Longevity is connected to aging, but its root cause is not yet defined. "The Hallmarks of Aging", which were defined by European scientists provide a common understanding of aging. The hallmarks include genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, altered intercellular communication, and protein crosslinking. The genome is the complete genetic information of an organism made up of DNA and arranged in specific order to form genes, which are the instructions for making proteins. Humans have 23 pairs of chromosomes with an estimated 20,000-25,000 genes, half inherited from each parent, leading to unique variations in traits and disease susceptibility. Mapping the human genome has advanced genetic research, but also raised ethical questions. Questions in regard to the improvement of people's lives through diagnosis, prevention, treatment, and mitigation of illnesses, medical technologies encompass services, goods, infrastructure, and solutions. It includes three main categories: medical devices, digital health, IVDs. These are non-invasive tests using biological samples to determine a person's health, classified into risk-based categories A to D with Class B being the most commonly used due to fast results, best cost-effectiveness, highest accuracy, highest reliability, and highest validity. DTC genetic testing allows individuals to purchase genetic testing kits and receive their results directly, without a doctor's prescription or counseling. These tests are marketed to learn about ancestry, health risks, or traits. DTC tests analyze a small sample of DNA and results are provided online with limitations in accuracy and reliability, privacy concerns, and a lack of comprehensive analysis as well as high costs. WGS is a laboratory technique that determines the entire DNA sequence of an organism's genome. It can be used to find genetic abnormalities linked to specific diseases and pinpoint genetic variants that raise risk for particular diseases. There are several techniques like Next-generation sequencing (NGS) and Sanger sequencing that are used to read the order of nucleotides. WGS is becoming more affordable, but still costly and requires specialists to interpret the results.

3. State of the art

This chapter presents a brief overview of currently available technologies for detecting genetic mutations that lead to severe diseases and products humans nowadays use to diagnose age-related genetic mutations. Out of these technologies the chapter will introduce products and services that are used to diagnose such diseases and turn out as the most promising ones. Furthermore, it is described how they work, what are their advantages and disadvantages as well as provide an answer to the question why these selected technologies are mentioned to represent state of the art technology.

3.1. Next generation sequencing (NGS)

Next-generation sequencing (NGS) is a powerful technology that allows for the rapid and cost-effective sequencing of large stretches of DNA. It is considered a state-of-the-art technology due to its ability to generate large amounts of high-quality sequencing data in a relatively short period of time (Hu, et al., 2012).

NGS works by breaking the DNA sample into small fragments, and then using a combination of enzymes and primers to make millions of copies of these fragments. These copies are then attached to a solid surface, such as a bead or a chip, and the sequence of each fragment is determined by reading the order of nucleotides, or bases, in each fragment. The process of reading the sequence is called sequencing by synthesis, which is a method that uses fluorescent dyes to label the nucleotides as they are added to the growing strand of DNA (Bentley, 2008).

NGS has several advantages over traditional sequencing methods, such as Sanger sequencing. One of the biggest advantages is its ability to generate large amounts of data in a relatively short period of time. This means that NGS can be used to sequence an entire genome in just a few days, whereas traditional methods can take several months or even years. Additionally, NGS has a higher accuracy than traditional sequencing methods, which is important for identifying disease-causing mutations (McCombie, McPherson, & Mardis, 2023). Another advantage of NGS is that it allows for the simultaneous sequencing of multiple samples at once, which can be useful for studying large groups of people or for identifying variations in a population. Additionally, NGS can be used to sequence both the coding and non-coding regions

of the genome, which can provide insights into the function of certain genes and how they may be involved in disease (Qin, 2019).

However, NGS also has some disadvantages. One of the biggest is that it is relatively expensive compared to traditional sequencing methods. Additionally, the large amount of data generated by NGS can be difficult to analyze, which can be time-consuming and require specialized software and expertise. Another disadvantage is that the sequencing platforms have limited read lengths, which means that not all regions of the genome can be sequenced with the same accuracy. This can be especially problematic for certain types of genetic disorders, such as repeat expansions, where the mutations are relatively large and not captured well by the short reads. Despite these disadvantages, NGS is considered a state-of-the-art technology due to its ability to generate large amounts of high-quality sequencing data in a relatively short period of time. This has made it a valuable tool for a wide range of applications, such as identifying disease-causing mutations, studying population genetics, and understanding the function of specific genes. Additionally, NGS is widely adopted in clinical diagnostic and research settings and is a key component in precision medicine (Morash, Mitchell, Beltran, Elemento, & Pathak, 2018).

In conclusion NGS is a powerful and state-of-the-art technology that rapidly and cost-effectively sequences large stretches of DNA, providing high-quality sequencing data with the ability to identify disease-causing mutations and study population genetics, despite some disadvantages such as cost and limited read lengths.

3.2. Whole genome sequencing (WGS)

The entire DNA sequence of an organism's genome can be ascertained using the laboratory technique known as whole genome sequencing. Adenine, guanine, cytosine, and thymine are the four basic building units (referred to as nucleotides) that make up DNA. Advanced DNA sequencing methods are used to read the order of these nucleotides. The genome is the entirety of an organism's genetic makeup, and it contains all the data required for its growth, operation, and reproduction. The DNA that makes up the genome is bundled into units known as chromosomes. There are 46 chromosomes in all, or 23 pairs in humans.

Scientists can establish the order of all the DNA in an organism's genome using WGS. Regions with coding and without coding areas are included in this. In the fields of health, genetics, and even forensic research, this technology has many use cases. WGS for instance gets used to find genetic abnormalities linked to specific diseases, such as cancer, or inherited disorders. Additionally, it can be used to pinpoint the precise genetic variants that raise a person's risk of developing particular diseases. The genetic make-up of microorganisms, such as bacteria and viruses, can also be studied using whole genome sequencing to better understand how they evolve and cause infections, but are not part of this thesis.

There are other approaches to genome sequencing, however the following are the most popular ones:

- Next-generation sequencing (NGS): This technique reads a large number of tiny DNA fragments simultaneously. It produces millions or billions of short reads in parallel, which are subsequently put together to rebuild the entire genome. The process of WGS is labor-intensive as well as complex. The resulting data set can be substantial.
- Sanger sequencing: This technique reads the sequence of a little portion of DNA at a time using chemical reactions.

WGS is becoming substantially less expensive, making it more affordable for academics, healthcare professionals and private persons. The operation is still costly, and specialists in the field are required to interpret the results.

3.3. Clustered regularly interspaced short palindromic repeats (CRISPR)

CRISPR-based genome editing is a revolutionary technology that allows for the precise modification of specific genetic sequences. It is considered a state-of-the-art technology due to its ability to make highly specific changes to the genome with great precision and efficiency.

The CRISPR system is a naturally occurring defense mechanism found in bacteria that allows them to recognize and destroy invading viral deoxyribonucleic acid (DNA). The CRISPR system is composed of two main components: a guide ribonucleic acid (gRNA) and an enzyme called Cas9. The gRNA is a short RNA molecule that binds

to a specific location in the genome, while the Cas9 enzyme acts like a pair of molecular scissors that cuts the DNA at the specific location where the gRNA is bound.

CRISPR-based genome editing works by delivering the gRNA and Cas9 enzyme into a cell, where they will bind to and cut a specific location in the genome. Once the DNA is cut, the cell's own repair mechanisms are activated, and the DNA can be repaired in one of two ways: non-homologous end joining (NHEJ) or homology-directed repair (HDR). NHEJ results in insertions or deletions (indels) in the genome, which can disrupt the function of a gene and therefore be used to knock out a gene. HDR allows researchers to introduce specific changes to the genome, such as replacing a disease-causing mutation with the correct version of the gene.

One of the biggest advantages of CRISPR-based genome editing is its precision and efficiency. This technology allows for highly specific changes to be made to the genome, which is important for identifying the function of specific genes and how they may be involved in disease. Additionally, CRISPR-based genome editing is relatively inexpensive and easy to use, which makes it accessible to researchers in a wide range of fields. Another advantage of CRISPR-based genome editing is that it can be used to edit a wide range of organisms, from bacteria to plants to animals to humans. This makes it a valuable tool for a wide range of applications, such as developing new treatments for genetic disorders, studying the function of specific genes, and understanding the underlying causes of disease (Rodríguez-Rodríguez, Ramírez-Solís, Garza-Elizondo, Garza-Rodríguez, & Barrera-Saldaña, 2019).

However, CRISPR-based genome editing also has some disadvantages. One of the biggest concerns is the potential for off-target effects, where the gRNA and Cas9 enzyme bind to and cut the genome at unintended locations. This can result in unintended changes to the genome, which could lead to serious health problems. Another disadvantage is that CRISPR-based genome editing is not yet fully understood and there is still much research to be done to fully understand the long-term effects of this technology. Additionally, there are also ethical concerns surrounding the use of CRISPR-based genome editing, particularly when it comes to editing the human genome (Omodamilola & Ibrahim, 2018).

Despite these disadvantages, CRISPR-based genome editing is considered a state-of-the-art technology due to its ability to make highly specific changes to the genome with great precision and efficiency. This technology has the potential to revolutionize the field of genetics and medicine, and it is likely to play an increasingly important role in the development of new treatments for genetic disorders and the understanding of the underlying causes of disease.

In conclusion, CRISPR genome editing allows precise modification of genetic sequences with high efficiency, but potential off-target effects and ethical concerns exist.

3.4. Genome wide association studies (GWAS)

Genome-wide association studies (GWAS) is a method used to identify genetic variations that are associated with a particular trait or disease. It is a powerful tool for identifying genetic risk factors for complex diseases such as diabetes, cancer, and heart disease.

The basic principle behind GWAS is to compare the genetic makeup of individuals who have a particular trait or disease with those who do not. This is typically done by genotyping hundreds of thousands of single nucleotide polymorphisms (SNPs) in the genome, which are small variations in the DNA sequence. By looking for patterns of association between the SNPs and the trait or disease, researchers can identify genetic variations that are associated with the trait or disease.

One of the major advantages of GWAS is that it allows researchers to identify genetic risk factors for complex diseases that were previously unknown. This can lead to a better understanding of the underlying biology of the disease and may lead to the development of new treatments. Another advantage of GWAS is that it can be used to study a wide range of traits and diseases, including both common and rare conditions. This makes it a versatile tool that can be applied to a wide range of research questions (Uffelmann, et al., 2021).

