SEMMELWEIS EGYETEM

DOKTORI ISKOLA

Ph.D. értekezések

3149.

MADARÁSZ BÁLINT

Nép- és közegészségtudományok

című program

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Comparison of lifespans of historic populations emphasizing especially dietary and geographic factors

An analysis between 1268-2022

PhD thesis

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Budapest

2025

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List of abbreviations

GDP	Gross Domestic Product
SIRT-1	Sirtuin 1
Nrf2	Nuclear factor erythroid 2-related factor
BC	Before Christ
WHO	World Health Organization
RR	Rate Ratio
95% CI	95% Confidence Interval
IQR	Interquartile Range
AD	Anno Domini

1 Introduction

1.1 Life expectancy and factors shaping it

In Europe, life expectancy at birth is overall high compared to other parts of the world, but certain national and regional differences can be observed here too. In 2020, the highest ones in Europe were registered in Switzerland (83.1 years) and Norway (83.3 years), while the lowest ones in Bulgaria (73.6 years) and Romania (74.2 years) (1). When focusing on European regions instead of individual countries, the Epirus region of Greece (83.8 years), the Balearic Islands of Spain (83.9 years), and French Corsica (84 years) have the highest life expectancy, while the lowest one can be observed in the North-Western Region of Bulgaria (72.1 years) (1).

Life expectancy is influenced by several factors, one of the most significant being a country's level of development, which is often measured by its gross domestic product (GDP). Even though a higher GDP often correlates with higher life expectancy (2), it is noteworthy to mention that this relationship is not necessarily linear. For example, in both the Netherlands and Greece life expectancy at birth is 81.4 years, yet Greece's GDP is only half of the Netherlands' (3, 4). The same phenomenon is observed when comparing Germany to Portugal (3, 4).

A possible explanation to this phenomenon may reside in national differences regarding certain lifestyle factors. Among lifestyle factors, tobacco **smoking** is one of the most significant risk factor to health (5). According to Eurostat data 2019, Bulgaria had the highest percentage of daily smokers (people above age 15), at 28.7%, followed by Greece at 23.6%, Latvia at 22.1%, Germany at 21.9%, and Croatia at 21.8%. In contrast, Sweden reported the lowest smoking prevalence, at 6.4%, followed by Finland at 9.9%, Luxembourg at 10.5%, and Portugal at 11.5% (6).

Physical activity is another lifestyle factor that has a strong correlation with life expectancy. In 2022, a survey conducted by the European Commission revealed that Finland (71%), Luxembourg (63%), and the Netherlands (60%) were the countries with the highest levels of physical activity, in contrast with Portugal (73%), Greece (68%), and Poland (65%) that reported the highest levels of physical inactivity (7).

The data show that Northwestern Europe generally enjoys better longevity outcomes. However, despite its lower GDP per capita, higher smoking rates, and less frequent physical activity, Southern countries like Greece are still competitive with

Northern and Western regions in terms of life expectancy. This could be partially attributed to differences in cuisine and **diet**, as diet is another important factor that influences life expectancy, and the Mediterranean region follows a unique one.

The Mediterranean diet is a dietary pattern typically practiced in countries bordering the Mediterranean Sea, including Spain, Italy, and Greece in Europe (8). The Mediterranean diet is distinguished by its emphasis on abundant intake of fruits, vegetables, whole grains, legumes, nuts, and olive oil (9). It also includes moderate consumption of fish and seafood, limited to moderate consumption of dairy products, and minimal intake of red meat and processed foods (9).

The Mediterranean diet has been extensively researched for its potential health benefits in slowing down aging and lowering the risk of age-related chronic diseases (8, 10), and may partially explain the relatively high life expectancy observed in Greece, Italy, and the broader Mediterranean area (8, 10).

An increasing body of evidence suggests that specific components of the Mediterranean diet have diverse anti-aging effects, as demonstrated in both preclinical and clinical studies. Resveratrol, a polyphenolic compound found in grapes, red wine, and various berries, exhibits anti-inflammatory, antioxidant, and anticancer properties (11-27). Resveratrol may also contribute to longevity by activating specific enzymes and transcription factors (such as SIRT-1 (28), and Nrf2 (29, 30)) that regulate cellular and molecular processes associated with aging. Apart from resveratrol, various other compounds abundantly found in the Mediterranean diet have demonstrated notable anti-aging properties. One example is hydroxytyrosol (31-34), which is abundant in extra virgin olive oil, a staple ingredient in the Mediterranean diet. Hydroxytyrosol is known for its potent antioxidant effects, which can potentially safeguard against oxidative stress and inflammation. Furthermore, flavonoids like quercetin, which is highly abundant in onions, apples, berries, citrus fruits, leafy green vegetables, tomatoes, and broccoli, have also demonstrated strong antioxidant and anti-inflammatory properties. These qualities may all contribute to the anti-aging benefits associated with the Mediterranean diet (35-37).

Based on data from 2019, countries like Italy, Spain, and Greece often report high fruit and vegetable consumption, with over 75% of the population consuming these goods regularly, meanwhile countries like Latvia and Romania reported the lowest rates, below 50% (38). This may partially explain the higher life expectancy found in Mediterranean countries hence that often have a relatively lower GDP per capita, higher prevalence of smoking, and higher rates of physical inactivity.

Even though the aforementioned factors shape the present life expectancy in Europe, it is also interesting to observe how life expectancy changed throughout history and what factors influenced this change historically. In prehistoric times, life expectancy was estimated at around 30 years (39) and increased only by approximately 10 years across antiquity until the onset of Medieval Period (5^{th} – 15^{th} century) (40, 41). During this period, life expectancy was estimated at 40 years of age, and this did not increase significantly up until the 18^{th} –19^{th} century (40, 41). In the following section, we will provide an overview about important events and advancements in the field of medicine that greatly shaped the life expectancy of Europe. Since the statistically analyses of the present thesis begin with the Black Death, our overview will begin with this catastrophic event.

1.2 Important events and medical advancements that affected life expectancy

The increase of life expectancy was not always linear throughout history and certain events even contributed to its decrease, for instance the Black Death (1346-1353). This epidemic was responsible for the extinction of a significant part of Europe's population, leaving a notable impact on the population's health and longevity (42). Furthermore, the long-term effects also led to significant social and economic transformations, including changes in the labor force, food availability, and more.(43).

During the Middle Ages (5^{th} –15^{th} century), European medical knowledge was primarily based on the works of Hippocrates (460-370 BC) and Galen (129-199). This knowledge was later expanded by the contributions of Avicenna (Ibn Sina) (980-1037) (44). The flourishing Renaissance era (14^{th} – 17^{th} century) and the Early Modern Period (16^{th} – 18^{th} century) were rich and fruitful times for humankind in terms of development and medical knowledge (45).

During the Renaissance, scientists began questioning the medical knowledge of antiquity and supplemented the medical canon with new discoveries. For instance, Andreas Vesalius (1514–1564) published his work *De Humani Corporis Fabrica* in 1543, while William Harvey (1578–1657) discovered the circulation of blood and the role of the heart as a pump, publishing his groundbreaking work *De Motu Cordis* in 1628 (45). Ambroise Paré (1510-1590) also added a pioneer discovery to medicine in the field surgery techniques and discovered the use of ligatures to stop bleeding during amputations, which was also a significant innovation in his time (45). These discoveries facilitated a better understanding of the human body, and helped physicians improve their knowledge and treatments.

The Industrial Revolution (18th – 19th century) brought a new level of development. Urbanization and technological advancements in all areas significantly transformed the population and changed the economic and social aspects of life (43). The rapidly growing populations and urbanization resulted in crowded housing conditions, which led to an increase in cases of infectious diseases, such as cholera and typhoid fever (46). However, these challenges also facilitated developments in public health and led to John Snow's (1813–1858) discovery, which helped to understand and control the spread of cholera (47). As a result of this, the establishment of sewage systems and the development of water main systems, along with public health policies, greatly influenced the quality of life and mortality rates in urbanized environments (48). Medical discoveries also brought significant innovations such as Edward Jenner's (1749-1823) new vaccination technique instead of variolation (49), Joseph Lister’s (1827-1912) use of carbolic acid in antiseptic surgeries, and Louis Pasteur's (1822-1895) and Robert Koch’s (1843-1910) germ theory, (50). Together, these advancements and discoveries all contributed to a gradual increase of life expectancy as well.

Breakthrough discoveries continued into the late 19th and early 20th centuries, marking a golden age of scientific advancement and almost doubling of life expectancy. Wilhelm Conrad Roentgen (1845-1923) discovered X-rays in 1895 (51), which became essential for medical diagnosis. Alexander Fleming (1881-1955) discovered penicillin in 1928, revolutionizing the treatment of bacterial infections (52). The World Wars of the 20th century led to significant population decreases and economic instability. However, they also spurred notable medical advancements (53). Moreover, prosperity after the second World War led European countries to become welfare states, providing citizens with affordable access to healthcare, education, and social security (53). These improvements all had long-term positive effects on public health and longevity of the population (53, 54). The discovery of the DNA structure by James Watson (1928-), Francis Crick (1916-2004), and Rosalind Franklin (1920-1958) in 1953 marked a brand new level in medicine, opening up fields such as genetic research and biotechnology (55). Establishing the World Health Organization (WHO) in 1948 advanced the field of public health (54). Incidence of polio, measles, mumps, rubella, and other infectious diseases decreased as a result of vaccine development (54). Thanks to these efforts, smallpox was also eradicated in 1977 through global vaccination campaigns (54). At the end of the 20th century, the development of Magnetic Resonance Imaging and Computed Tomography scans also revolutionized medical imaging and recognizing diseases (56).

In the 21st century, mankind continues to experience improvements in healthcare, technology, and social policies, which continuously contribute to a gradual and steady increase of life expectancy (53).

1.3 Historic changes in nutrition

1.3.1 Regional differences

As mentioned before, a region's diet greatly affects the life expectancy of a country. Over the centuries, nutrition also changed significantly.

In **Southern Europe**, even in medieval times, the cultivation of olives and viticulture has always been important (57). The Arab Agricultural Revolution, part of the Islamic Golden Age from the 8th to the 13th centuries, introduced significant advancements in agriculture, which had a lasting impact on the Iberian Peninsula. During this period, many new crops were brought to the region, including sugar cane, rice, figs, and citrus fruits. These crops became integral to local agriculture and continued to thrive even after the Reconquista (58). The dry summers of the region limited the availability of animal feed, thus sheep and goats were the main farm animals along with seafood thanks to the proximity of the Mediterranean sea (57).

In the Middle Ages, **Central Europe** had a very different natural geography characterized by a temperate climate and vast, seemingly endless forests. These deciduous forests, dominated by oak and beech trees, created favorable conditions for sustenance. The nutrient-rich humus soils supported robust cereal production, and the temperate climate provided an ideal environment for livestock farming (59). In addition, animal husbandry, especially cattle farming, provided a large amount of milk for everyday meals, which was used to make cheese and butter (60). Producing butter and cheese was particularly important on monastic estates, as monastic rules allowed the consumption of only moderate quantities of meat (60). Butter was mainly used for baking and cooking in contrast to Southern Europe, where olive oil was more commonly used (60).

In Medieval **Western Europe**, animal husbandry was the mainstay of the agricultural economy, and meat was considered as one of the most important foods (61). According to some estimates a person consumed at least 100 kilograms of meat per year on average (62), which is much higher than the yearly per capita consumption of 69.8 kg in Europe according to data form 2018 (63). In addition to livestock farming, agriculture in Western Europe was also practiced in the Middle Ages in forest clearings and along river banks (64). In the West, cattle farming created large dairy farms providing plenty of meat for royal courts and feasts (65). Fish from the North and Baltic Seas, especially herring and cod, played a major role in the food supply of the poorer social classes of medieval Western Europe. Around the 14th century, the Dutch fisherman Willem Beukelszoon (?-1397) devised a process whereby fishing boats set sail with empty barrels and salt so that the herring that was gutted and cleaned on board could be directly salted as well, making it a cheap mass meal for the whole of Europe (66). This innovation later became one of the cornerstone of the Hanseatic economy (67).

In **Northern Europe**, the harsh weather and living conditions made very few areas suitable for farming (68). The western half of the Scandinavian peninsula is dominated by mountain ranges in many places with altitudes surpassing 2000 meters (69). The scarce arable land was mainly used for barley and millet, while pastures were mainly used for cattle and sheep. Agriculture was not the only way to make a living; in addition to farming and animal husbandry, hunting and fishing were also alternatives (70). Poorer classes made their living from fishing in the Norwegian coast, while the ruling classes hunted for moose, deer, roe deer, bears, and smaller animals in the forests (71). The climate in the Swedish areas is much colder than in Norway, with short summers and long and cold winters, and unfortunately there was very little land suitable for agriculture, so livestock farming was the basis of sustenance (mainly cattle) (72). Hunting played a big role in the royal circles too, even for specialties such as reindeer, caribou, or even whales, polar bears, and seals. Sustenance was based on animal husbandry and partly on hunting and fishing (70).