However, GWAS also has some limitations. One of the major limitations is that it can only identify genetic variations that are associated with a particular trait or disease, it does not prove causality. This means that the identified genetic variations may only be

associated with the trait or disease and not directly responsible for causing it. Another limitation of GWAS is that it can only identify common genetic variations. Rare genetic variations that have a large effect on the trait or disease may not be detected by GWAS. Additionally, GWAS is based on the assumption that the genetic variation is the cause of the trait or disease, which is not always the case. It may be that the genetic variation is only associated with the trait or disease but not causally responsible for it (Tam, et al., 2019).

Despite these limitations, GWAS remains a state-of-the-art technology because of its ability to identify genetic risk factors for complex diseases that were previously unknown. It has led to a better understanding of the underlying biology of many diseases and has the potential to lead to the development of new treatments.

GWAS is also a cost-effective way of identifying genetic risk factors for complex diseases, as it can be done on a large scale with many participants. This allows researchers to identify genetic variations that are associated with the trait or disease in a large population, which increases the statistical power of the study (Uffelmann, et al., 2021).

In conclusion, GWAS is a powerful method for identifying genetic variations that are associated with a particular trait or disease. It has led to a better understanding of the underlying biology of many diseases and has the potential to lead to the development of new treatments. However, it also has some limitations, including the inability to prove causality and the inability to detect rare genetic variations. Despite these limitations, GWAS remains a state-of-the-art technology because of its ability to identify genetic risk factors for complex diseases that were previously unknown and its cost-effectiveness.

3.5. Whole exome sequencing (WES)

Whole exome sequencing (WES) is a method used to sequence all of the exons, or protein-coding regions, of an individual's genome. It is a powerful tool for identifying genetic variations that are associated with a particular trait or disease.

The basic principle behind WES is to isolate and sequence all of the exons in an individual's genome. This is typically done using a technique called capture-based

sequencing, in which a panel of probes is used to capture and isolate the exons from the genome. Once the exons are isolated, they are then sequenced using next-generation sequencing technology.

One of the major advantages of WES is that it allows researchers to identify genetic variations that are associated with a particular trait or disease, including both common and rare genetic variations. This is because WES sequences the entire exome, which includes all of the protein-coding regions of the genome, rather than just a subset of the genome like GWAS. This increases the chances of identifying genetic variations that are associated with the trait or disease. Another advantage of WES is that it can be used to study a wide range of traits and diseases, including both common and rare conditions. This makes it a versatile tool that can be applied to a wide range of research questions. Additionally, WES allows researchers to identify genetic variations that are associated with a particular trait or disease that are not necessarily in coding regions of the genome. This is because the exome contains not only the coding regions but also the untranslated regions (UTRs) and intron-exon boundaries that are important for regulation of gene expression.

However, WES also has some limitations. One of the major limitations is that it can be expensive and time-consuming. This is because it requires a significant amount of computational power and data storage to analyze the large amount of data generated by the sequencing process. Another limitation of WES is that it can only identify genetic variations that are associated with a particular trait or disease, it does not prove causality. This means that the identified genetic variations may only be associated with the trait or disease and not directly responsible for causing it.

Finally, WES is based on the assumption that the genetic variation is the cause of the trait or disease, which is not always the case. It may be that the genetic variation is only associated with the trait or disease but not causally responsible for it.

Despite these limitations, WES is still considered a state-of-the-art technology because of its ability to identify genetic variations that are associated with a particular trait or disease. It has led to a better understanding of the underlying biology of many diseases and has the potential to lead to the development of new treatments. WES is also useful

in rare genetic disease research, in which it is often difficult to identify the genetic cause of the disease.

In conclusion, WES is a powerful method for identifying genetic variations that are associated with a particular trait or disease. It can be used to study a wide range of traits and diseases, including both common and rare conditions. However, it is also an expensive and time-consuming process. Despite these limitations, WES remains a state-of-the-art technology because of its ability to identify genetic variations that are associated with a particular trait or disease and its usefulness in rare genetic disease research.

3.6. Targeted sequencing

Targeted sequencing is a method used to sequence specific regions of an individual's genome. It is a powerful tool for identifying genetic variations that are associated with a particular trait or disease.

The basic principle behind targeted sequencing is to isolate and sequence specific regions of an individual's genome, such as genes or exons, rather than sequencing the entire genome. This is typically done using a technique called polymerase chain reaction (PCR)-based sequencing, in which primers are used to amplify the specific regions of interest from the genome. Once the regions are amplified, they are then sequenced using next-generation sequencing technology.

One of the major advantages of targeted sequencing is that it allows researchers to focus on specific regions of the genome that are known or suspected to be associated with a particular trait or disease. This increases the chances of identifying genetic variations that are associated with the trait or disease and reduces the cost and time required to analyze the data. Another advantage of targeted sequencing is that it can be used to study a wide range of traits and diseases, including both common and rare conditions. This makes it a versatile tool that can be applied to a wide range of research questions.

Additionally, targeted sequencing allows researchers to use a smaller number of samples and still achieve a high level of resolution, making it more cost-effective than whole genome sequencing.

However, targeted sequencing also has some limitations. One of the major limitations is that it can only identify genetic variations that are present in the specific regions of the genome that are targeted for sequencing. This means that genetic variations outside of these regions will not be detected. Another limitation of targeted sequencing is that it requires prior knowledge of the specific regions of the genome that are associated with the trait or disease. This means that it is less powerful for the discovery of new genetic associations than whole genome sequencing methods.

Finally, targeted sequencing is based on the assumption that the genetic variation is the cause of the trait or disease, which is not always the case. It may be that the genetic variation is only associated with the trait or disease but not causally responsible for it.

Despite these limitations, targeted sequencing is still considered a state-of-the-art technology because of its ability to identify genetic variations that are associated with a particular trait or disease. It has led to a better understanding of the underlying biology of many diseases and has the potential to lead to the development of new treatments. Targeted sequencing is also useful in genetic disease research as it allows researchers to focus on specific regions of the genome that are known or suspected to be associated with the disease.

In conclusion, Targeted sequencing is a powerful method for identifying genetic variations that are associated with a particular trait or disease by focusing on specific regions of the genome. It can be used to study a wide range of traits and diseases, including both common and rare conditions. However, it also has some limitations such as the inability to detect genetic variations outside of the targeted regions and the need for prior knowledge of the specific regions of the genome associated with the trait or disease. Despite these limitations, targeted sequencing remains a state-of-the-art technology because of its ability to identify genetic variations that are associated with a particular trait or disease and its usefulness in genetic disease research.

3.7. Digital PCR (dPCR)

Digital PCR (dPCR) is a laboratory technique used to quantitatively measure the amount of a specific DNA or RNA molecule in a sample. It is a variation of polymerase chain reaction (PCR), a method used to amplify a specific DNA or RNA sequence.

The main difference between PCR and dPCR is that while PCR amplifies a sample to generate millions or billions of copies of a specific sequence, dPCR partitions a sample into thousands of tiny droplets, each containing one or a few copies of the target sequence. By counting the number of droplets that contain the target sequence, dPCR can determine the original concentration of the target sequence in the sample with high precision and accuracy.

dPCR works by partitioning a sample into thousands of small droplets using a device called a thermal cycler. The droplets are then sealed and amplified using PCR. After amplification, the droplets are analyzed to determine which ones contain the target sequence. This is typically done by adding a fluorescent probe that binds to the target sequence, and then measuring the fluorescence of each droplet using a specialized camera. The number of droplets that contain the target sequence is then divided by the total number of droplets to determine the original concentration of the target sequence in the sample.

One of the main advantages of dPCR is its high precision and accuracy. Because each droplet contains a small number of copies of the target sequence, the measurement is less affected by noise and variation in the reaction. This makes dPCR particularly useful for applications where a precise measurement of a small number of target sequences is required, such as in the detection of rare mutations or the quantification of viral loads in patients with infections. Another advantage of dPCR is its ability to detect very low levels of target sequences. Because each droplet is amplified independently, dPCR can detect target sequences that are present in as few as one or a few copies per droplet. This makes dPCR useful for applications such as the detection of low levels of cancer cells in a blood sample or the quantification of viral loads in patients with infections.

dPCR also has some disadvantages. One of the main disadvantages is that it is a more labor-intensive and time-consuming process than PCR. Because each droplet must be amplified and analyzed separately, dPCR requires a large number of droplets, which can take a significant amount of time to generate and analyze. Additionally, dPCR requires specialized equipment, such as a thermal cycler and a specialized camera, which can be expensive.

Despite these disadvantages, dPCR is considered to be a state-of-the-art technology because of its high precision and accuracy, as well as its ability to detect very low levels of target sequences. This makes it useful for a wide range of applications, such as the detection of rare mutations, the quantification of viral loads in patients with infections, and the detection of low levels of cancer cells in a blood sample. In addition, dPCR is widely used in the field of genetic research, where precision and accuracy are crucial. In conclusion, dPCR is a powerful tool that enables researchers to make highly accurate and precise measurements of target sequences, making it an important tool in the field of molecular biology and genetics.

In conclusion, Digital PCR (dPCR) is a lab technique that partitions a sample into tiny droplets to accurately quantify DNA or RNA with high precision and accuracy. It is useful for detecting rare mutations, quantifying viral loads, and detecting low levels of cancer cells. However, dPCR is time-consuming, labor-intensive, and requires expensive equipment. Despite its disadvantages, it is considered a state-of-the-art technology in genetic research.

3.8. Summary

NGS is a powerful, cost-effective technology that generates large amounts of high-quality sequencing data quickly, with advantages such as high accuracy, but also some disadvantages such as high cost and limited read lengths. Despite these limitations, it is widely used in clinical and research settings. CRISPR-based genome editing is a powerful, precise, and efficient method for modifying specific genetic sequences. It has potential to revolutionize genetics and medicine, but also has limitations such as potential off-target effects and ethical concerns. Despite these limitations, it is still considered a state-of-the-art technology. GWAS is a method that identifies genetic variations associated with a particular trait or disease. It is a powerful tool for identifying genetic risk factors for complex diseases and has the potential to lead to new treatments. Despite some limitations, such as inability to prove causality and only identifying common genetic variations, it is considered a state-of-the-art technology due to its ability to identify unknown genetic risk factors and its cost-effectiveness. WES is a powerful tool for identifying genetic variations associated with a particular trait or disease, including rare variations, but can be expensive and time-consuming. Despite limitations, it remains state-of-the-art due to its ability to identify genetic variations and usefulness in rare disease research. Targeted sequencing is a powerful method for identifying genetic variations associated with a particular trait or disease by focusing on specific regions of the genome. It has limitations and the need for prior knowledge but is still considered a state-of-the-art technology.