1.3.2 The table of the European aristocracy

The cuisine favored by European nobility of the time was different than that of the general population's diet and may have remained relatively stable over time, influenced more by contemporary trends and trade than the availability of food. The capacity to consume large quantities of food and drinks was considered a display of strength and valor with meat being especially esteemed among the nobility (73). It was typical to serve and carve whole roasted animals directly at the table just before they were eaten and smaller animals such as lambs and rabbits, along with ingredients like eggs, mushrooms, and vegetables, were frequently stuffed inside larger animals like deer, cattle, or pigs, and then roasted whole (74). Over the centuries, new ingredients and dishes, such as sugar and later exotic goods followed. The quality and quantity of food became a symbol of social status and were used as tools of power and diplomacy, not just as a source of pleasure (75). According to John Dickie the culinary preferences of royalty across Europe remained relatively uniform during this period too (76). Danielle De Vooght claims "fashions spread from court to court through their continuing contact with each other" (77), supporting the assertion that the food preferences of courts were probably more uniform than different, marked by abundant consumption of meat, extravagant goods, and both fermented beverages and strong distilled spirits.

To understand the diet of the nobility, the most valuable sources are accounts of feasts and cookbooks that feature recipes from the upper classes (76). Based on the recipes of one of the earliest post-antiquity cookbooks from the mid-1300s, *The Book for Cook* (*Libro per cuoco*) by an anonymous author, we can assume that the nobility in Venice enjoyed a wide access to a diverse array of luxurious spices. This is not surprising, since Venice was one of the central trade hubs of the time in Europe (78). For instance, recipe LXXIII in *The Book for Cook* details a blend of cinnamon, pepper, cloves, ginger, and saffron, which was used as a pre-prepared spice mixture in other recipes (78). The extensive use of spices and herbs can be attributed to two main factors: firstly, their high cost made them a symbol of social status, and secondly, they were also consumed as medicines influenced by the humoral pathology concept of the era (76, 79). Recipe collections from the fourteenth and fifteenth centuries in Western Europe and Italy shared many similarities especially the widespread cultural practice of adding spices into a wide range of dishes (76). The nobility indulged in large quantities of meat seasoned with exotic spices, accompanied by white bread and delicacies such as almonds, dates, and other luxury items (76).

From the Age of exploration and geographic discoveries (late 15th century), the nobility reduced their consumption of herbs and spices, as accessible spices like black pepper lost their status-symbolizing significance. Instead, colonial goods such as coffee, tea, tobacco, chocolate, and strong, distilled and flavored spirit beverages became the new luxurious commodities. Moreover, rulers began to include a diverse selection of fresh vegetables and fruits like artichokes, peas, beans, bell peppers on their dining tables (43). Later, thanks to the explorations and agricultural advancements, potato, tomato, and corn also appeared on the table from the eighteenth century (76). Frank Spooner conducted a comparison of the dietary habits of nobles with those of the local hospital and found that while the hospital's diet was predominantly cereal based (81% of calories derived from cereals), the Spinola family's diet consisted only of 53% cereals. Additionally, the Spinola family consumed twice as much meat and three times as much dairy products as in the hospital (43, 80). This could also indicate that the diet of the nobility was different than the diet of the general population with a relatively higher consumption of proteins and fats and a lower consumption of complex carbohydrates, however, this comparison should be approached with caution, as medical dietary considerations played a significant role for the patients in the local hospital. For a long time, diet was a key component of their therapy prior to the introduction of iatrochemistry, and it’s important to note that the average person's diet did not necessarily align with the hospital diet.

During the eighteenth century, there was a noticeable gap between economic progress and population expansion, resulting in intermittent shortages of food and periods of starvation among the general population (43). It required time for production and consumption rates to realign once more. However, due to improvements in animal husbandry and agriculture, the elimination of fallow land, the adoption of crop rotation involving cereals and legumes, and the introduction of new fertilization techniques coupled with the dissemination of new high-yield crops like rice, maize, and potatoes, the threat of a famine crisis was mitigated. Nevertheless, despite the improved security of food supply, it also became more unevenly distributed and stratified socially (43). The diet of the impoverished became more basic and limited as wheat and meat became less accessible and were substituted with corn and potatoes among the commoners. Some information regarding what a Hungarian Benedictine monks consumed in the 18th century supports these tendencies, but it has to be mentioned that monks also consumed not only fish (8, 10, 81) but also beef and wild meat (82). We also know that beans, lentils, peas, prunes, strawberries, oats and wheat were also often consumed in the community (83, 84). Sugar first appeared around 1745, before that only honey was available as sweetening substance (85, 86). Chestnut, lemon, and olive would also have appeared on special occasions on the table of the Hungarian brothers (87, 88).

By the late nineteenth century, the adoption of new refrigeration and canning methods, alongside advancements in milling techniques that resulted in refined wheat, increased the accessibility of white bread to a broader swath of the population (43). Advancements in technology ultimately enabled broader access to meat and bread, ensuring a more reliable food supply for the general populace, however, the nobility persisted in their preference for sophisticated and extravagant dishes, transforming mealtime into a spectacle centered around social presentation (43). While economic processes had minimal direct impact on the dietary choices of the nobility, they indirectly influenced the food preferences and provisions served at noble tables across the different regions.

2 Objectives

To better understand longevity patterns today, it is also important to analyze the lifespans of people from the past. However it is challenging to find homogenous groups from the past where individuals' lives were properly recorded, including information on their lifestyle, birth, and death (46). There are some exceptional groups in this regard, however, whose entire lives were recorded, for instance the nobility, artists, or religious groups like monks and nuns (89). The latter group's lifestyle was humbler and closer to the average population's, yet still well documented. By focusing on these exclusive groups, we can minimize the possible variability of socioeconomic status, lifestyle, and other factors influencing longevity. Thus, the objectives of the present thesis are as follows:

1. Our **primary objective** is to perform a retrospective study analyzing the differences in the lifespan of European rulers who ruled after the Black Death (1346-1353) until today with special emphasis on differences in survival in-between different geographic areas using the Southern European region as reference where Mediterranean diet was characteristic.

2. Our **secondary objective** is to compare the survival of *Hungarian Benedictine monks* with the lifespan of *Southern European* and *Central and Eastern European rulers*. Like rulers, monks represent a relatively well-documented population whose lifestyle follows a set of standard rules.

3 Methods

3.1 Primary analysis: Survival of rulers by geographic regions

3.1.1 Population of the primary analysis

To collect our data on European rulers, we utilized various online sources, including Encyclopedia Britannica and cross-referenced our population of rulers with the dynastic tables found in Morby's *Dynasties of the World* (2002) (90, 91). We started our data collection with rulers who were already in power by 1354, a year after the end of the devastation of the Black Death (1346–1353), which often caused rulers to succumb to infection (42). Our data collection continued until the last ruler for countries that ceased being a monarchy or until the first ruler still alive if the given country persisted as a monarchy to this day. We limited our analysis to European rulers to maintain consistency of our sample population.

3.1.2 Variables of the primary analysis

We extracted various kinds of information for each ruler, including their sex, birth and death date, age, age of enthronement, duration of ruling, country, and cause of death (natural vs. violent death). The definition of violent death included deaths caused by unexpected events, poisoning, accidents, murders, execution, or war. If we did not have any specific information regarding the cause of death, we assumed a natural death. We coded the residency of each ruler based on where they would have lived at the present day (2023). If a ruler governed in more than one country or moved to another country, their residency was coded according to where they lived the longest. Finally, we classified the countries into the following regions based on the *EuroVoc* Geographical classification: Northern, Western, Southern, Central and Eastern Europe (as shown in **Figure 1**) (92).

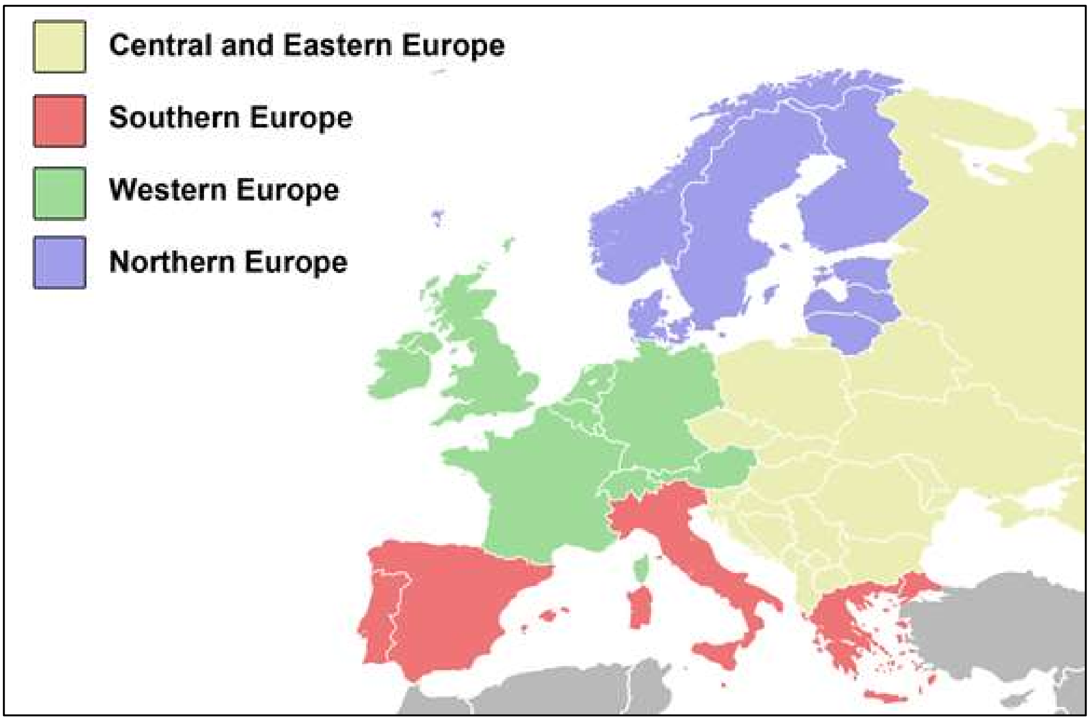

Figure 1. Classification of European sub-regions based on EuroVoc, with country borders representing the divisions as of 2023. Although the European part of Turkey is classified as part of the Southern region, we exclude Turkey from our analysis due to cultural reasons.

3.1.3 Statistical analysis of the primary analysis

Normal distribution of continuous variables was tested with Shapiro-Wilk test. As continuous variables followed a non-normal distribution, Kruskal-Wallis tests were used to compare continuous variables (age, age of enthronement, and duration of rule) among regions. Cox-regression models were created for natural vs. violent death as outcome and age as follow-up. Only those participants were included in the analysis who reached at least the age of 40 years, the approximate life expectancy up until the twentieth century (40, 41). We considered death before age 40 as premature and more likely to be associated to non-natural causes;. Since the Mediterranean diet is often associated with health benefits (9), we used the Southern region as reference in all our analyses.

First, Cox regression models were built including all European rulers who ruled between 1354–2022 and reached the age of at least 40 years. In the regression model, covariates included birth year, sex, and region. Birth year was centered around 1700.

Linear and quadratic time terms were also introduced in the regression models. From the regression models, rate ratios (*RR*s) and 95% confidence intervals were calculated. The rate ratios show how much more likely it is for a comparison group to die of natural death as compared to the reference.

Kaplan-Meier curves were then plotted to depict the differences in survival across regions. The Kaplan-Meier curves show the probability of survival over time, where each step down corresponds to an event, in our case the event of death. The vertical axis represents the survival probability, ranging from 0 to 1, while the horizontal axis shows the time elapsed since the start of the study. The curve remains flat if no events occur and drops when an event is recorded. It is important to note that the Kaplan-Meier curves show each death event, regardless of whether the cause was violent or natural, and include both sexes. In the Cox regression analysis, these variables are adjusted for.

Since life expectancy changed significantly from 1354 to 2022, it may be reasonable to divide the aforementioned period into the following 3 shorter time periods to better capture differences regarding life expectancy:

- 1354–1499: End of the Black Death until the Discovery of Americas
- 1500–1749: The discovery of Americas until the Industrial Revolution
- 1750+: From the Industrial Revolution onwards

Descriptive tables and Cox regression models were built for the three time periods separately, as described above. Kaplan-Meier curves by region were also plotted for these analyses as well. Moreover, Kaplan-Meier curves were also plotted showing how survival changed over the three time periods by region, and how survival of every region compared to each other over the three time periods.

For all analyses, statistical significance was set at $p<0.05$. All statistics were conducted by IBM-SPSS 24. Kaplan-Meier survival curves were constructed using R (“survminer” package).

3.2 Secondary analysis: Survival of Hungarian Benedictine monks and rulers

Similarly to rulers, monks represent a relatively well-documented group of people with recorded data of date of birth and death and a well-defined lifestyle. This is why we decided to run an additional analysis to compare the survival of Hungarian Benedictine monks to Southern European rulers and Central and Eastern European rulers. The reason for the comparison of these three groups is that the monks come from the previously mentioned Central and Eastern European region, making it worthwhile to compare them to the ruling class of the same region. Additionally, we also included the Southern region in the analysis to examine how the survival of monks compared to that of rulers in the Mediterranean region.

Figure 3. The Abbey of Pannonhalma, Hungary (Photograph by: Bálint Madarász, 2022).

3.2.1 Population of the secondary analysis

Data of Hungarian Benedictine monks was obtained from the *Directory of the Order of St. Benedict of Pannonhalma 1802-1986* collected by Pál Berkó and Norbert Legányi (Pannonhalmi Szent Benedek-Rend Névtára 1802-1986) (93) (**Figure 3**). This directory provides information about Hungarian monks who served the order between 1802 and 1986. Since the earliest birth date in this directory is from 1728, we decided to restrict our analyses to also only include rulers born after 1728. Additionally, we also excluded all monks who left the order from our analyses, all rulers whose death was coded as violent death, and finally also all female rulers. We included only the monks born between 1728 and 1850. Although the dataset extends beyond this period, the population becomes less consistent after 1850 due to historical factors, such as world wars and significant emigration.

3.2.2 Variables of the secondary analysis

The following variables were collected for our secondary analysis: birth and death date, age, country, and residency of monks (and rulers).

3.2.3 Statistical analysis of the secondary analysis

Normal distribution of continuous variables was tested with Shapiro-Wilk test. As continuous variables followed a non-normal distribution, Kruskal-Wallis tests were used to compare continuous variables (age). In our descriptive analysis, age was presented as years and interquartile range. Cox regression analyses were constructed similarly to previous analyses by including linear and quadratic time terms for birth year for only monks and rulers who reached the age of at least 40 years. From the regression models, rate ratios (*RR*s) and 95% confidence intervals were extracted. Kaplan-Meier curves were also plotted for this analysis as well. Statistical significance was set at $p<0.05$. All statistics were conducted by IBM-SPSS 24. Kaplan-Meier survival curves were constructed using R (“survminer” package).

4 Results

4.1 Results of our analyses examining the survival of European rulers by regions

A total of 989 rulers were identified in the database. We decided to exclude Popes (n = 59) and Doges of Venice (n = 67) from our analysis, since they were significantly older when first elected, and thus their inclusion would have led to bias, as seen by the following results. The Popes and Doges of Venice stood out with a median age of enthronement at 64 and 70, and a median age of death of 70 and 77, respectively, indicating significantly better survival rates than rulers in other regions. For comparison, the median age of enthronement and median age for rest of the rulers in the Southern region was 27 and 57, respectively (**Table 1.** and **Fig**. **2.**). The Cox regression analyses reveals that the risk of the event occurring (death) among the popes is 61% lower and 73% lower among the Doges as compared to the Southern region. This is corroborated by the Kaplan-Meier survival curves.

Table 1. Descriptive data and Cox regression analysis for rulers of the Southern Region, popes, and Doges of Venice (89)

Group	Participants n (%)	Age of death* years (IQR)	Age of enthronement* years (IQR)	Duration of rule years (IQR)	Cox regression analysis RR (95% CI)
Rulers of the Southern Region	166 (56.8)	57.00 (49.75–66.00)	27.00 (18.00–37.25)	27.00 (13.00–38.00)	ref.
Popes	59 (20.2)	70.00 (67.00–81.00)	64.00 (55.00–68.00)	9 (5.00–15.00)	0.39 (0.28–0.55)*
Doges of Venice	67 (22.9)	77.00 (70.00–82.00)	70.00 (65.00–75.00)	9 (5.00–15.00)	0.27 (0.20–0.38)*

Kruskal-Wallis tests were used to compare continuous variables among regions. Rate ratios and 95% Confidence Intervals were calculated from Cox-regression models.

*p<0.05

Abbreviation: 95% CI: 95% Confidence Interval; IQR: Interquartile Range, ref.: reference; RR: Rate Ratio

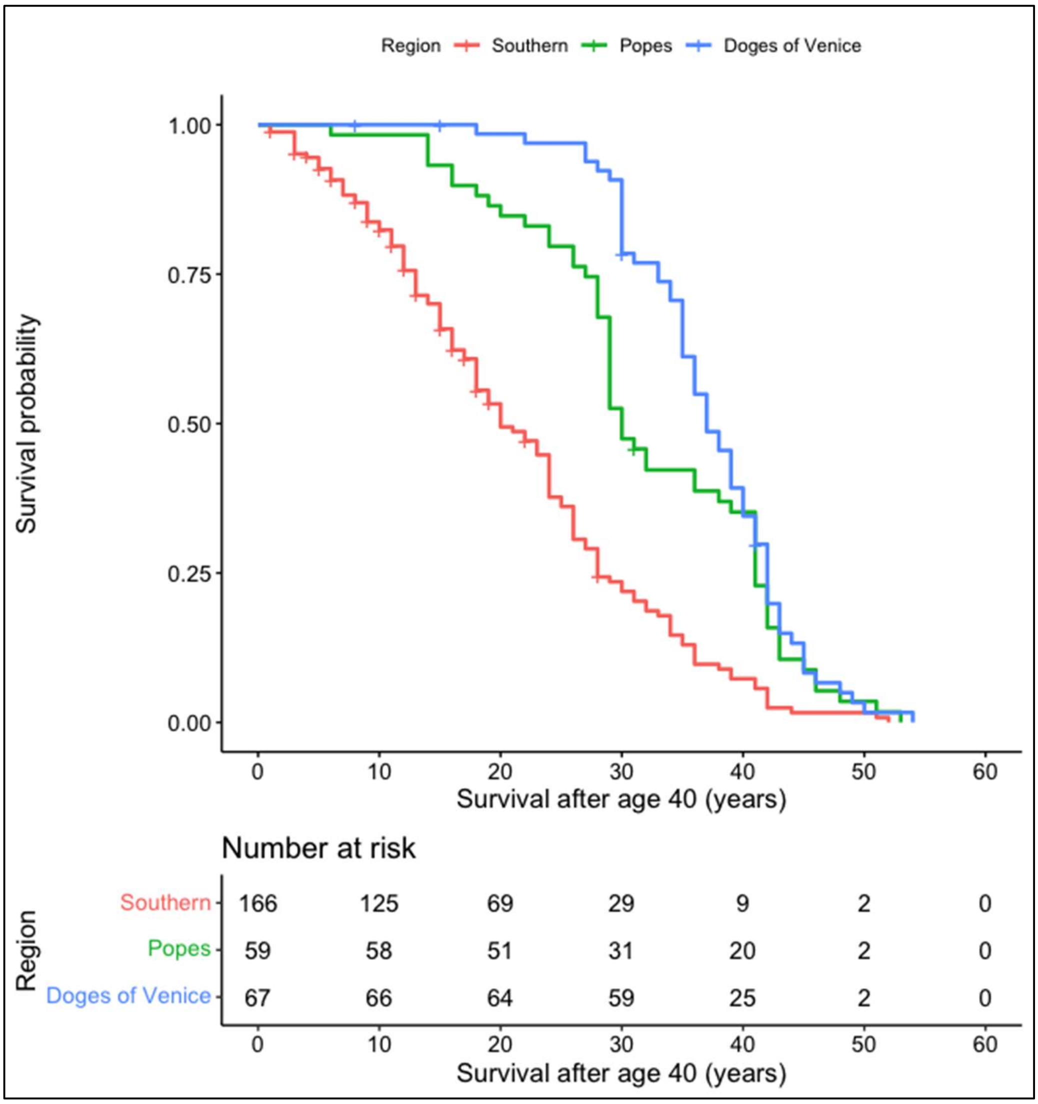

Figure 2. Kaplan-Meier survival curves for rulers in the Southern region, as well as for popes and Doges of Venice who reached the age of at least 40 years.

After the exclusion of Popes and Doges of Venice, 863 European rulers were left. A total of 190 were excluded because they died before the age of 40, resulting in a final sample of 673 rulers from the four European regions: Northern (*n*=57), Eastern and Central (*n*=76), Western (*n*=377), and Southern (*n*=166). A total of 582 rulers died of natural causes, while 91 were recorded as violent death. The earliest born ruler in our sample was Luigi Gonzaga, born in 1268, and the latest ruler added was Elizabeth II, who passed away in 2022. The majority of the rulers in our sample were male (94%). We observed significant differences in age of death of rulers among the regions, but age of enthronement and duration of rule were similar across regions **(Table 2**). It is important to note that based on our database there were 18 Southern rulers, who were potentially assassinated by poison, meanwhile only 4 potential cases in the Central and Eastern European region, 3 in the Northern, and 7 in the Western Region.

When examining our Cox regression models that included all study participants between 1354 and 2022, we found that that hazards did not differ significantly among geographic regions (**Table 2**), and these findings were supported by the Kaplan-Meier curves (**Fig**. **4**).

Table 2. Descriptive data and Cox regression analysis for rulers who ate least reached the age of 40 years by region

Region	Participants n (%)	Male n (%)	Age of death* years (IQR)	Age of enthronement years (IQR)	Duration of rule years (IQR)	Cox regression analysis RR (95% CI)
Southern	166 (24.7)	153 (92.2)	57.00 (49.75–66.00)	27.00 (18.00–37.25)	27.00 (13.00–38.00)	ref.
Western	377 (56.0)	359 (95.2)	62.00 (53.00–71.00)	29.00 (20.00–41.00)	27.00 (16.50–39.00)	0.86 (0.70–1.06)
Northern	54 (8.0)	51 (94.4)	62.00 (55.00–75.50)	31.50 (23.00–45.75)	27.00 (15.00–37.00)	0.73 (0.52–1.03)
Central and Eastern	76 (11.3)	72 (94.7)	57.00 (49.00–66.00)	31.50 (21.00–38.75)	24.00 (13.00–37.00)	1.07 (0.77–1.46)

Kruskal-Wallis tests were used to compare continuous variables among regions. Rate ratios and 95% Confidence Intervals were calculated from Cox-regression models.

*$p<0.05$

Abbreviation: 95% CI: 95% Confidence Interval; IQR: Interquartile Range, ref.: reference; RR: Rate Ratio

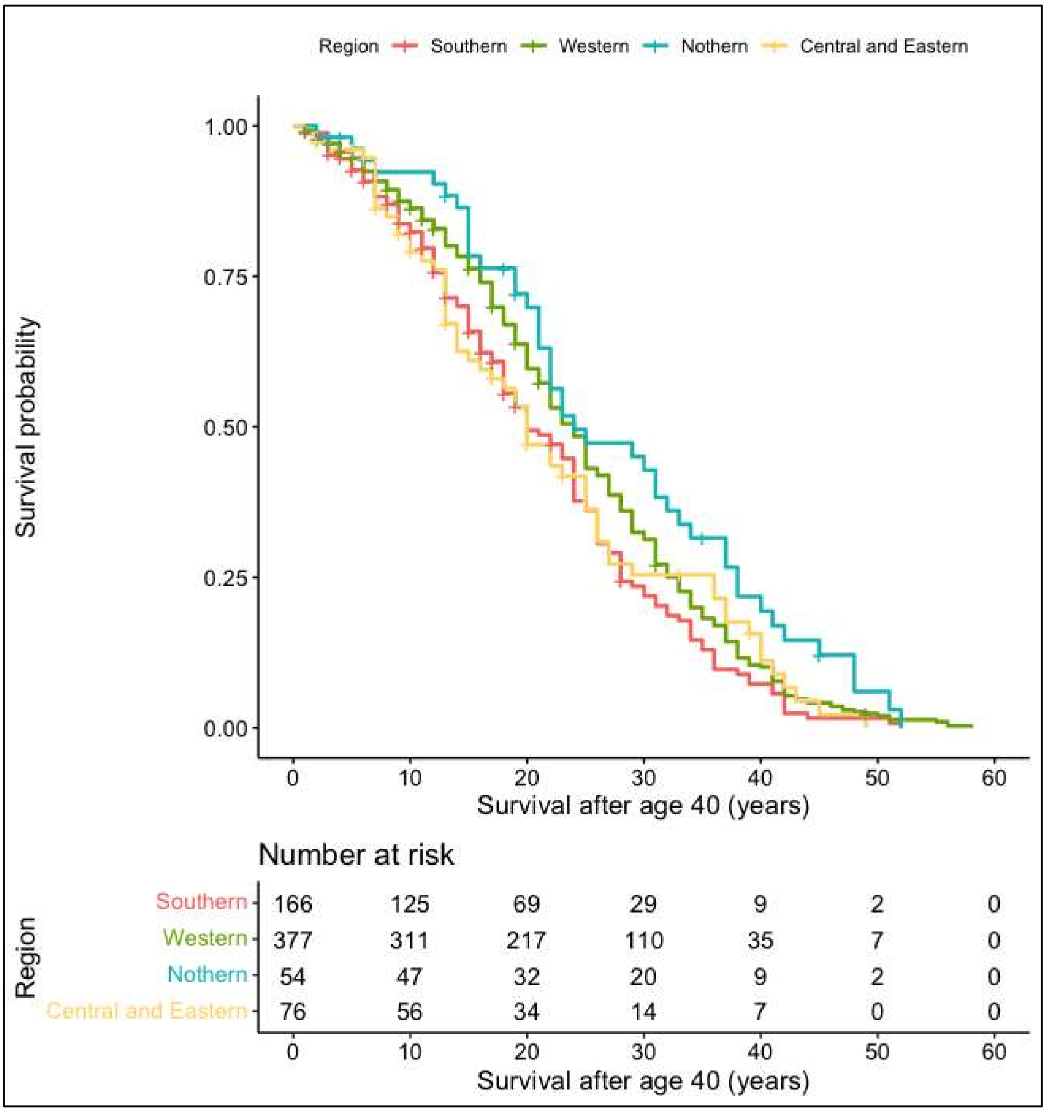

Figure 4. Kaplan-Meier survival curves for rulers who reached the age of at least 40 years by regions between 1354–2022.