4. Problem description

The main aim of this thesis is to give a highly relevant answer to the key question "what direct-to-consumer medical technology to use in 2023 within the area of diagnosis to live for 150 years". For the average consumer, patient, or healthcare enthusiast it is hard to define out of the currently more than 500,000 medical technologies what technologies turn out as the most promising ones with the most valuable impact on longevity. It has to be added that even though this thesis presents a selection of the four medical technologies, not every human being can be treated equally when it comes to healthcare due to his or her individual biology, lifestyle, social background, and geographical location.

4.1. Research approach

In order to be able to compare the most promising medical technologies the research approach for this thesis is divided into two steps. First, relevant data and information gets collected and gathered from different journals, scientific papers, presentations, websites, and books. Being able to do a comparison of each essential parameter that describes the product and/or services and furthermore analyze it, the gathered data subsequently is transferred into a comparable format, which can be seen in Table 3. As previously discussed in chapter 2.5, Medical technology can be divided into medical devices, IVDs, and digital health. For the purpose of this thesis, only IVDs will be considered. From these IVDs only those which consumers can use on their own without any clinicians will be discussed. These DTC medical devices can then be split further into the area of their use case or diagnostic area. Based on (Young, Diagnosing Early, 2021) most promising and noninvasive diagnostic areas are liquid biopsy as well as genetic, epigenetic and microbiome diagnostics. For further comparison the discussed data exclusively cover genetic diagnostics. The most essential parameters for DTC genetic tests and their impact on longevity are shown and cover the company, product, type of sample, number of users, price, included reports and/or services, number of times and percentage of genome or exome sequenced, and number of detected diseases. Based on data from 2016 there are currently around 246 companies providing some form of DNA testing (Philips, 2016). Out of this huge number of genetic testing possibilities, the thesis will deal with a product from four different

companies, which are Nebula Genomics, Dante Labs, Circle DNA and 23andMe. An overview can be seen in Table 2. These providers are selected based on the criteria of fulfilling either providing a WGS or WES and its usage determined by the number of users. This preselection of DTC genetic tests allows a comparison of the products and/or services, that turn out as the most promising ones in the area of diagnosis and therefore reaching healthy 150 years of live. This comparison is subject of the following chapters 5 Results and 6 Discussion.

4.1.1. Data collection

In order to be able to compare selected DTC genetic tests and services out of the currently more than 500,000 available medical technologies a preselection is necessary for the thesis. The result can be seen in Table 2. These are selected out of 250 DTC genetic testing companies that currently provide any kind of genetic tests (Wysocki & Osier, 2019). Within the following chapter 4.1.2 Data formation the preselected products and services fulfill the following defined criteria:

1) highest number of times and percentage that a single product sequences the whole genome or exome and therefore creates the biggest amount of DNA data as well as

2) highest number of users compared to other solutions.

Both preselection criteria lead to an increased amount of stored DNA within the database which increases the accuracy of detecting a mutation caused disease as well as identifying rare diseases. Based on the results, the four companies Nebula Genomics, Circle DNA, Dante Labs and 23andMe with their representative products are selected and data supporting or describing their solution gets collected. This information is retrieved through various media channels like journals, scientific papers as well as presentations, websites, and books. This provides enough input for doing a comparison as described in the previous chapter 4.1. No DTC genetic diagnostic test that is listed within Table 2 is bought or tested for the formation of given results within this thesis. Furthermore, no additional genetic testing technologies or traditional testing methods are tested or taken into consideration within this comparison. Traditional methods are not taken into consideration within this comparison either

since DTC genetic test have several advantages over these methods and therefore have a more significant impact on longevity. The differences between traditional or clinical and DTC genetic tests are accuracy, costs, and accessibility. The price (around 919 - 1838 euros for clinical genetic testing without any additional reports or consultation and 169 - 744 euros for given DTC genetic test with a variety of reports and personalized consultation) for testing is the main argument supporting the preselection and why conventional genetic tests are not considered within this thesis.

Overview DTC genetic diagnostics		
Company	**Product**	**Website**
Nebula Genomics	Ultra-Deep Whole Genome Sequencing	https://nebula.org/whole-genome-sequencing-dna-test/
Circle DNA	Premium DNA Test	https://circledna.com/premium
Dante Labs	MyGenome Sequencing Test	https://dantelabs.com/products/whole-genome-sequencing
23andMe	Health + Ancestry Service	https://www.23andme.com/en-eu/dna-health-ancestry/

Table 2 – Overview DTC genetic diagnostic providing companies and their products

4.1.2. Data formation

In this subchapter, gathered data is put into a comparable format as it can be seen in Table 3. In the first two rows of the table, the mentioned companies and their product that fulfills the defined criteria of highest number of times and percentage the whole genome or exome was sequenced as well as highest number of users are listed. The row “Type of sample” shows how the sample that is needed for the sequencing gets collected from the consumer at home. Samples are collected via salvia or blood. It gets followed by the number of users that already used the product or service and contributed to or set the foundation for companies DNA database. The next row within the table shows the price for each technology that is given. This value represents the price for one product with all its necessary tools for collecting DNA samples, shipping costs as well as additional support after sequencing. The data in row “Included reports

and/or services" represent which add-ons come along with the product. There all kinds of follow up information, or personalized support after receiving the results from analyzing the genome or exome are mentioned. These cover various reports that mention diseases or recommendations for how to start living a healthier lifestyle as well as a membership that further supports consumers after their genome or exome was sequenced. Out of the sequenced genome massive amounts of data (DNA data) get generated and stored in DNA databases. This data is used for identification and interpretation of mutations in disease causing genes as well as personalizing and optimizing recommendations in the area nutrition, sports, and many more. With the sequencing of the human genome it is now possible to identify diseases due to mutations in disease causing genes. Next row "Number of times and percentage of genome or exome sequenced" states how many times and what percentage of the genome or exome gets sequenced. This data indicates how often genes out of more than 20,000 genes within the human genome (Watson, 1990) gets sequenced as well as the accuracy to determine a mutation that causes a disease. Using the enormous, gathered data helps the providers detect and identify a high number of different diseases. Within the row "Number of detected diseases" each company provides a certain depth of detected diseases meaning how many diseases can be detected in total. In the following chapter 5 Results are described in more detail and compared to each other.

Company	Nebula Genomics	Circle DNA	Dante Labs	23andMe
Product	Ultra-Deep Whole Genome Sequencing	Premium DNA Test	MyGenome Sequencing Test	Health + Ancestry Service
Type of sample	Salvia	Salvia	Blood	Salvia
Number of users	-	> 600,000	300,000	> 12,000,000
Price	744 €	539 €	599 €	169 €
Included reports and/or services	• Ancestry report • Oral microbiome report • Support by geneticists • Exploration tool to examine any of your ~20.000 genes • Access to data of whole genome • Membership (new DNA reports based on the latest scientific discoveries	• More than 500 personalized reports • 2 complimentary 1-on-1 consultations with health and genetic professionals	• 4 personalized reports (possibility of additional 125 reports) • Genome Manager to examine the whole genome • Access to data of whole genome • Regular updates as science progresses • 1-hour genomic consultation service session with a genetic counselor	• More than 150 personalized reports • Personalized recommendations
Number of times and percentage of genome or exome sequenced	100x (100%) whole genome	1x (100%) whole exome	30x (100%) whole genome	1x (~ 0.02%) of the whole genome
Number of detected diseases	213 diseases	115 diseases	> 50 diseases (~ 350.000 conditions)	14 diseases

Table 3 – Comparison matrix of four different DTC genetic diagnostic products

4.2. Summary

The aim of the is to compare the most promising medical technologies in the area of DTC genetic testing and how those impact longevity in order to live for 150 years. The research approach covered gathering data and information from various sources such as journals, scientific papers, websites and putting them into a comparable format for analysis. The data gets narrowed down to DTC genetic testing companies and products with a focus on liquid biopsy and genetic, epigenetic as well as microbiome diagnostics. Four companies which are Nebula Genomics, Circle DNA, Dante Labs, and 23andMe are selected based on the highest number of times and percentage of sequencing the genome or exome as well as the number of users compared to other solutions. The collected data covers information about the company, product, type of sample, number of users, price, included reports and/or services and number of detected diseases. For the comparison of each product, none of the mentioned DTC genetic tests are purchased or tested. Traditional genetic testing methods are not considered due to the advantages of DTC genetic testing for the customers.

5. Results

Following the data collection and data formation the purpose of this section is an objective comparison of previously introduced DTC genetic tests. In order to provide a meaningful comparison of found data, the previously mentioned products get compared to each other based on one parameter at a time.

Each upcoming chapter starts with an short introduction. Following the introduction each parameter that is given in Table 3 gets addressed individually for every company before continuing with the next characteristic.

5.1. Type of sample

In this section the types of samples which are necessary for the genome sequencing are described for each company individually. For the purpose of this thesis the region from where the sample of human salvia originates from (e.g., throat, cheek, etc.) does not affect any parameter in the comparison.

Nebula Genomics state on their website that the collection of customers sample for the "ultra-deep whole genome sequencing" product can be taken at home by rubbing a swap against the inner side of consumers cheek (Nebula Genomics, 2023).

Similar to Nebula Genomics as well Circle DNA mentions on their website that the sample for their product "Premium DNA Test" originates from salvia. They additionally mention that all kits include a non-invasive, Federal Drug Administration (FDA)-approved salvia collection swab (Circle DNA, 2023).

Dante Labs on the other hand states on their website that for their product "MyGenome Sequencing Test" a blood sample is taken. This happens by an innovative home blood collection kit which is part of the product (Dante Labs, 2023).

23andMe states on their website that for their product "Health + Ancestry Service" consumers need a salvia sample in order to be able to sequence their genome. The sample will not be taken with a swap. Customers need to spit into a collection tube (23andMe, 2023).

5.2. Number of users

Within this chapter the number of users that already use the products from the companies are described. As discussed in previous chapters the number of users has an direct impact on how accurate the identification and classification of disease is. Furthermore, the amount of gathered DNA data increases the accuracy and reliability of the diagnosis.

As of now, there is no publicly available information or indication of the number of users or customers that Nebula Genomics has. It is possible that the company has not disclosed this information or that it is not easily accessible on purpose.