When we stratified our analysis by the three time periods (1354–1499, 1500–1749, 1750+), we found that age of rulers and age of enthronement were similar across regions from 1354 to 1749 but differed significantly after 1750. Duration of rule was similar across the three periods. Within the Western and Northern regions, age of rulers and age of enthronement significantly increased over time, while they remained stable in the Southern region and Central and Eastern European region. Duration of rule significantly decreased over time in the Southern and Western regions but remained stable in the other two regions **(Table 3**).

Our Cox regression analyses show that from 1354 to 1499, the Northern region had significantly better survival compared to the Southern region (*RR*: 0.48; 95% *CI*: 0.28–0.84). Between 1500 and 1749, the survival of rulers was overall similar. After 1750, the Western (*RR*: 0.44; 95% *CI*: 0.28–0.68), Northern (*RR*: 0.39; 95% *CI*: 0.20–0.76), and Central and Eastern European (*RR*: 0.52; 95% *CI*: 0.28-0.98) regions all exhibited better survival than the Southern region (**Table 4**). These findings are supported by the Kaplan-Meier curves (**Figure 5-7)**.

When we examined each region separately, we found that survival of rulers in the Southern region was stable over the three periods. In the Northern region, survival initially declined between 1500 and 1749 and then increased, while in both the Western and Central and Eastern European regions, survival increased prominently only after 1750 (**Figure 8-11**).

Table 3. Descriptive statistics by *EuroVoc* regions through different periods

Region	Age of death, years (IQR)			
	1354–1499	1500–1749	1750+	Heterogeneity p-value
Southern	56.00 (49.00–64.00)	60.00 (50.00–68.00)	58.00 (51.25–68.00)	0.399
Western	57.00 (50.00–66.50)	60.00 (51.00–68.00)	71.00 (65.50–79.50)	<0.001
Northern	64.00 (58.00–77.50)	55.50 (46.75–61.00)	73.00 (60.00–88.00)	0.001
Central and Eastern	57.50 (50.25–61.50)	54.50 (50.50–65.75)	59.50 (47.25–77.00)	0.855
Heterogeneity p-value	0.013	0.191	<0.001	
Region	**Age of enthronement, years (IQR)**			
	1354–1499	**1500–1749**	**1750+**	**Heterogeneity p-value**
Southern	29.00 (18.00–38.50)	25.00 (17.50–37.50)	26.50 (19.25–37.25)	0.731
Western	25.00 (17.50–34.00)	27.00 (18.00–42.00)	40.00 (28.00–49.00)	<0.001
Northern	30.00 (17.50–46.00)	26.00 (17.00–31.25)	45.00 (40.00–53.00)	0.003
Central and Eastern	23.00 (16.50–37.75)	32.50 (22.25–40.50)	32.00 (22.50–38.50)	0.242
Heterogeneity p-value	0.377	0.530	<0.001	
Region	**Duration of rule, years (IQR)**			
	1354–1499	**1500–1749**	**1750+**	**Heterogeneity p-value**
Southern	29.00 (13.50–37.50)	33.00 (17.00–43.00)	18.50 (6.00–29.75)	0.006
Western	30.00 (21.00–39.00)	29.00 (16.00–43.00)	22.00 (12.50–33.00)	0.009
Northern	33.00 (14.00–39.50)	23.00 (19.00–32.50)	25.00 (15.00–35.00)	0.504
Central and Eastern	34.00 (19.50–40.00)	23.00 (10.25–36.25)	21.50 (11.50–26.00)	0.122
Heterogeneity p-value	0.381	0.338	0.373	

Kruskal-Wallis tests were used to compare continuous variables among regions.

*p<0.05

Abbreviation: IQR: interquartile range

Table 4: Result of the Cox regression models by different periods and regions

Region	Participants n (%)	Male n (%)	Cox regression analysis RR (95% CI)
	1354–1499		
Southern	77 (29.3)	68 (88.3)	ref.
Western	141 (53.6)	135 (95.7)	0.96 (0.70–1.31)
Northern	21 (8.0)	20 (95.2)	0.48 (0.28–0.84)*
Central and Eastern	24 (9.1)	24 (100)	0.83 (0.48–1.43)
	1500–1749		
Southern	53 (21.5)	51 (96.2)	ref.
Western	147 (59.8)	141 (95.9)	1.06 (0.75–1.49)
Northern	18 (7.3)	16 (88.9)	1.45 (0.77–2.72)
Central and Eastern	28 (11.4)	24 (85.7)	1.53 (0.94–2.51)
	1750+		
Southern	36 (22.0)	34 (94.4)	ref.
Western	89 (54.3)	83 (93.3)	0.44 (0.28–0.68)*
Northern	15 (9.1)	15 (100)	0.39 (0.20–0.76)*
Central and Eastern	24 (14.6)	24 (100)	0.52 (0.28–0.98)*

Rate ratios and 95% confidence intervals were calculated from Cox-regression models.,

*p<0.05

Abbreviation: 95% CI: 95% Confidence Interval; IQR: Interquartile Range, ref.: reference; RR: Rate Ratio

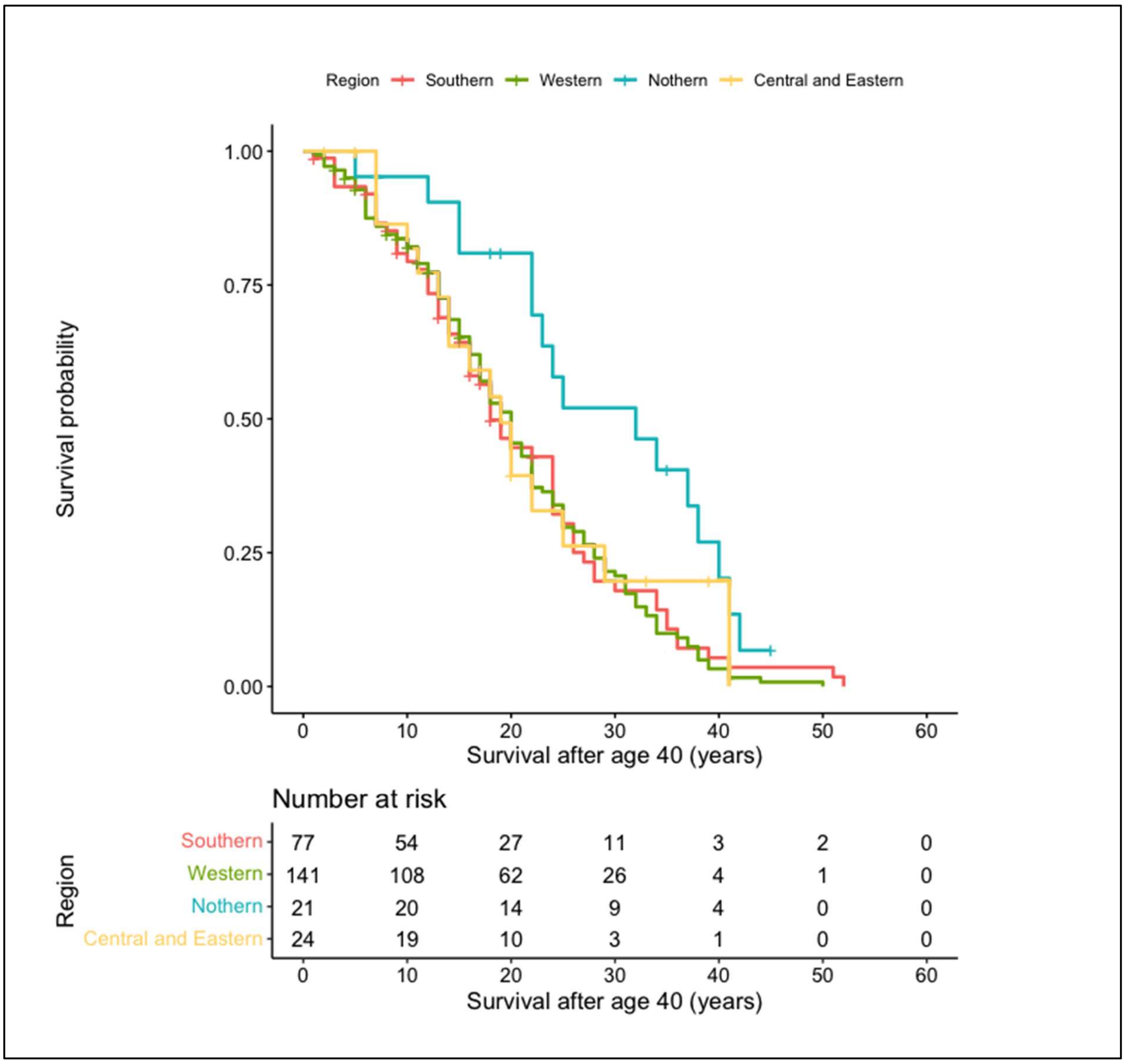

Figure 5. Comparison of Kaplan-Meier survival curves for rulers who reached the age of at least 40 years by regions between 1354–1499

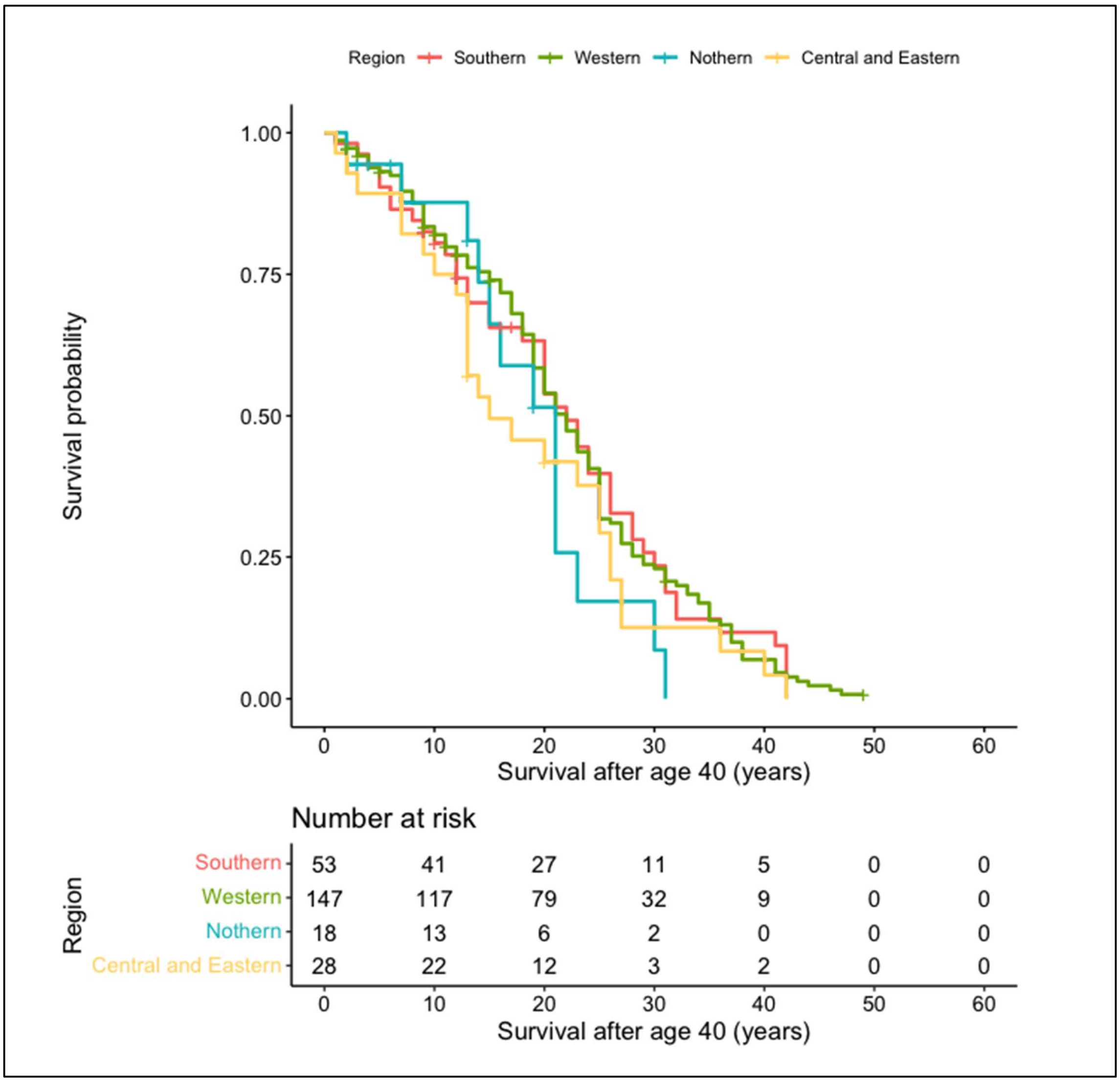

Figure 6. Comparison of Kaplan-Meier survival curves for rulers who reached the age of at least 40 years by regions between 1500–1749

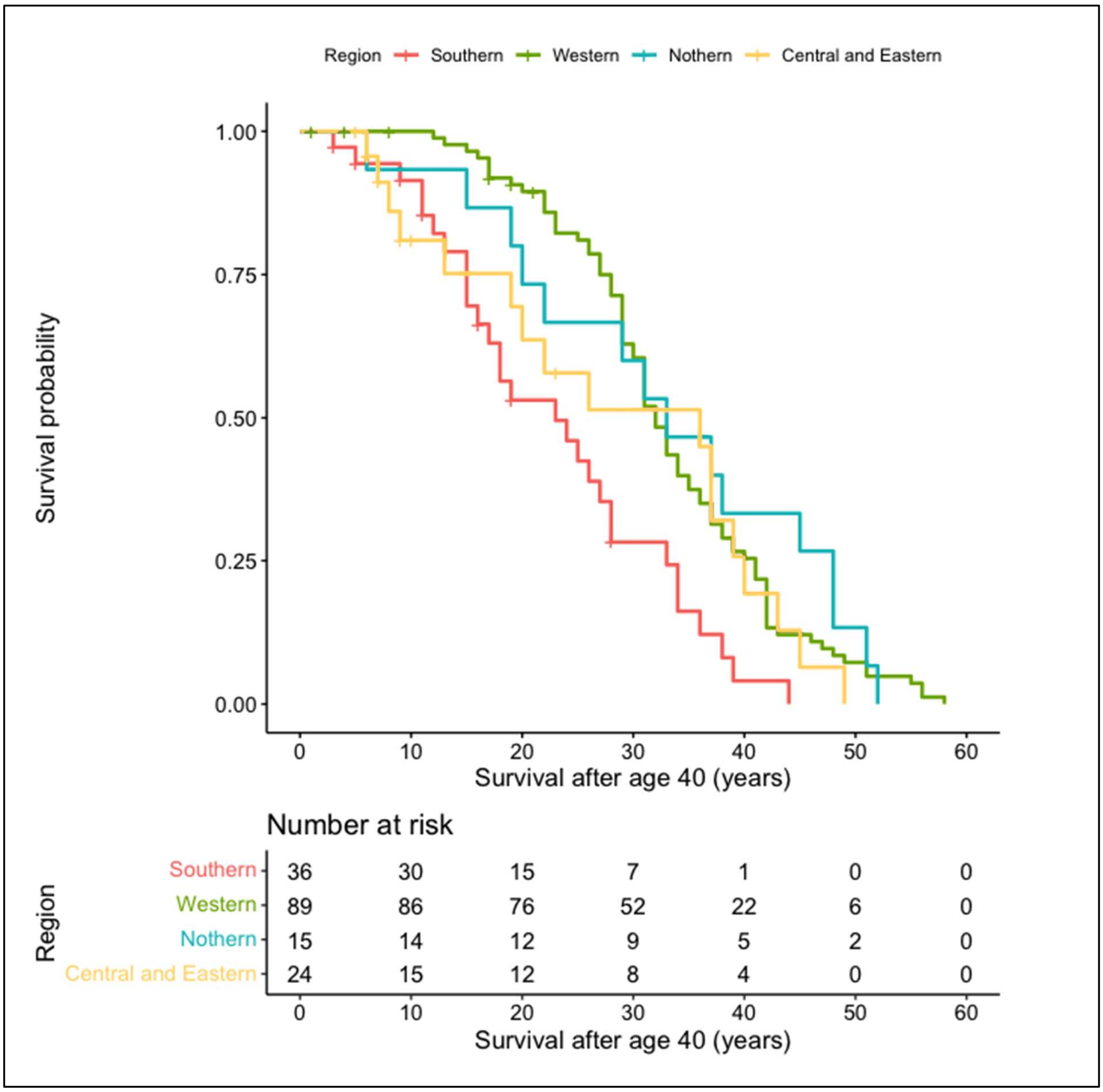

Figure 7. Comparison of Kaplan-Meier survival curves for rulers who reached the age of at least 40 years by regions between 1750–2022

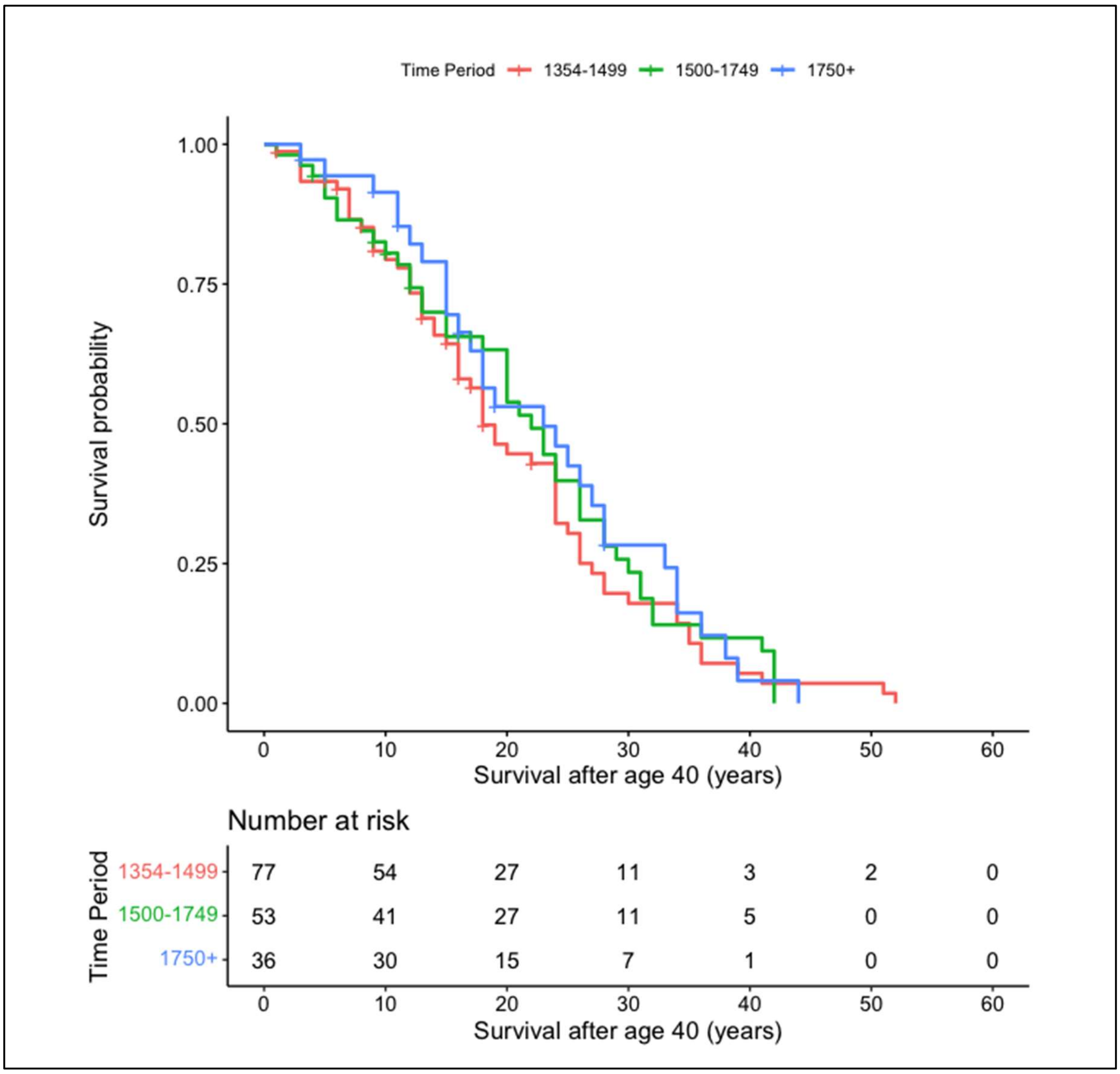

Figure 8. Changes in survival rates for the **Southern European region** over three distinct (1354–1499, 1500–1749, and 1750–2022) time periods for rulers who reached the age of at least 40 years

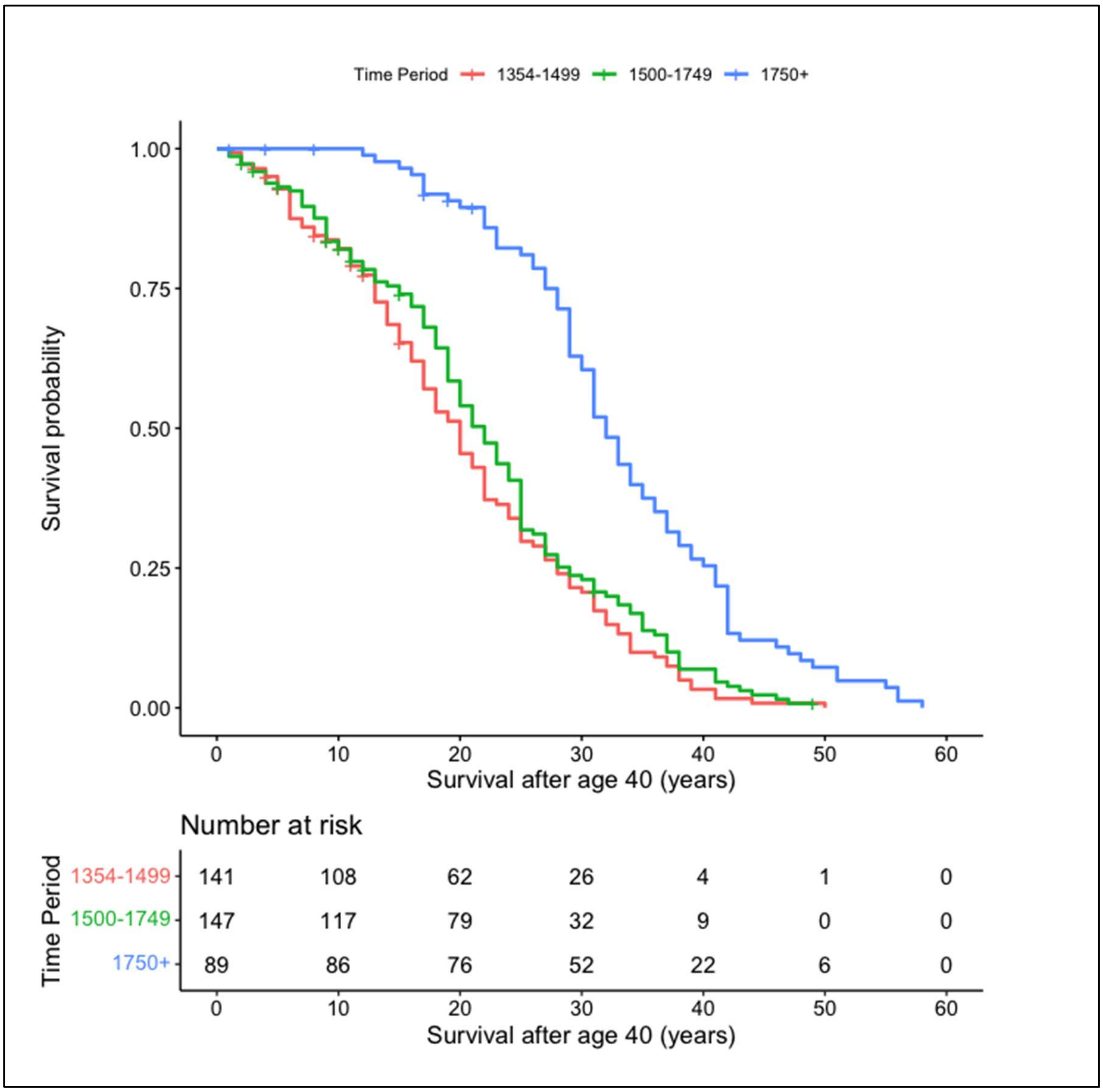

Figure 9. Changes in survival rates for the **Western European region** over three distinct time periods (1354–1499, 1500–1749, and 1750–2022) for rulers who reached the age of at least 40 years