Circle DNA states on their website that the company currently has more than 600,000 customers. Anyhow a direct allocation to their product "Premium DNA Test" is not possible since their portfolio covers more test besides the given one. For the purpose of this thesis, it was assumed that all 600,000 users at least sequenced their exome once (Circle DNA, 2023).

As of 2023, Dante Labs has reported that they have performed a significant number of genome analyses with a total of 300,000 whole genomes being analyzed and processed through their systems. This is indicated on their website (Dante Labs, 2023).

23andMe mentions on their page "About us" that the company sold more than 12,000,000 DNA kits until now. For the purpose of this thesis, it is assumed that all kits that are sold to consumers cover at least 0.02% of each customers genome (23andMe, 2023).

5.3. Price

Within this chapter the price tag of each product from the companies is described. Price has an impact on the decision of purchasing a DTC genetic test. The higher the price tag of a genetic test the higher its additional provided products and/or services.

The "Ultra-Deep Whole Genome Sequencing" with all its addons costs around 744 euros. On the Nebula Genomics website the currency for all products is given in dollar. For the purpose of this thesis all prices are converted to euros by using a factor of 0.93

euro/dollar. Within this 744 euros no membership fee is included although a purchase requires a yearly or lifetime paid membership (Circle DNA, 2023).

The price for the product "Premium DNA Test" from Circle DNA is 539 euros. Due to the fact that Circle DNA's website provides a conversion from dollars to euro no conversion is necessary. Within the given price there is no membership included, but access to every offered report and a 1-on-1 consultation (Circle DNA, 2023).

"MyGenome Sequencing Test" from Dante Labs costs 599 euros. No conversion from dollar to euro is needed. This price includes access to a variety of reports and unlimited genomic consultation services (Dante Labs, 2023).

The product "Health + Ancestry Service" of 23andMe costs 169 euros. Here as well no conversion from dollar to euro is necessary. This price covers more than 150 reports, but no membership or additional support is included (23andMe, 2023).

5.4. Included reports and/or services

Within this chapter the included reports and/or services of each product from the compared companies are described. After receiving the results from sequencing, companies have the possibility to support the customers by giving further insights into the gathered data.

Within the price of "Ultra-Deep Whole Genome Sequencing" product additional reports like an ancestry and an oral microbiome report are provided. Furthermore, an unlimited support from geneticists is included. To examine any of consumers approximately 20.000 genes, Nebula Genomics provides exploration tools doing exactly that. Access to the data of customers whole genome is given. A necessary condition that comes along with purchasing the product is a membership that offers new DNA reports based on the latest scientific discoveries and is charged either one time or monthly (Nebula Genomics, 2023).

The product "Premium DNA Test" from Circle DNA comes together with more than 500 personalized reports. Out of these, 125 reports examine diet and fitness routines, more than 115 detect disease risks, 163 research conditions that might get passed on to consumers' unborn child and 73 of them analyze ancestral roots and genetic traits.

Furthermore, two complimentary 1-on-1 consultations discussing customers results with health and genetic professionals are included (Circle DNA, 2023).

Dante Labs product "MyGenome Sequence Test" includes four personalized reports which are dealing about the topics health and predispositions, wellness, fitness as well as nutrition. Additionally to these reports, the consumer has the possibility to purchase further 125 reports that target different organs (e.g., hearth, liver, etc.) or diseases (e.g., cardiovascular diseases, autoimmune disorders, etc.). Access to whole genome data is given and can be examined with a genome manager. As science progresses, Dante Labs provides regular updates that come along with the product. Finally, a 1-hour genomic consultation service with a genetic counselor is included (Dante Labs, 2023).

23andMe offers more than 150 personalized reports for the customers when choosing "Health + Ancestry Service" as a product. Out of these reports more than 10 reports talk about how customers DNA might be affected by mutations that increases the likelihood of developing certain health conditions, more than 5 talk about lifestyle factors like diet, exercise as well as sleep, and more than 40 reports about what inherited health condition might be passed to consumers unborn (23andMe, 2023). Furthermore, there is the possibility to choose to receive personalized recommendation which cover custom health and wellness recommendations as well as medical consultations (23andMe, 2022).

5.5. Number of times and percentage of genome or exome sequenced

Within this chapter the number of times and percentage of genome or exome get sequenced of each product from the companies are described. With an increasing number of sequences, the accuracy and reliability to detect disease causing mutations in customers DNA increase. Therefore, a high number of whole genome or exome sequences are preferred.

Nebula Genomics mentions that their product "Ultra-Deep Whole Genome Sequencing" reads over 6,000,000 positions in the genome, which represent nearly 100% of it. This the company does 100 times. Practically, this means that every letter within the DNA gets read 100 times. This increases the accuracy drastically and generates approximately 300 gigabytes of DNA data (Nebula Genomics, 2023) .

Circle DNA conducts a full scan of all protein-coding genes with a high validated accuracy. The technology the company uses is a WES. The exome gets sequenced once (Circle DNA, 2023). With Circle DNA's WES 3 million DNA data points get collected. For purpose of this thesis 1 data point translates to 1 byte of DNA data. This results into 3 gigabytes of DNA data, which is generated by Circle DNA's genetic test (Nebula Genomics, 2023).

With Dante Labs "MyGenome Sequencing Test" consumers genome gets sequenced 30 times. By that method every letter in customers DNA is read 30 times. This increases accuracy and therefore reduce mistakes. According to Dante Labs website which states that the whole genome gets sequenced 30 times and the fact that the whole genome consists out of around 3,000,000,000 data points "MyGenome Sequencing Test" generates about 90 megabytes of DNA data (Dante Labs, 2023).

The product "Health + Ancestry Test" from 23andMe analyzes around 0.02% of the whole genome. This means that the company sequences less than the whole genome of every customer. With this 0.02% of the whole genome around 600,000 to 1,000,000 DNA markers get analyzed (Nebula Genomics, 2023). With the assumption that the whole genome consists out of 3,000,000,000 data points this results in 60 megabytes of DNA data points (Know your DNA, 2022).

5.6. Number of detected diseases

Within this chapter the number of detected diseases of each product from the companies are described. With an increasing number of detected diseases the customer feels safer when it comes to identifying what condition might lead to premature death. The more diseases are identifiable by the companies the higher is the chance of being able to detect even rare diseases that are usually not covered by DTC genetic tests.

The Nebula Library, a compilation of diseases and conditions available on the Nebula Genomics website, currently lists 213 different diseases according to information available on the website as of 2023. The library includes a wide range of diseases and conditions from common conditions such as multiple sclerosis and gallstones up to more rare and complex conditions. (Nebula Genomics, 2023).

On Circle DNA's website there are 115 reports dealing with common health conditions and cancer risk, brain, and dementia health as well as other disease risks. Beside these reports there are as well services that deal with allergies, pollution sensitivities and other areas which might have an impact on customers health, but are not further considered within this thesis (Circle DNA, 2023).

The" MyGenome Sequencing Test" detects around 50 diseases in its standard version. Due to the fact that there are 101 so-called "panels" which Dante Labs offers additionally to their product, extends the range of detection of diseases and conditions (e.g., epilepsy, hemiplegic migraine, etc.) to around 350.000. Out of those more than 50 diseases are detected by the "MyGenome Sequencing Test". Anyhow, there is no indication how many diseases are covered in total with all panels (Dante Labs, 2023).

23andMe, a well-known player in the DTC genetic testing space, states on their website that through their various genetic reports they are able to detect 14 different diseases and conditions. These include type 2 diabetes and celiac disease. The detection of those diseases is achieved by analyzing customers' genetic data and comparing it to known genetic variations associated with these conditions. (23andMe, 2023).

5.7. Summary

As it can be seen within this chapter, there are many differences, but as well similarities in the parameters between each product and its representative company. When looking at the type of sample that needs to be collected, Nebula Genomics, Circle DNA and 23andMe use saliva samples for their genetic tests. Dante Labs is the only company that uses a blood sample for genetic sequencing. This sample is taken with an innovative home blood collection kit. The number of users varies between each company as well. Circle DNA sold to over 600,000 customers, Dante Labs having analyzed 300,000 whole genomes, and 23andMe having sold over 12,000,000 DNA kits. The prices for each company's products differ. Nebula Genomics' "Ultra-Deep Whole Genome Sequencing" costs 744 euros, Circle DNA's "Premium DNA Test" costs 539 euros, Dante Labs' "MyGenome Sequencing Test" costs 599 euros, and 23andMe's "Health + Ancestry Service" costs 169 euros. Each company provides a variety of different included reports and/or services for each product. Differences start by the type and number of provided reports and reaches up to the private consultation for each customer after receiving the results.

6. Discussion

Following the comparison of previously introduced companies and products from chapter 5, the purpose of this section is a comparison of introduced DTC genetic tests. The comparable data gets analyzed with the goal to identify advantages and disadvantages. Furthermore, the results are put into context of scientific literature and connect to the problem statement in chapter 4. With this connection a first indication what product has the highest impact or importance in regard to longevity is possible. This linkage gets supported by a weighted score that is given to each product and parameter to finally arrive at an overall total score, which indicates the most recommended DTC genetic test that is discussed within this thesis.

As it can be seen in Table 3, there are two types of customer DNA samples in order to sequence consumers genome and suit the given DTC genomic test products. One type of sample is salvia. Next to a salvia sample there is also the possibility to provide a blood sample. As it can be seen in Table 1, every product except the one from Dante Labs, which uses blood, needs salvia as a sample for genome or exome sequencing. When comparing the two types of samples, the purity of genomic DNA extracted from salvia is not really different from a blood sample. When looking at the DNA yield between both samples, literature states that the yield from blood samples are significantly higher than the one from salvia samples by a factor 10. Additionally, the human amplifiable DNA is higher in blood samples than salvia samples (Hu, et al., 2012). Advantages of collecting salvia samples for DNA extractions are to get a non-invasive ability to collect the sample. Furthermore, the salvia samples can be stored for years under room temperature and shipped batchwise. DNA extraction does not need to happen immediately after taking the sample (Yao, Akinrinade, Marie, & Mital, 2020).