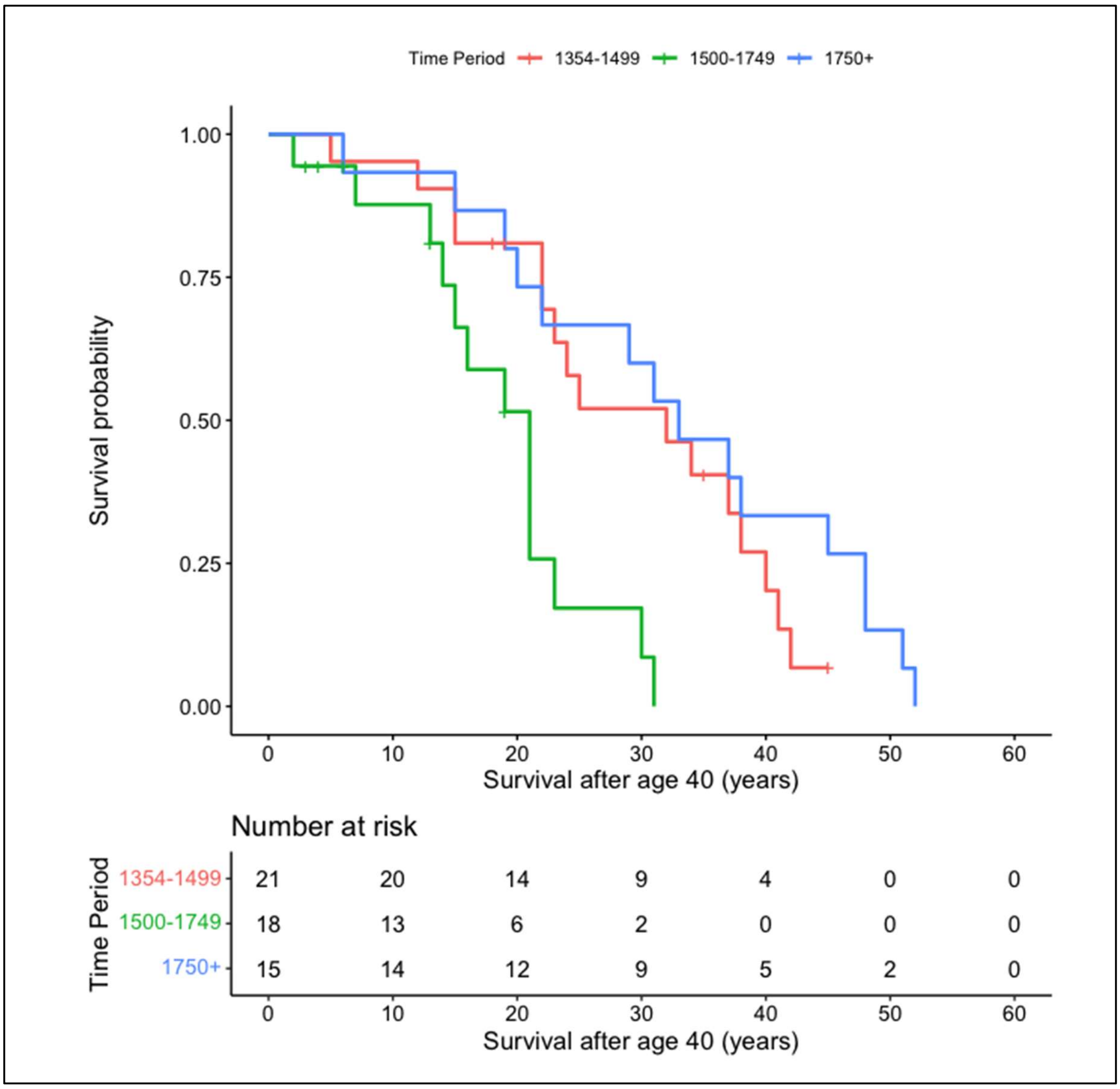

Figure 10. Changes in survival rates for the **Northern region** over three distinct time periods (1354–1499, 1500–1749, and 1750–2022) for rulers who reached the age of at least 40 years

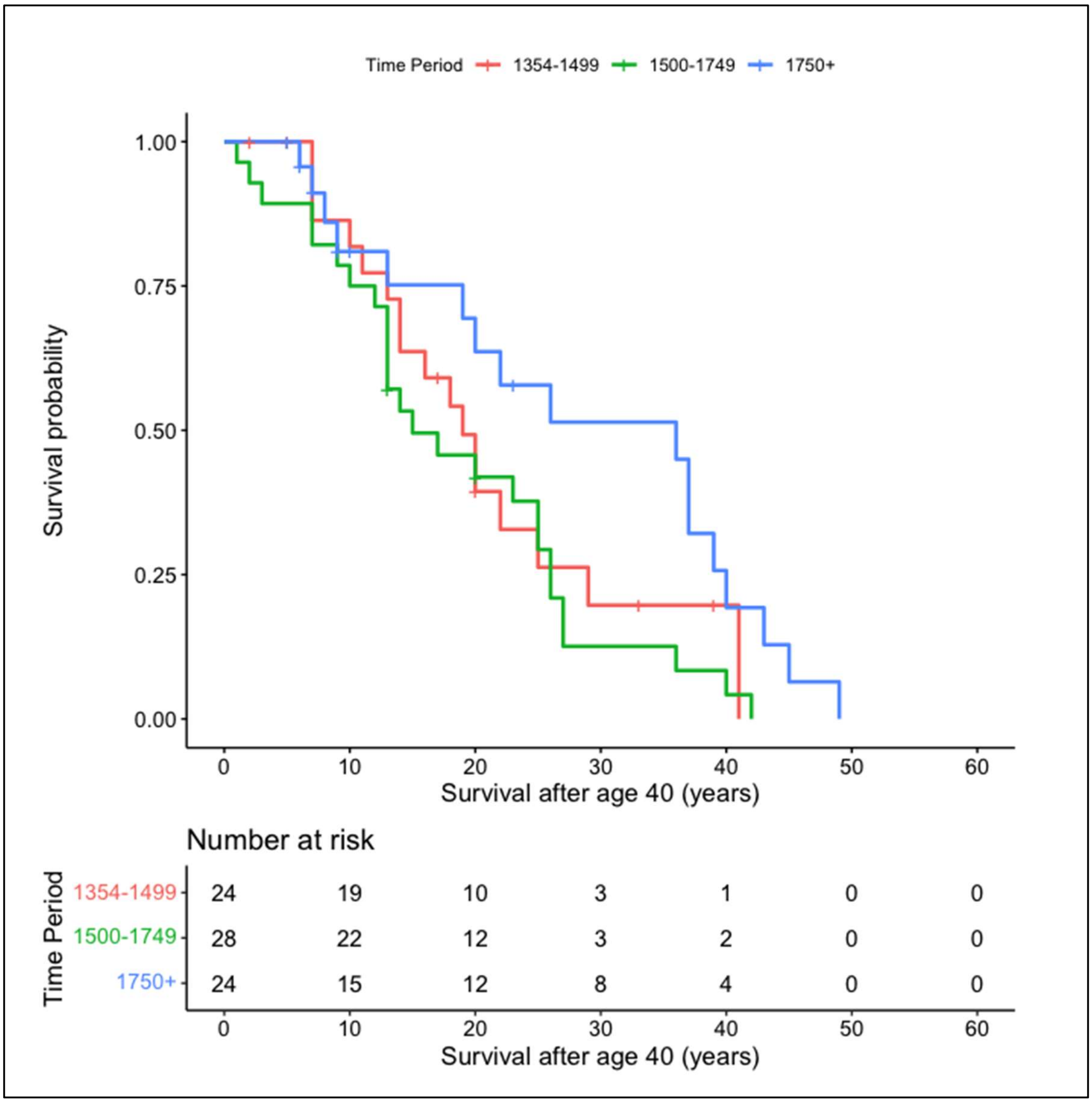

Figure 11. Changes in survival rates for the **Central and Eastern European region** over three distinct time periods (1354–1499, 1500–1749, and 1750–2022) for rulers who reached the age of at least 40 years

4.2 Secondary analysis: Comparing the survival of rulers and monks

In our secondary analysis, we included a total of 883 Benedictine Monks born in different parts of the historic Hungary but died in relatively fewer locations associated with the order's activities (**Figure 12)** between 1728-1850**.**

Figure 12. The most common places of death place of the Hungarian Benedictine monks born between 1728-1850 in our database. (The city names are indicated using the Hungarian names from the analyzed period. In present days: Pozsony is Bratislava, Nagyszombat is Trnava.)

After the exclusion of monks who left the order and did not reach the age of at least 40 years, 318 monks were left along with 34 Southern European rulers and 21 Central and Eastern European rulers. (**Table 5**). The ages of the three groups were similar and did not differ statistically. Our Cox regression analysis of Hungarian and Benedictine monks reveals that compared to monks, Southern rulers had a significantly worse survival (*RR: 1.50, 95% CI:1.02–2.20*), while survival was similar for Central and Eastern European rulers. The Kaplan Meier curves further support these findings (**Figure 13).**

Table 5. Descriptive characteristics and results of Cox regression analysis for the comparison of monks and rulers

Group	Participants n (%)	Age of death years (IQR)	Cox regression analysis RR (95% CI)
Hungarian Benedictine monks	318 (85.3)	64.00 (56.00–70.00)	ref.
Southern European rulers	34 (9.1)	66.00 (56.00–74.25)	1.50 (1.02–2.20)*
Central and Eastern European rulers	21 (5.6)	63.50 (54.50–73.25)	0.99 (0.63–1.56)

Kruskal-Wallis tests were used to compare continuous variables among regions. Rate ratios and 95% Confidence Intervals were calculated from Cox-regression models.

*p<0.05

Abbreviation: 95% CI: 95% Confidence Interval; IQR: Interquartile Range, ref.: reference; RR: Rate Ratio

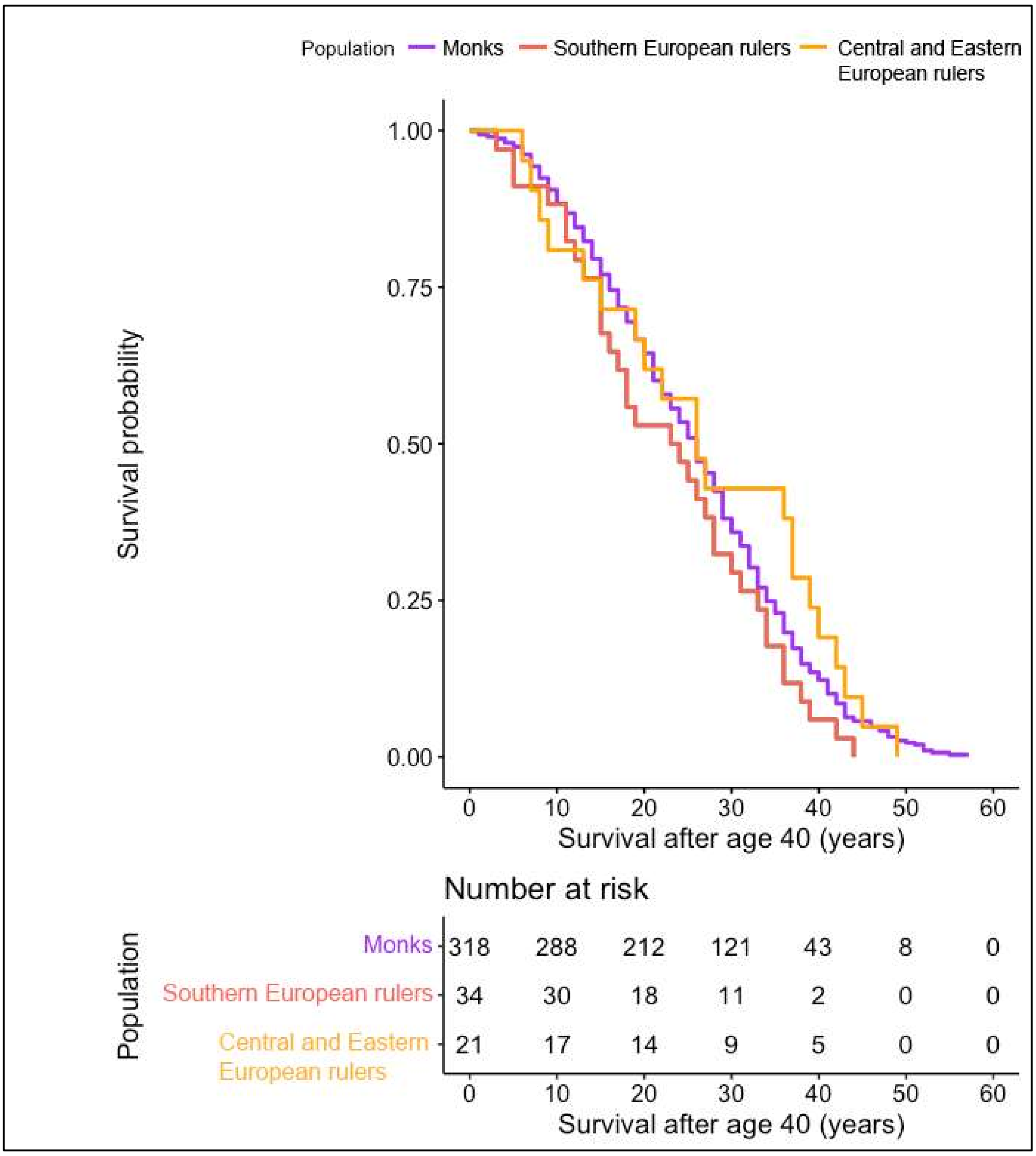

Figure 13. Kaplan-Meier survival curves for rulers in the Southern region, as well as for the Central and Eastern European rulers for rulers and monks who at least reached the age of 40 years.