Looking at the given products and its number of users there is one company that stands out when it comes to consumers. It is 23andMe. With more than 12,000,000 customers it is the most used or requested genetic diagnosis test within the comparison. Following with more than 600,000 consumers is Circle DNA and their product. Dante Labs has 300,000 customers. Within the literature there is no information about Nebula Genomics customer base, which can be explained either by the fact that since it is a

rather young company (foundation in 2018) there is still no competitive data or number of products sold so the given number would not be competitive enough to represent value if publicly available. 23andMe is founded in 2006 and is the oldest companies out of the comparison. Circle DNA is founded in 2014, Dante Labs in 2016. Nebula Genomics is the youngest company since it is founded in 2018. When looking at the foundation date of 23andMe the high number of customers can be explained with the argument that the company as well as its products and services already exist for years and therefore provides them a competitive advantage. Another reason for the high number of consumers that purchased a genetic diagnostic test from 23andMe can also be reasoned by the price for the test, as it can be seen in a study from China showing that an increase of prices for a DTC results in a decrease of customer demand (Zhu, 2022). Demand for DTC genomic tests increased during the last years, which can be reasoned by the greater availability and the expansion of DTC testing (ACMG, 2016). Circle DNA with their more than 600,000 customers might differentiate from Dante Labs, because of the small price difference (539 euros to 599 euros) and their numerous personalized reports (500) which is more than the 129 reports from Dante Labs.

In the different given data about the price for each product, there are two products "Premium DNA Test" from Circle DNA and "MyGenome Sequencing Test" from Dante Labs which cost nearly the same. Circle DNA`s product costs 539 euros. Dante Lab's product costs 599 euros. When those get compared to each other, the small difference in price can be explained with an increased number of sequences of the whole genome (1 time genome sequencing versus 30 times WGS) as well as additional supportive tools like the so-called "Genome Manager". It allows customers to dig deeper into their sequenced genome. As it can be seen with 23andMe`s "Health + Ancestry" genetic diagnostic product, the price does have an impact on the number of customers. With as low as 169 euros, this product represents a cheaper alternative to "MyGenome Sequencing Test" and "Premium DNA Test". Even though 23andMe`s product costs about a third of the DTC genetic test from Dante Labs and Circle DNA, it still delivers a lot of value. This can be seen by the number of reports for example, in which 23andMe provides even more personalized reports than Dante Labs basic version without any additional panels. On the other end of the price spectrum there is

Nebula Genomics' "Ultra-Deep Whole Genome Sequencing" which costs 744 euros. The increased costs for the customers can be explained by the 100 times sequencing of genome instead of less than 30 times when looking at the other companies, which results in a higher data output as well as additional services that come along with the product. Anyhow, for the purpose of getting an indication about what diseases the consumer might be most likely to get, 30 times genome sequencing is sufficient. Since 100 times sequencing lowers the probability of a sequencing error and at the same time increase reliability, the usual use case for this precision of genetic testing is in medical environments. There a completely clear and accurate identification of the mutation is needed (Marian, 2014). Of course, this does not mean that customers do not want to be 100% safe when it comes to detecting all potential diseases.

Along with the different prices there are also variations in the included reports and/or services that each company provides to the customer. Nebula Genomics "Ultra-Deep Genome Sequencing" and Dante Labs "MyGenome Sequencing Test" offer a low number of reports that interpret diseases or give the consumer personalized reports. Anyhow, Dante Labs offers the possibility to get additional 125 reports talking about diseases and other conditions. Circle DNA`s and 23andMe's product on the other hand provides hundreds of personalized reports. Every of the given products include some kind of consultation or support by either a geneticist or health and genetic professional. Except of 23andMe, which only provides personalized recommendations within their reports, but offers no in person consultation. Customers have the possibility to explore their sequenced genome in more detail with the products from Nebula Genomics and Dante Labs. "MyGenome Sequencing Test" does not give any qualitative information regarding how many genes or DNA points the customer can examine. Nebula Genomics' exploration tool enables the consumer to examine around 20,000 genes. Besides that, both previously mentioned companies offer accessibility to the whole genome. Nebula Genomics and Dante Labs offer the consumer to stay up to date by providing new version of their reports or adapt them based on scientific findings. Nebula Genomics covers that with a membership, which is necessary as soon as the product gets purchased. Dante Labs provides those updates without paying for a membership. When looking at the number of customers in relation to the number of sequences of the whole genome or exome as well as included reports and/or services,

the number indicates as well that the cheaper and more precise offers are preferred. The less options the customer has the easier it is for him or her to choose a preferred product or service. A phenomenon known as “decision fatigue”. It seems like that for most customers the possibility to examine the whole genome or exome is not from highest value.

When looking at the compared companies and their products, there is a difference in the number of times the genome or exome gets sequenced. Each of the given product has a different number of included sequences of the genome or exome. An increasing number of sequences increases the accuracy of reading each letter of customers DNA correct. This means that it is possible to decrease a sequencing error and at the same time increase reliability by the number of times the genome or exome gets sequenced. Nebula Genomics represent one of the few companies that offer 100 times DTC WGS, besides Sanos Genetics and FullGenomes. 23andMe sequences around 0.02% of the genome and represents the only company within this comparison that do not offer at least a full WGS or WES. When it comes to the necessary range of genome or exome sequencing, literature says that just 1% of the genome is covering 85% of all mutations which cause disease-related traits (Choi, Scholl, Ji, Liu, & Lifton, 2009). This represents a valid reason why most consumers are satisfied with the sequencing of a just small part of their DNA. Similar to the efforts that are provided by 23andMe.

Circle DNA’s “Premium DNA Test” together with Nebula Genomics “Ultra-Deep Whole Genome Sequencing provide the customer with insights into hundreds of different diseases that both companies can identify. These diseases are described and explained within the provided reports. Additionally, the consumer also receives recommendations for individual improvements based on the results and next steps how to avoid the disease to break out. Having the mutation within customers DNA does not mean that the consumer develops this disease. In 23andMe’s “Health + Ancestry Service” reports 14 diseases get detected. When comparing the number of detected diseases to the number from Circle DNA and Nebula Genomics, it is lower. An outstanding variety and number of diseases get detected by Dante Labs product and its WGS. With “MyGenome Sequencing Test” and all the additional panels purchased, the customer can get information about more than 350,000 conditions. This enormous and additional pool of insights when compared to the other companies can be reasoned

because of the following. As previously mentioned, the type of sample is blood and has a higher yield of readable DNA. This might support the fact that the number of reports is drastically higher than the one from the other companies. Furthermore, the amount of the gathered data which originates from already sequenced genomes and is used to build a DNA database explains the difference. Another reason for having such a difference in provided reports might also be explained by the fact that each company does not have to provide more information about diseases even if they could. The most asked and researched diseases that are not many, but at the same time the biggest reason for all age-related deaths worldwide as seen in Figure 2. Therefore customers are satisfied by the portfolio of predetermined detected diseases of the providers. Anyhow, Dante Labs provides an option to get more information by purchasing additional panels.

Based on the discussed points above, the following paragraphs discuss the impact of each individual parameter to human longevity. These individual characteristics are given a score which represents a weighting considers the relative impact on longevity. After summarizing the scores of each individual parameter, a total weighted sum results and indicates the impact on how the genetic testing from the given company extends the human lifespan. In the individual score next to each parameter is shown. This score ranges from 1 to 5. 1 means that this parameter has the lowest impact and 5 means it has the highest impact on the lifespan.

Looking at the type of sample that gets used for genetic testing, there are salvia and blood samples. As discussed in a previous paragraph, literature indicates (Hu, et al., 2012) that 37.3% of the salvia samples have human amplifiable DNA which furthermore leads to a 88.8% genotyping call rate (percentage of samples in which a confident genotype call rate can be made) when compared to a blood-derived DNA with a genotype detection of 99.1%. Anyhow, if the DNA samples contain more than 31.3% of human amplifiable DNA, it performs very well. The genotype call rate is at least 96%. Since the blood is slightly more accurate due to a higher amplifiable DNA content, it scores a 5, where the salvia sample scores a 4. The score is based on the fact that the genotype call rate is almost 100% and therefor just a low percentage of not working samples for genotyping occur. Since the sequencing will take place within

days after the customers sends it back to the laboratory, transportation has no significant impact.

The number of costumers of a given product within this thesis determines the size of the database created from DNA data, which makes it easier to identify and analyse the diseases that are caused by mutations in genes (Liu, Li, Zhu, & Qi, 2020). When comparing the products, the most consumers bought the genetic test from 23andMe. The number of customers is more than 12,000,000. Scoring it with a 2 can be explained the following. Even though the number is high, still they only offer to detect 14 diseases when looking at the number of customers. “MyGenome Sequencing Test” scores a 2. Reasons for the score are the same as for Circle DNA. More than 600,000 customers are using the “Premium DNA test” from Circle DNA which represents a high number of gathered DNA data that furthermore and as previously explained can be valuable in detecting mutations in a gene that might cause various diseases. Anyhow there is no scientific literature that talks about the amount of DNA data that needs to be stored for sufficient disease detection since the main challenge is to explore further genomic variants that are not yet discovered. Publicly available databases like DisGeNET represent resources to discover genes and variants associated to human diseases (DisGeNET, 2023) (Pinero, Saüch, Sanz, & I. Furlong, 2021). For the purpose of this thesis, the number of customers of Circle DNA scores a 2. This can be explained by the fact that comparable high number of customers provide more insightful details for every additional consumer, but does not have a significant impact on detecting a disease. When compared to Dante Labs for example, which has a lower number of customers (300,000) on the other side, the services provide the possibility to detect more than 350,000 conditions out of which at least more than 50 are diseases. An advantage of having a wide customer base is the possibility to participate in a community as a user and having someone to talk to and exchange further information with.

Looking at the price range from 169 euros (23andMe) to 744 euros (Nebula Genomics) it can be seen, that within the given comparison there are three price areas. The most expensive product “Ultra-Deep Whole Genome Sequencing” comes from Nebula Genomics with a price of 744 euros. The second price area is around 500 – 600 euros where products from Circle DNA and Dante Labs are located. The cheapest product

within the given comparison is the “Health + Ancestry Service” from 23andMe which costs 169 euros. Given the fact that Nebula Genomics offers not only a 100 times WGS, but also detects 213 diseases when compared to Dante Labs “MyGenome Sequencing Test”, which detects more than 50 diseases and sequences the whole genome 30 times. The reasoning for the higher price point is understandable. When comparing Dante Labs product to Circle DNAs “Premium DNA Test” the customer can choose between a more personalized and information centered service from Circle DNA and a more genetic insightful and personalized approach from Dante Labs “MyGenome Sequencing Test” for nearly the same price. Given the fact that the product of 23andMe sells for 169 euros, it is very attractive to the curious customer who is not interested to go too much into detail, but wants to have an overview of the most common diseases with additional personal support. Objectively speaking, 23andMe’s product scores a 4. Reason for this is that even though the offer covers a rather low amount of genetic information, the detection of most common diseases is included and represents the most essential benefit for the customer by providing the customer encouragement to modify their behavior in order to avoid getting any disease (C Howard & Borry, 2008). Looking at Nebula Genomics product, which covers an enormous amount of genetic information, 100 times WGS and detection of 213 diseases the score is 2. The product is still expensive compared to others. The “Premium DNA Test” from Circle DNA scores a 3. It is still expensive compared to 23andMe’s product (169 euros), but offers a lot of personalized support and reports as well as insight into 115 diseases that include the most common diseases. Same score is given to Dante Labs product. Main reason for this result is the high price, since all other services are in favor of the customer even though a 30 times WGS would not be from importance as long as the accuracy is high enough to get an first indication about the genetic mutations of the consumer.

Included reports and/or services are the key feature besides the number of detected diseases. Taking into consideration to get the most information out of each product or service the one from Nebula Genomics offers clearly the most information and personalized support for the customers who want to dig into details by their own. Considering only the number of services and provided outputs, the score for this product is a 4. Even though there are no personalized reports except ancestry and oral

microbiome reports, the detection of all predispositions and rare genetic mutations are covered as well as personalized support and the possibility to get frequent updates based on scientific discoveries are included and represent a valuable insight for the customer. This explains the score 4. Close to the scope of reports and services to Nebula Genomics is Dante Labs product. Similar to "Ultra-Deep Whole Genome Sequencing" the product of Dante Labs provides a variety of additional services and covers the most common diseases and scores a 4 as well. Another solution represents Circle DNA. Its product is distilled down to a more comprehensive portfolio of services. Anyhow, there are more than 500 personalized reports that are included and cover a wide spectrum of information for the customer. Taking into consideration the high informational output and the possibility to get professional consultation, the product scores a 2. The consultation and the possibility to dig deeper into details is missing. Finally, 23andMe offers more than 150 personalized reports which in comparison to the other products is high. Given the fact that there is no consultation and no possibility to dig deeper into customers genome as well as the fact that the covered diseases are limited, even though the most common diseases get identified, the product scores a 1.

In regard to the number of times the genome or exome is sequenced the range of given parameters are wide. Nebula Genomics offers a WGS for 100 times covering 100% of the genome whereas on the other side of the spectrum 23andMe sequences only 1 time around 0.02% of the genome. In between there are two products that either sequence the whole exome once ("Premium DNA Test") or 30 times the whole genome ("MyGenome Sequencing Test"). Anyhow, as research claims approximately 1 – 2 % of the genome is causing 85% of disease-causing mutations (Edelson, Dugoff, & Bromley, 2019). Given this fact, with every time a whole genome gets sequenced, the accuracy of detecting a disease-causing mutation increases and the more often it gets done the more accurate the diagnosis. Furthermore, it can be seen in Figure 5 that if the genome gets sequenced 30 times, the callable genomic data is stagnating.

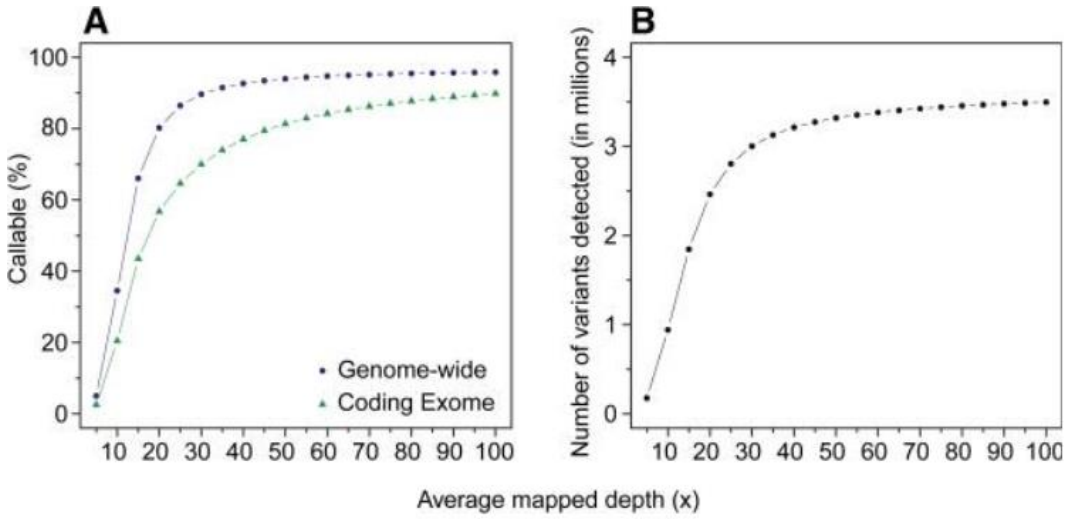

Figure 5 – Callable portion of the genome per average mapped depth (Ajay, et al., 2011)

Even though the data that gets generated through this numerous sequences, the reference data which the customers data gets compared to is lacking. There is not a lot of information that can be gained from the DNA data since research is not that far ahead yet. Online available tools and platforms as the one from DisGeNET (DisGeNET, 2023) will grow further in its importance. Scoring the compared product and starting with Nebula Genomics, it scores a 5. Reason for that is screening the whole genome 100 times the probability of missing a gene during sequencing is close to 0. Nearly the same stands for Dante Labs 30 times of sequencing which comes with an acceptably low error rate and therefore scores a 4. Circle DNA sequences the exome once which suggests a low accuracy when it comes to detecting disease-causing mutations and by that scores a 1. Even though 23andMe covers just 0.02% of the genome and sequences it only once, the accuracy is low, but satisfies customers that want to get a first indication. Following the low accuracy due to a single genome sequence, “Health + Ancestry Service” scores a 1 as well.

When considering the impact of the parameter of detected diseases in correlation with extending human lifespan, it is preferred to detect as many diseases as possible to minimize the chance of developing a disease. Comparing the discussed products within this thesis, the product with the most detected diseases is preferred. According to a statement of a World Health Organization (WHO) representative which was referenced within a Washington Post article there are currently more than 10,000

diseases that are known worldwide (Kessler, 2016). Looking at the Nebula Genomics product and its statement of being able to detect 213 diseases, which represents the highest number of detected diseases when compared to the other products, is given a score of 4. Reason for this is since there is a small number of common diseases like cardiovascular diseases as it can be seen in Figure 2, that are responsible for the majority of deaths caused by age-related diseases worldwide, detecting the most common ones has still a big impact when it comes to extending the human lifespan. Anyhow there are still diseases that are not known yet and can be deadly on the one hand. Various other diseases that do not fall into the group of common diseases can lead to deaths on the other hand as well. Following Circle DNAs "Premium DNA Test" which detects 115 diseases scores as well a 4. Dante Labs and 23andMe`s products detect a lower number of diseases, but still cover the most common diseases and therefore both score a 3.

Based on the previous discussed results and given scores to each parameter within our comparison there is a final result, which is presented in within the last row "total score". Dante Labs "MyGenome Sequencing Test" achieves a total score of 20. Followed by Nebula Genomics "Ultra-Deep Sequencing Test" with a total score of 18 and 23andMe's "Health + Ancestry Service" as well as Circle DNA's "Premium DNA Test" with a total score of 16. Based on these results there is one recommended product. Dante Labs "MyGenome Sequencing Test". It has to be noted that one score of Nebula Genomics product is not given a score due to a lack of publicly available information, which would have an impact on the final total score. Dante Labs product reaches a total score of 20, because of many reasons. Most extensive reports and services, additional support from a specialist, frequent updates based on scientific discoveries, a high number of detected diseases and high accuracy in detection of mutations within the genome to mention a few. Even though the price tag is high, the insights and expertise provided is extensive. Slightly worse in the score of 18 is Nebula Genomics product, due to its lower number of reports and a higher price tag (+145 euros). 23andMe's product together with Circle DNAs product result in a total score of 16, due to the reason of a lower accuracy of detection, less detected diseases, and less additional services like a consultation-based discussion in regard to the results of the genetic test. Anyhow, the difference between the "Premium DNA Test" and the

“Health + Ancestry Service” is the missing consultation and a lower number of personalized reports, the sequenced area of the genome on the side of 23andMe’s solution, the much higher price (+370 euros) as well as the smaller community on the side of Circle DNAs DTC genetic test. Differences compensate on each side which results in an equal score between these two products.

Company	Nebula Genomics	Score	Circle DNA	Score	Dante Labs	Score	23andMe	Score
Product	Ultra-Deep Whole Genome Sequencing	-	Premium DNA Test	-	MyGenome Sequencing Test	-	Health + Ancestry Service	-
Type of sample	Salvia	4	Salvia	4	Blood	5	Salvia	4
Number of users	-	-	> 600,000	2	300,000	2	> 12,000,000	3
Price	744 €	2	539 €	3	599 €	3	169 €	4
Included reports and/or services	• Ancestry report • Oral microbiome report • Support by geneticists • Exploration tool to examine any of your ~20.000 genes • Access to data of whole genome • Membership (new DNA reports based on the latest scientific discoveries	4	• More than 500 personalized reports • 2 complimentary 1-on-1 consultations with health and genetic professionals	2	• 4 personalized reports (possibility of additional 125 reports) • Genome Manager to examine the whole genome • Access to data of whole genome • Regular updates as science progresses • 1-hour genomic consultation service session with a genetic counselor	4	• More than 150 personalized reports • Personalized recommendations	1
Number of times and percentage of genome or exome sequenced	100x (100%) whole genome	4	1x (100%) whole exome	1	30x (100%) whole genome	3	1x (~ 0.02%) of the whole genome	1
Number of detected diseases	213 diseases	4	115 diseases	4	> 50 diseases (~ 350.000 conditions)	3	14 diseases	3
Total score		**18**		**16**		**20**		**16**

Table 4 – Comparison matrix of four different DTC genetic diagnostic products with weighting based on its impact on longevity

6.1. Summary

Within this chapter previously introduced genetic diagnostic products get compared and the advantages and disadvantages of each is analyzed. The two types of samples used for genome sequencing are saliva and blood. Literature states that the yield of genomic DNA from blood samples is significantly higher than from saliva samples by a factor 10 as well as that the human amplifiable DNA is higher in blood samples. However, the advantages of using saliva samples include non-invasiveness and the ability to store and ship samples at room temperature. Looking at number of customers the company with the highest number is 23andMe with over 12,000,000 customers. Circle DNA has over 600,000 customers, Dante Labs has 300,000. There is no publicly available information on Nebula Genomics' customer base due to its recent establishment. The high number of customers for 23andMe can be linked to its long existence and competitive pricing. Circle DNA's high number of customers may be due to its small price difference and the fact that it offers 500 personalized reports when compared to Dante Labs' 129 reports. The "Premium DNA Test" from Circle DNA and "MyGenome Sequencing Test" from Dante Labs have similar prices. The small difference likely being due to Circle DNA's additional support tools and genome sequencing. The price of a product also appears to have an impact on the number of customers. 23andMe's "Health + Ancestry" genetic diagnostic is priced at 169 euros and therefore more affordable than the other options. The product from Nebula Genomics offers the most information and personalized support whereas Dante Labs offers a variety of additional services. Circle DNA's product is distilled down to a more comprehensive portfolio of services, but lack consultation and the ability to dig deeper into details. 23andMe offers more than 150 personalized reports, but lack consultation and has limited covered diseases within their reports. In terms of the number of times the genome or exome is sequenced, Nebula Genomics offers the most extensive service with 100 times, while 23andMe sequences the least. They sequence the genome once and only 0.02% of it. It is noted that as research claims that approximately 1-2% of the genome causes 85% of disease-causing mutations and therefore the more often a genome is sequenced the more accurate the diagnosis. However, currently there is not a lot of information that can be gained from DNA data as the reference data is lacking and research is not that far ahead yet.