5 Discussion

5.1 Primary analysis: Rulers of Europe and tendencies of longevity

The results of our primary analysis concerning the longevity of European rulers indicate that overall rulers exhibited similar survival irrespectively of their geographic regions. This, however, can be misleading, as life expectancy changed significantly from 1354 to 2022. This is why dividing this period into shorter time periods was reasonable. In the first analyzed time period (1354-1499), the Southern region was similar in terms of lifespan to the other regions with the exception of the Northern region, whose rulers exhibited significantly better lifespans than the south. In the second period (1500-1749), the survival rates were overall similar, suggesting that the longevity of rulers across Europe became more evenly distributed up until the third examined period. After 1750, all regions showed significantly better survival rates compared to rulers in the Southern regions. These differences in survival may be explained most probably by healthcare improvements, nutrition, and socio-economic and cultural factors. Thus, in the upcoming sections we will examine the possible role of these factors in shaping the longevity of rulers with a special emphasis on diet.

5.1.1 During the late Medieval Ages (1354-1499)

During the first time period (1354–1499), the Northern region exhibited a significantly better survival compared to the Southern region. One potential reason for this could be that Nordic countries were possibly less involved in military activities compared to other regions during this period. The lower frequency of conflicts and greater economic stability, exemplified by events such as the foundation of the Kalmar Union in 1397, contributed to this stability and could potentially explain the better survival rates observed in the Northern region (94, 95). Another possible factor that may have contributed to the better survival of rulers in the Northern region is the absence of malaria in this region, since malaria is not endemic beyond the summer isothermic line of +15.5 degrees Celsius (96, 97), which is corroborated by our results, as only rulers from the Southern and Western regions were documented to have died from malaria during this period. Another factor may be related to the Black Death, since the Scandinavian region experienced one of the highest estimated overall mortality rates in Europe due to Black

Death, according to Remi Jedwab and his colleagues (98), which led to a drastic decrease in population size that consecutively led to a relative prosperity and an increase in food availability in the following years (43). Be as it may, it is improbable that this directly affected the survival of the rulers in this region, as they consistently had access to food regardless of the prosperity of the general population.

5.1.2 The age of exploration and geographic discoveries (1500–1749)

The survival rates across different regions became similar during the Age of Discoveries between 1500 to 1749. The advantage previously held by Northern rulers vanished during this period. Several factors could explain this, including shifts in dietary habits, geopolitical changes, conflicts, and weather conditions. For instance, the Nordic countries were involved in more conflicts than before, which could have negatively impacted their economy, especially after the dissolution of the Kalmar Union in 1523 (94). The Thirty Years' War (1618 – 1648) also profoundly affected Europe, leading to significant loss of life, extensive destruction of property, and boosted hard drinks and tobacco consumption (99). Additionally, the Little Ice Age, spanning from the mid-16th to the mid-19th century, brought colder temperatures across the Northern Hemisphere (100). As a result, famine struck in Finland, leading to the death of approximately one-quarter to one-third of its population between 1696 and 1697 (43, 101).

During the second time period (1500–1749), there were notable changes in culinary practices too, however feasts still continued to serve as symbols of power and opportunities for diplomacy. For example, Cristofor da Messisbugo, steward of the Duke of Ferrara in the 16th century, recorded the four courses served at a banquet hosted by the Este family in Ferrara in 1529 (102). The menu featured a diverse array of meats, pastries, fruits, and spices, including different types of fish, whole meats, sausages, salamis, ham, small pastries, as well as assorted blancmanges, fritters, and salads, all in vast amounts (102).

5.1.3 The life since the Industrial Revolution (1750–2022)

The third analyzed period showed a noticeable trend of rising life expectancy among rulers in Northern and Western regions after 1750, whereas the Southern region did not experience a comparable increase in longevity. In contrast to what we initially hypothesized, our study revealed that rulers from regions, where the Mediterranean diet was common, did not exhibit longer lifespans compared to those from other regions. The reasons for this are likely complex and may be related to the complicated interaction of diet, lifestyle, politics, and socio-economic factors. The significant rise in the lifespan of rulers in Northern and Western regions after 1750 are particularly remarkable. During this period, the Industrial Revolution started in Great Britain and introduced numerous technological advancements that significantly enhanced the economy and quality of life across many regions (103). The Southern region also experienced the new achievements of the Industrial Revolution, especially in sea transportation and seaport infrastructures, thus these areas (and other areas that were connected to these zones by railroads) experienced relative prosperity and development (104). Conversely, internal parts of the countries were lagging behind, which may have negatively impacted health, economy, and quality of life (105).

After 1750, there were also notable advancements in the field of medicine and public health. Transformation in hygiene was also significant, especially in terms of personal hygiene, piped drinking water availability, sewage systems, and food hygiene. Edward Jenner's discovery of smallpox vaccination in 1796 represented a significant breakthrough in the prevention of infectious diseases (49). The introduction of general anesthesia in 1846 transformed surgery and enabled the performance of complex surgical procedures (106). Moreover, Louis Pasteur's microbiological discoveries in the late nineteenth century laid the foundation for later development of antibiotics, which saved numerous lives (107). Throughout the eighteenth and nineteenth centuries, Western countries such as the predecessors of modern France and Germany, the Habsburg Empire, and the United Kingdom were at the forefront of these advancement and their populations may have profited first in terms of life expectancy. The medical progress in these geographic areas could have also extended the lifespans of rulers in these areas, as enhanced medical knowledge and practices likely improved healthcare for rulers in these societies.

Another element which is important to note among the possible reasons of the lower lifespan of rulers in the Southern Region is the higher prevalence of criminal poisonings (108). There is a long history and tradition of poisonings in this region, dating back to the Roman Empire (27 BC – AD 476) (109-111). In the early 18th century, arsenic-based poisoning became known in Italy, with Aqua Tofana being the most infamous poison in the region (110). The core component of this poison was arsenic which was also used as a medicine. As a poison, it could be used for both acute and chronic criminal poisonings. Acute poisoning could have been mistaken for hyperacute bacterial gastroenteritis (112) at the time, while chronic poisoning resulted in slow, gradual death that was difficult to recognize. Additionally, arsenic was cheap, widely available, and, most importantly, untraceably at that time (110, 113, 114). Consequently, it became a popular tool for those looking to influence fate in favor of the poisoners and their clients. Since in the South there were more cases of poisoning compared to other regions, it is plausible that some deaths in the Southern region were mistaken for natural death, and decreased objectively the overall lifespan in this geographic area (89).

Another possible factor that may explain the lower survival of rulers in the Southern region may be linked to plague outbreaks, as this could both directly and indirectly have an impact on the survival of rulers by affecting the food availability, quality, and the overall quality of life (43). The Italian historian Guido Alfani claims that the Italian peninsula was more affected by infectious diseases than other regions in the seventeenth century (115), which could have been mainly due to their exposure to sea trade with the Eastern Mediterranean and warmer climate. However, over time, the number of outbreaks decreased in Europe and quarantine measures played a crucial role in controlling these plague outbreaks (115, 116). This most probably increased the lifespan of the general population, but may not have affected the nobility as much, since they frequently sought refuge in their more private countryside properties in time of pestilence (117).

5.2 Secondary analysis: Survival and lifestyle of Hungarian Benedictine monks

Our results from our secondary analysis in which we compared the survival of Hungarian Benedictine Monks with that of Southern European and Central and Eastern European rulers between the 18th and 19th century, indicate that Benedictine monks in Hungary also had a significantly better survival than Southern European rulers. Their survival was very similar to that of Central and Eastern European rulers. This is somewhat surprising but can probably be explained by the rigorous yet healthy lifestyle of this monastic order.

The Benedict Order is one of the oldest catholic monk orders (118). St. Benedict's (480-547) rules offer guidance for the monastic life (118). The daily routine of Hungarian Benedict monks is displayed in **Table 6.** (81). This schedule was followed in Bakonybél, but it is not unique to this monastery, since it is based on St. Benedict's Rule that were also followed by other monasteries in the Benedictine Order throughout Europe (118).

St. Benedict's rules prescribe moderation in all parts of life, for instance alcohol consumption and diet, only two meals a day, work intensity, fasting periods, and religious events (118). As for religious fasting (118), this could have also been an important factor contributing to healthy longevity of monks, as studies indicate that intermittent fasting has a positive impact on health and longevity (119). Other explanations may be that monks were relatively more protected from physical assault and war, they led a lifestyle defined by moderation in their diet and performed physical activity regularly in the form of work around the monastery. Benedictine monks may have also had better mental health, as certain studies show that religion and spirituality are connected to improved mental health mediated through religious coping strategies, sense of community, mutual support, and positive beliefs (120). These, however, are only a hypothesis and further research is needed to better elucidate the reason of the relatively higher lifespan of this specific population.

Table 6. A regular day of a benedict monk in Bakonybél Monastery, Hungary in the 2nd half of the 18th century.

Activity	Time
Awakening	3:45
Matutinum and Laudes (praying)	4:00
Contemplation	5:30
Prima and Martyrologium and Penance (spiritual practices)	6:00
Terce, Sext, Nones, Convent Mass (prayers)	7:00
Work then later lunch, which was followed by recreation	8:00
Evening prayers and practices	14:00
Compline and Lectio Divina - Spiritual practices, Dinner	17:00
Silentium and going to bed	20:00

5.3 Limitations

5.3.1 Limitations of the rulers' dataset

One of the major challenges of our study concerning the lifespan of rulers is the inability to eliminate properly the impact of immortal time bias. We considered age as the underlying time and included only crowned rulers implying that they were effectively immortal until their time of coronation. Immortal time bias (121) is a type of bias that occurs in observational studies, when there is a period of time during which the outcome of interest (e.g., death) cannot happen. This "immortal" time is incorrectly included in the analysis in a way that may distort the true association between an exposure and the outcome. Thus, rulers crowned later in life had a clear advantage over those crowned at younger ages, as they had already lived longer and were more likely to reach an older age. Another limitation is the arbitrary categorization of Europe into larger geographic regions that do not necessarily reflect uniform cuisines. Cuisines could vary between countries within the same region, potentially affecting our results. Another limiting factor is the accuracy of historical records, which could lead to possible misclassifications of the cause of death. Additional limitation is the lack of access to potential confounding factors that can also significantly affect lifespan, such as smoking, alcohol consumption, diseases, or differences in dietary habits during upbringing that may have also influenced later eating habits of an individual. Furthermore, we did not account for genetic relationships either, which may also have significantly influenced longevity, especially in case of dynastic intermarriages, frequent relocations, and consanguineous marriages, especially prevalent among the Habsburg dynasty and a key reason for the extinction of the Spanish line (122). Finally, from a statistical perspective, the Central and Eastern region and the Northern region had less rulers too, which led to challenges related to statistical power.

5.3.2 Limitations of the monks' datasets

One major limitation of our analysis regarding the life expectancy of monks is that we had no information on the cause of their death. Moreover, we also do not know the exact lifestyle of each individual and to which extent he respected the rules of St. Benedict. This is also true for the examined monasteries, as they may have exhibited heterogeneity in their daily activities and cuisine. Another limiting factor is the overall low number of rulers compared to the monks in the secondary analysis, which may have also led to low statistical power as mentioned before.

6 Conclusions

6.1 Main conclusion

In conclusion, our study highlights the complex relationship between geographic location, period, and lifespan of European rulers. Results of our study indicate that the lifespan of Southern European rulers was not longer than that of rulers in other regions. In fact, after 1750, the lifespan of Southern rulers was even lower than the lifespan of other rulers, especially compared to the rulers in the Northern regions.

While the Mediterranean diet is coupled frequently with health advantages, our results suggest that it in itself does not necessarily explain the variations in ruler longevity across different regions. It is also important to consider that rulers in Southern Europe might not have adhered to the Mediterranean diet, and they led a physically less active lifestyle, as common people. This is also corroborated by the diet of Benedictine monks who not only followed a rigorous diet consisting of fish, beans, lentils, peas, prunes, strawberries, oats, wheat, and sigh in moderation – similarly to the Mediterranean diet – but also performed physical activity regularly, which may explain why their lifespan was on par with the ruling classes of the same region.

Overall, our results point in the direction that the cuisine and lifestyle of the courts may have been more alike than distinct from one another (76, 77). Rulers across Europe had access to a wide variety of foods in plentiful amounts consistently, therefore the dietary habits of the Southern elite may not have been representative of the Mediterranean diet. Additional factors, such as protection against infectious diseases and physical assault, economic security, and access to the best possible healthcare of a given era, could have also played a pivotal role in the differences observed in the survival of the European elite. These elements might have offset the effect of any regional dietary differences.