7. Conclusion and outlook

There is a growing body of evidence and scientific research as well as books that show humans already today how to reach 150 years or how to reach biological immortality in a not-so-distant future. Since there is not yet the one solution that fits all, there are many proposed ways, methods, products, lifestyles how to reach these states. This makes humankind optimistic.

Even though the fact that our life expectancy increased during the last years, still 55% of the 55.4 million people die on cardiovascular, respiratory, and neonatal diseases, which are seen as age-related conditions. When looking at age-related diseases, scientists currently do not yet know the single key process that causes aging and therefore agreed on a variety of causes also known as "The Hallmarks of Aging". Knowing these hallmarks exist makes research and in the following the treatment and prevention easier. There are a lot of different products and services in regard to detection, prevention, and treatment of age-related diseases. Out of the currently existing solutions, researchers and experts in that field argue that early and accurate detection of age-related diseases is one of the biggest lever when it comes to preventing premature death and therefore increase individuals' longevity. Even though scientific literature that examines the relationship between DTC genetic tests and longevity is still missing, there is a growing body of research on the use of genetic testing in general and its impact on health outcomes. Some studies have suggested that genetic testing can lead to improved health behaviours and increased adherence to recommended medical interventions, which in turn may lead to improved health outcomes (Roberts, Kuller, & Nease Jr, 2009) (Green, Gollust, Goddard, & Fiske, 2015).

The products that are compared as part of this thesis suggest four possible solutions to take a step into the direction of increasing customers longevity by detecting potential disease-causing mutation in customers genome early. Even though the difference between each of the given DTC genetic tests are marginal, still Dante Labs "MyGenome Sequencing Test" reaches a total score of 20 and therefore represents the most recommended test discussed within this thesis to use and live for healthy 150 years. Reasons are the brought area of additional reports and services, the high accuracy (30 times WGS) as well as wide the huge number of diseases and conditions

detected. Nevertheless, when considering that each of the compared products provide the customer with insightful details about disease-causing mutations that exist within his or her genome, every product is great. The most important step to take for everyone is to sequence his or her genome. This helps to understand what diseases might affect customers life now or in some years from now, if not prevented early. Getting rid of drinking alcohol, quit smoking, reducing sugar consumption, eat less and more vegetables, do frequent health check-ups, supplement, be physical active, get enough sleep, meditate, and educate represent all the basics that can be put in place for living to 150 years. If customers do not know that they might get a rare type of cancer, because there is a mutation within his or her genome, the necessary steps to act against the gene's activation might be too late.

When looking into the not-so-distant future there are a lot of new innovations that will change the biological immortality as known today. Biologically speaking there is no rule given by nature that prevents immortality as it can be seen in Turritopsis jellyfish, which needs about three days to reverse-age itself into a polyp state and start growing all over again (Young, Extreme Longevity Meets Technical Inevitability, 2021). Today there is already the possibility to reprogram age-associated changes which are a huge leap into biological immortality. A scientific paper from March 2022 shows the successful reprograming of the epigenetic clock of aging cells in mice (Horvath, Belmonte, & Browder, 2022). It is only an issue of time when this reprograming is available for humans. Furthermore, the line between man and machine will blur. In Germany, Metin Sitti a microroboticist released a proof-of-concept robot that can be swallowed like a pill. It will move around the gastrointestinal system using magnets, releasing drugs exactly where they are needed, is taking pictures and collects issue for doing biopsies (Young, Man and Machine Become One, 2021). MIT professor Sangeeta Bhatia designed nanoparticles that are roaming through the human body on the way to detect cancerous cells, which react to certain enzymes that only these cancer cells release (Young, Extreme Longevity Meets Technical Inevitability, 2021). Technology like that is already getting used to successfully detect lung, colon, and ovarian cancer in mice at a very early state (Trafton, 2020).

Due to the increasing life expectancy, which is estimated to reach eighty to nighty years by 2100 (Roser, Ortiz-Ospina, & Ritchie, 2022), it is anyhow just a matter of

time to reach longevity escape velocity. Since technological breakthrough and developments (e.g., more powerful computer, artificial intelligence, etc.) at some point in time progresses drastically, it does not matter how quickly one ages or what kind of illness humans get. The scientific development will always be a step ahead, which provides an available and universally affordable new solution to restore health and youth. Based on Ray Kurzweil, an "oracle" in Silicon Valley, the longevity escape velocity is "just another ten to twelve years away" (H. Diamandis & Kotler, 2020).

Bibliography

23andMe. (2022, January 11). *23andMe*. Retrieved from Personalized Recommendations: https://customercare.23andme.com/hc/en-us/articles/9295505340183-Personalized-Recommendations

23andMe. (2023, January 10). *23andMe*. Retrieved from How it works: https://www.23andme.com/howitworks/

23andMe. (2023, January 10). *23andMe*. Retrieved from About us: https://circledna.com/about-us

23andMe. (2023, January 11). *23andMe*. Retrieved from DNA Health and Ancestry Service: https://www.23andme.com/en-eu/dna-health-ancestry/

23andMe. (2023, January 11). *23andMe*. Retrieved from What Countries Do You Ship To?: https://int.customercare.23andme.com/hc/en-us/articles/214806628-What-Countries-Do-You-Ship-To-

23andMe. (2023, January 12). *23andMe*. Retrieved from How Can I See The Status Of My DNA Sample?: https://customercare.23andme.com/hc/en-us/articles/202904780-How-Can-I-See-the-Status-of-My-DNA-Sample-#:~:text=Actual%20sample%20processing%20times%20may,is%20received%20at%20the%20lab

A. Gaev, J. (2020). Technology in health care. In E. Iadanza, *Clinical Engineering Handbook* (pp. 428-435). United States: Academic Press. doi:https://doi.org/10.1016/C2016-0-04298-5

ACMG, B. o. (2016). Direct-to-consumer genetic testing: a revised position statement of the American College of Medical Genetics and Genomics. *Genetics in Medicine*, 207-208.

Ajay, S. S., C. J. Parker, S., Abaan, O., Hatice, Fajardo, F., V., K., & Margulies, E. H. (2011). Accurate and comprehensive sequencing of personal genomes. *Genome Research*, 1498-1505.

author, L. n. (year of publication). *Full title of the publication* (Vol. Edition (except 1st edition)). place of publication: publisher.

Bentley, D. J. (2008). The Illumina sequencing platform: an overview. *Nature Reviews Genetics*.

C Howard, H., & Borry, P. (2008). Direct-to-consumer genetic testing: more questions than benefits? *Personalized Medicine*.

Choi, M., Scholl, U. I., Ji, W., Liu, T., & Lifton, R. P. (2009). Genetic diagnosis by whole exome capture and massively parallel DNA sequencing. *PNAS*.

Circle DNA. (2023, January 10). *Circle DNA*. Retrieved from https://circledna.com/about-us: https://circledna.com/about-us

Circle DNA. (2023, January 11). *Circle DNA*. Retrieved from Do you deliver to my country?: https://circledna.zendesk.com/hc/en-us/articles/360019804552-Do-you-deliver-to-my-country-

Circle DNA. (2023, January 10). *Circle DNA*. Retrieved from Premium DNA Test: https://circledna.com/premium

Comfort, A. (1956). *The Biology of Senescence.* London: Routledge & Kegan Paul.

Dante Labs. (2023, January 10). *Dante Labs*. Retrieved from MyGenome Sequencing Test: https://dantelabs.com/products/whole-genome-sequencing

Dante Labs. (2023, January 12). *Dante Labs*. Retrieved from FAQs: https://dantelabs.com/pages/faqs#:~:text=I'm%20currently%20waiting%20for,your%20sample%20in%20our%20lab.

Davida, Y., M. Juddb, T., & Zambutoc Raymond, P. (2020). Introduction to medical technology managment practices. In E. Iadanza, *Clinical Engineering Handbook* (p. 694). Academic Press. doi:https://doi.org/10.1016/C2016-0-04298-5

De Benedictis, G., & Franceschi, C. (2006). The unusual genetics of human longevity. *Science of aging knowledge environment 10*, 20.

DisGeNET. (2023, January 21). *DisGeNET*. Retrieved from https://www.disgenet.org/home/

Edelson, P. K., Dugoff, L., & Bromley, B. (2019). Chapter 11 - Genetic Evaluation of Fetal Sonographic Abnormalities. In M. E. Norton, J. A. Kuller, & L. Dugoff, *Perinatal Genetics.* Elsevier.

European Union. (1998). *Directive 98/79/EC of the Euopean Parliament and of the Council on in vitro diagnostic medical devices.*

Fedintsev, A., & Moskalev, A. (2020). Stochastic non-enzymatic modification of long-lived macromolecules - A missing hallmark of aging. *Ageing Research Reviews*, 1-18.

Green, R., Gollust, E., Goddard, J., & Fiske, N. (2015). Direct-to-consumer genetic testing and changes in health behaviors. *Journal of Genetic Counseling*.

H. Diamandis, P., & Kotler, S. (2020, Februar 25). *MarketWatch*. Retrieved from We are nearing 'longevity escape velocity' — where science can extend your life for more than a year for every year you are alive: https://www.marketwatch.com/story/we-are-nearing-longevity-escape-velocity-where-science-can-extend-your-life-for-more-than-a-year-for-every-year-you-are-alive-2020-02-24

Horvath, S., Belmonte, J. C., & Browder, K. C. (2022). In vivo partial reprogramming alters age-associated molecular changes during physiological aging in mice. *Nature*, 243-253.

Hu, T., Chitnis, N., Monos, D., & Dinh, A. (2021). Next-generation sequencing technologies: An overview. *Human Immunology*, 801-811.

Hu, Y., A. Ehli, E., Nelson, K., Bohlen, K., Lynch, C., Huizenga, P., . . . Davis, G. E. (2012). Genotyping Performance between Saliva and Blood Derived Genomic DNAs on the DMET Array: A Comparison. *PLoS ONE*.

Kessler, G. (2016, 2022 21). *The Washington Post*. Retrieved from Are there really 10,000 diseases and just 500 'cures'?: https://www.washingtonpost.com/news/fact-checker/wp/2016/11/17/are-there-really-10000-diseases-and-500-cures/

Know your DNA. (2022, January 12). *Know your DNA*. Retrieved from Nebula Genomics Review: Your Complete Guide to Their Whole Genome Sequencing Kit: https://knowyourdna.com/nebula-genomics/#:~:text=While%2023andMe%20and%20Ancestry%20read,and%20100X%20whole%20genome%20sequencing

Liu, Y., Li, N., Zhu, X., & Qi, Y. (2020). How wide is the application of genetic big data in biomedicine. *Biomedicine & Pharmacotherapy*.

López-Otín, C., Blasco, M. A., Partridge, L., Serrano, M., & Froemer, G. (2013). The Hallmarks of Aging. *CellPress*, 1194-1217. doi:https://doi.org/10.1016/j.cell.2013.05.039

Marian, A. J. (2014). Sequencing Your Genome: What Does It Mean? *Methodist Debakey Cardiovascular Journal*, 3-6.

Marwaha, S., W. Knowles, J., & A. Ashley, E. (2022). A guid for the diagnosis of rare and undiagnosed disease: beyond the exome. *Genome Medicine*, 23.

McCombie, W. R., McPherson, J. D., & Mardis, E. R. (2023). Next-Generation Sequencing Technologies. *Cold Spring Harbor Perspectives in Medicine*.

MedTech Europe. (2021). *MedTech Europe Survey Report analysing the availability of In vitro Diagnostic Medical Devices (IVDs) in May 2022 when the new EU IVD regulation applies.* MedTech Europe.

MedTech Europe. (2022). *The European Medical Technology Industry in figures.* MedTech Europe.

Morash, M., Mitchell, H., Beltran, H., Elemento, O., & Pathak, J. (2018). The Role of Next-Generation Sequencing in Precision Medicine: A Review of Outcomes in Oncology. *Journal of personalized medicine*, 30.

National Cancer Institute. (2023, January 5). *Surveillance, Epidemiology, and End Results Program*. Retrieved from National Cancer Institute: https://seer.cancer.gov/statfacts/html/breast.html

Nebula Genomics. (2022, January 11). *Nebula Genomics*. Retrieved from International availability: https://nebula.org/blog/international-availability/

Nebula Genomics. (2023, January 10). *Nebula Genomics*. Retrieved from https://nebula.org/whole-genome-sequencing-dna-test/

Nebula Genomics. (2023, January 11). *Nebula Genomics*. Retrieved from 30x Whole-Genome Sequencing is here!: https://nebula.org/blog/30x-wgs/

Nebula Genomics. (2023, January 12). *Nebula Genomics*. Retrieved from CircleDNA review – Is Whole Exome Sequencing worth a premium price?: https://nebula.org/blog/circledna-review/#:~:text=Its%20whole%2Dexome%20sequencing%20collects,processed%20over%20300%2C000%20DNA%20samples.

Nebula Genomics. (2023, January 12). *Nebula Genomics*. Retrieved from Nebula Library – Unlocking Genetic Research: https://nebula.org/blog/nebula-library-unlocking-genetic-research/

Omodamilola, O. I., & Ibrahim, A. U. (2018). CRISPR Technology Advantages, Limitations and Future Direction. *Journal of Biomedical and Pharmaceutical Sciences*.

Papadopoulos, A. (2023, January 11). *Ceoworld Magazine*. Retrieved from CEO Spotlight: Andrea Riposati of Dante Labs: https://ceoworld.biz/2022/12/05/ceo-spotlight-andrea-riposati-of-dante-labs/#:~:text=The%20company%20grew%20quickly%20on,medical%20practices%20in%2097%20countries

Philips, A. M. (2016). Only a click away — DTC genetics for ancestry, health, love…and more: A view of the business and regulatory landscape. *Applied & Translational Genomics*, 16-22.

Pinero, J., Saüch, J., Sanz, F., & I. Furlong, L. (2021). The DisGeNET cytoscape app: Exploring and visualizing disease genomics data. *Computational and Structural Biotechnology Journal*, 2960-2967.

Qin, D. (2019). Next-generation sequencing and its clinical application. *Cancer Biology & Medicine*, 4-10.

Rabbani, B., Tekin, M., & Mahdieh, N. (2014). The promise of whole-exome sequencing in medical genetics. *Journal of Human Genetics*, 5-15.

Roberts, J. E., Kuller, J. L., & Nease Jr, R. L. (2009). The Impact of Genetic Testing on Health Behaviors: A Systematic Review. *Journal of Genetic Counseling*.

Robine, J.-M., & Paccaud, F. (2005). Nonagenarians and centenarians in Switzerland, 1860-2001: a demographic analysis. *Journal of Epidemiology and Community Health 59*, 31-37.

Rodríguez-Rodríguez, D. R., Ramírez-Solís, R., Garza-Elizondo, M. A., Garza-Rodríguez, M. D., & Barrera-Saldaña, H. A. (2019). Genome editing: A perspective on the application of CRISPR/Cas9 to study human diseases (Review). *International journal of molecular medicine*, 1559-1574.

Roser, M., Ortiz-Ospina, E., & Ritchie, H. (2022, January 23). *Our World in Data*. Retrieved from Life Expectancy: https://ourworldindata.org/life-expectancy

Rosner, M., Ortiz-Ospina, E., & Hannah, R. (2019, October). *Life Expectancy*. Retrieved from Our World in Data: https://ourworldindata.org/life-expectancy

Sinclair, D. A. (2019). *Lifespan: Why We Age—and Why We Don't Have To.* London: Thorsons.

Su, P. (2015). *Direct-to-Consumer Genetic Testing: A Comprehensive View.* California: PubMed Central.

Tam, V., Patel, N., Turcotte, M., Bossé, Y., Paré, G., & Meyre, D. (2019). Benefits and limitations of genome-wide association studies. *Nature Reviews Genetics*, 467-484.

Trafton, A. (2020, April 01). *MIT News*. Retrieved from New sensors could offer early detection of lung tumors: https://news.mit.edu/2020/urine-sensor-test-detect-lung-tumors-0401

Uffelmann, E., Huang, Q. Q., Munung, N. S., de Vries, J., Okada, Y., Martin, A. R., . . . Posthuma, D. (2021). Genome-wide association studies. *Nature Reviews Methods Primers*.

United Nations Department of Economic and Social Affairs, Population Division. (2022). *World Population Prospects 2022: Summary of Results.* UN DESA/POP/2022/TR/NO. 3.

Viegi, G., Maio, S., Simoni, M., Baldacci, S., & Annesi-Measano, I. (2009). the epidemiological link between ageing and respiratory diseases. *Respiratory Diseases in the Elderly: European Respiratory Monograph*, 1-17.

Waite, L. J. (2004). The Demographic Faces of the Elderly. *Popul Dev Rev.* , 3-16.

Watson, J. D. (1990). The Human Genome Project: Past, Present, and Future. *Science*, 44-49.

Wilmoth, J. (2000). Demography of longevity: past, present, and future trends. *Experimental Gerontology*, 1111-1129.

World Health Organization. (2020, December). *The top 10 causes of death*. Retrieved from www.who.int: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death

Wysocki, K., & Osier, N. (2019). Direct to consumer versus clinical genetic testing. *Journal of the American Association of Nurse Practitioners*, 152-155.

Yanagi, S., Tsubouchi, H., Miura, A., Matsuo, A., Matusomto, N., & Nakazato, M. (2017). The Impacts of Cellular Senescence in Elderly Pneumonia and in Age-Related Lung Diseases That Increase the Risk of Respiratory Infections. *International Journal of Molecular Science*, 1-16.

Yao, R. A., Akinrinade, O., Marie, C., & Mital, S. (2020). Quality of whole genome sequencing from blood versus saliva derived DNA in cardiac patients. *BMC Medical Genomics*.

Young, S. (2021). Diagnosing Early. In S. Young, *The Science and Technology of Growing Young.* Texas: BenBella Books, Inc.

Young, S. (2021). Extreme Longevity Meets Technical Inevitability. In *The Science and Technology of Growing Young* (pp. 150-151). Texas: BenBella Books, Inc.

Young, S. (2021). Man and Machine Become One. In *The Science and Technology of Growing Young* (pp. 151-156). Texas: BenBella Books, Inc.

Young, S. (2021). What is Aging, Anyway? In *The Science and technology of Growing Young* (pp. 34-36). Texas: BenBella Books, Inc.

Zauner, M. (2022). *Medical Engineering / Medical Device Technology.* Vienna.

Zhu, C. (2022). Demand for Direct-to-Consumer Genetic Testing Services in China and Its Implications for Precision Public Health — China. *China CDC Weekly*, 715-719.

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CRISPR	clustered regularly interspaced short palindromic repeats
DNA	deoxyribonucleic acid
dPCR	digital polymerase chain reaction
DTC	direct-to-consumer
e.g.	for example,
et al.	and others (Latin: et alii)
FDA	Federal Drug Administration
GWAS	genome wide association studies
HDR	homology-directed repair
IVD	in vitro diagnostics
NHEJ	non-homologous end joining
NGS	next generation sequencing
PCR	polymerase chain reaction
RNA	ribonucleic acid
SNP	single nucleotide polymorphisms
UTR	untranslated regions
WES	whole exome sequencing
WGS	whole genome sequencing