6.2 New findings

1. We conducted an analysis of European rulers over a long historical period (approximately 8 centuries) with a relatively large sample size. Based on our results we were not able to observe a higher lifespan of rulers of the Southern European region despite that this would otherwise be expected in the Mediterranean region. Overall, the survival of rulers in different geographic areas

was similar, indicating that rulers across Europe lived a similarly protected life in wealth and relative safety. One explanation for the similarity is that most activities of the rulers were considered public, or even international events. Therefore, in the competitive hierarchy of power among the monarchies, factors such as the quality and quantity of banquets were also decisive. This could have been one of the main factors contributing to the development of these similarities

2. When we divided our analysis into three distinct periods, we found that the lifespan of Southern rulers was sometimes significantly lower compared to other European regions. In our opinion, this may have been caused by several factors, for instance more common occurrence of outbreaks and criminal poisonings in this area, slower spread of the industrial revolution and some medical discoveries that arrived later to the Southern region, and warmer climate that may have favored the spread of infectious diseases in this area. In contrast to the Southern region, rulers of the Northern regions, especially between 1354–1499, performed better in terms of survival, which may partially be explained by the socioeconomic stability and lack of geopolitical conflicts observed in the area.
3. We also collected data about the survival of Hungarian Benedictine monks between the 18th and 19th century. Results about their survival and the comparison to the rulers' survival, was not published before, making our results unique in this area. Our results show that the survival of Central and Eastern European Benedictine monks was on par with the survival of rulers in Central and Eastern Europe and was significantly better than the lifespan of Southern rulers. In our opinion, this may be partially explained by their rigorous diet, regular physical activity, better mental health along with the more protected dwelling and safer and more closed living conditions of monks.

7 Summary

Life expectancy is not only different between specific regions in Europe, but it was also changing throughout history. In this work, I aimed to investigate the changes and differences of lifespan using well-defined historic groups of people, namely rulers and Benedictine monks.

My primary objective was to compare the survival of European rulers divided into different geographic areas with a special emphasis on the possible role of dietary differences. Rulers represent a rather homogenous group of individuals who had access to the best possible quality and quantity of food, best healthcare services, and led a life where starvation, lack of hygiene, plagues, and wars affected them less than their subjects. Overall, I found that the survival of rulers across different geographic regions was similar, indicating that rulers were more likely to have led a similar lifestyle. They were protected from infectious diseases and war, they consumed foods rich in protein and fat, consumed alcohol in excess, and were also mostly physically inactive. The Mediterranean diet, as it is known today, was not primarily preferred by the ruling classes. When we divided our time intervals into shorter periods, we often found that the survival of Southern rulers was lower than other regions. Although we do not know the exact causes behind this phenomenon, possible explanations may reside in the more common occurrence of plagues and criminal poisonings in the ruling classes in this area along with the delayed appearance of benefits of the industrial revolution and medical discoveries.

My secondary objective was to examine the lifespan of Benedictine monks and compare them to the lifespan of Central and Eastern European and Southern European rulers. Our results indicate that Benedictine monks lived longer than Southern European rulers and their lifespan was comparable to the survival of Central and Eastern European rulers. Monks, similarly to rulers, were a relatively well-protected group of people who practiced lifestyles beneficial to their physical and mental health alike. They worked regularly, prayed daily, and consumed healthy foods in moderation. This may partially explain why their survival was on par with the ruling classes.

The results published in this thesis can serve as a valuable tool for understanding the impact of the Mediterranean diet and geographical location on longevity from a historical perspective. It also brings us closer to understanding past longevity data, despite the challenges of collecting historical data.

8 References

8.1 Original archival and manuscript sources

(The items listed here also appear in the reference list below with the same numbers.)

82.. Pannonhalmi Főapátsági Levéltár [Pannonhalmi Archabbey Archives] - BAL GL Perceptio et erogatio 1739-1748, 9-14.

83. Pannonhalmi Főaptsági Lévéltár [Pannonhalmi Archabbey Archives] - BAL AA 8.22 327.

86. Pannonhalmi Főaptsági Lévéltár [Pannonhalmi Archabbey Archives] - PFL BAL GL Perceptio et erogatio 1739-1748, 31.

87. Pannonhalmi Főapátsági Levéltár [Pannonhalmi Archabbey Archives] - PFL BAL GL Perceptio et erogatio 1739–1748, 10., 13., 16–17., 23–24., 27., 38., 43., 47., .

88.. Pannonhalmi Főapátsági Levéltár [Pannonhalmi Archabbey Archives] - BAL GL Registrum proventus et erogationis 1764–1765, 25.

8.2 Original sources and contemporary printed material

(The items listed here also appear in the reference list below with the same numbers.)

47. Snow J. On the Mode of Communication of Cholera. Much enlarged. London: John Churchill, New Burlington St.; reprinted in Snow on Cholera: Being a Reprint of Two Papers by John Snow MD. New York: The Commonwealth Fund; London: Humphrey Milford. Oxford University Press; 1936.
https://wellcomecollection.org/works/twgega8g/items?canvas=4
Reprint from 1936
(The original papers are made in the 19th century.)

78. Veneziano Anonimo. Libro di cucina del sec. XIV a curoe di Ludovico Frati. Livorno 1899.
https://www.mori.bz.it/gastronomia/Anonimo%20Veneziano%20-%20Libro%20di%20cucina.pdf
(The 1899 edition is a reprint of the 14th-century cookbook.)

93. Légányi N. BP. Pannonhalmi Szent Benedek-Rend Névtára 1802-1986 1987.

102. Messisbugo C. Banchetti compositioni di vivande 1549.
https://books.google.hu/books?id=VSM8AAAAcAAJ
(A book which lists all the elements necessary to prepare a princely banquet, from the furnishings to the kitchen utensils, and contains numerous recipes form the 16th century.)

118. Nursiai Szent Benedek, Szent Benedek regulája. Pannonhalma: Bencés Kiadó; 1995. 143 p.
The Hungarian translations of the original work made available by the Hungarian Benedictine Order.
(The original text dates back to the 6th century)

8.3 References

1. Official website of the European Union, Eurostat - Life expectancy across EU regions in 2020 [cited 2024 Feb 27] [Available from: https://ec.europa.eu/eurostat/web/products-eurostat-news/-/ddn-20220427-1.
2. Deaton A. Income, health, and well-being around the world: Evidence from the Gallup World Poll. Journal of Economic perspectives. 2008;22(2):53-72.
3. Official website of the European Union, Eurostat - Life expectancy by age and sex in 2020 [cited 2023 Apr 12]: Eurostat; [Available from: https://ec.europa.eu/eurostat/databrowser/bookmark/e3f138df-5165-4db9-805c-f48ff25d621b?lang=en.
4. Official website of the European Union, Eurostat - Real GDP per capita of Europe 2020 [cited 2023 Apr 12] [Available from: https://ec.europa.eu/eurostat/databrowser/view/SDG_08_10/bookmark/table?lang=en&bookmarkId=c4de0f60-b965-4cb2-a890-79191b798c28.
5. Wynder EL, Graham EA. Tobacco smoking as a possible etiologic factor in bronchiogenic carcinoma; a study of 684 proved cases. Journal of the American Medical Association. 1950;143(4):329-36. https://doi.org/10.1001/jama.1950.02910390001001
6. Official website of the European Union, Eurostat - Daily smokers of the EU 2019 [cited 2023 Apr 12] [Available from: https://ec.europa.eu/eurostat/web/products-eurostat-news/-/edn-20211112-1.
7. Official website of the European Union, Eurostat - Sport and physical activity in the EU - Summary 2022 [cited 2023 Apr 12] [Available from: https://europa.eu/eurobarometer/surveys/detail/2668?fbclid=IwAR35CxWTqmFpwArx-cnPxrzGEi64m1BMoYLKrGDF0HpGVkE0MGJdR0Lje2k.
8. Guasch-Ferré M, Willett WC. The Mediterranean diet and health: a comprehensive overview. Journal of internal medicine. 2021;290(3):549-66. http://doi.org/10.1111/joim.13333
9. Bach-Faig A, Berry EM, Lairon D, Reguant J, Trichopoulou A, Dernini S, et al. Mediterranean diet pyramid today. Science and cultural updates. Public health nutrition. 2011;14(12a):2274-84. http://doi.org/10.1017/s1368980011002515

10. Keys A, Mienotti A, Karvonen MJ, Aravanis C, Blackburn H, Buzina R, et al. The diet and 15-year death rate in the seven countries study. J American journal of epidemiology. 1986;124(6):903-15. https://www.doi.org/10.1093/oxfordjournals.aje.a114480
11. Baur JA, Pearson KJ, Price NL, Jamieson HA, Lerin C, Kalra A, et al. Resveratrol improves health and survival of mice on a high-calorie diet. Nature. 2006;444(7117):337-42. https://doi.org/10.1038/nature05354
12. Baur JA, Sinclair DA. Therapeutic potential of resveratrol: the in vivo evidence. Nat Rev Drug Discov. 2006;5(6):493-506. https://doi.org/10.1038/nrd2060
13. Pearson KJ, Baur JA, Lewis KN, Peshkin L, Price NL, Labinskyy N, et al. Resveratrol Delays Age-Related Deterioration and Mimics Transcriptional Aspects of Dietary Restriction without Extending Life Span. Cell metabolism. 2008;8(2):157-68. https://doi.org/10.1016/j.cmet.2008.06.011
14. Aziz MH, Reagan-Shaw S, Wu J, Longley BJ, Ahmad N. Chemoprevention of skin cancer by grape constituent resveratrol: relevance to human disease? Faseb J. 2005;19(9):1193-5. https://doi.org/10.1096/fj.04-3582fje
15. Sale S, Verschoyle RD, Boocock D, Jones DJ, Wilsher N, Ruparelia KC, et al. Pharmacokinetics in mice and growth-inhibitory properties of the putative cancer chemopreventive agent resveratrol and the synthetic analogue trans 3,4,5,4'-tetramethoxystilbene. Br J Cancer. 2004;90(3):736-44. https://doi.org/10.1007/s12020-023-03458-9
16. Signorelli P, Ghidoni R. Resveratrol as an anticancer nutrient: molecular basis, open questions and promises. J Nutr Biochem. 2005;16(8):449-66. https://doi.org/10.1016/j.jnutbio.2005.01.017
17. Bernier M, Wahl D, Ali A, Allard J, Faulkner S, Wnorowski A, et al. Resveratrol supplementation confers neuroprotection in cortical brain tissue of nonhuman primates fed a high-fat/sucrose diet. Aging (Albany NY). 2016;8(5):899-916. https://doi.org/10.18632/aging.100942
18. Csiszar A, Labinskyy N, Olson S, Pinto JT, Gupte S, Wu JM, et al. Resveratrol prevents monocrotaline-induced pulmonary hypertension in rats. Hypertension. 2009;54(3):668-75. https://doi.org/10.1161/hypertensionaha.109.133397

19. Csiszar A, Labinskyy N, Pinto JT, Ballabh P, Zhang H, Losonczy G, et al. Resveratrol induces mitochondrial biogenesis in endothelial cells. Am J Physiol Heart Circ Physiol. 2009. https://doi.org/10.1152/ajpheart.00368.2009
20. Csiszar A, Labinskyy N, Podlutsky A, Kaminski PM, Wolin MS, Zhang C, et al. Vasoprotective effects of resveratrol and SIRT1: attenuation of cigarette smoke-induced oxidative stress and proinflammatory phenotypic alterations. Am J Physiol Heart Circ Physiol. 2008;294(6):H2721-35. https://doi.org/10.1152/ajpheart.00235.2008
21. Csiszar A, Smith K, Labinskyy N, Orosz Z, Rivera A, Ungvari Z. Resveratrol attenuates TNF-{alpha}-induced activation of coronary arterial endothelial cells: role of NF-{kappa}B inhibition. Am J Physiol. 2006;291(4):H1694-9. https://doi.org/10.1152/ajpheart.00340.2006
22. Csiszar A, Sosnowska D, Wang M, Lakatta EG, Sonntag WE, Ungvari Z. Age-associated proinflammatory secretory phenotype in vascular smooth muscle cells from the non-human primate Macaca mulatta: reversal by resveratrol treatment. J Gerontol A Biol Sci Med Sci. 2012;67(8):811-20. https://doi.org/10.1093/gerona/glr228
23. Mattison JA, Wang M, Bernier M, Zhang J, Park SS, Maudsley S, et al. Resveratrol prevents high fat/sucrose diet-induced central arterial wall inflammation and stiffening in nonhuman primates. Cell metabolism. 2014;20(1):183-90. https://doi.org/10.1016/j.cmet.2014.04.018
24. Toth P, Tarantini S, Springo Z, Tucsek Z, Gautam T, Giles CB, et al. Aging exacerbates hypertension-induced cerebral microhemorrhages in mice: role of resveratrol treatment in vasoprotection. Aging Cell. 2015;14(3):400-8. https://doi.org/10.1111/acel.12315
25. Toth P, Tarantini S, Tucsek Z, Ashpole NM, Sosnowska D, Gautam T, et al. Resveratrol treatment rescues neurovascular coupling in aged mice: role of improved cerebromicrovascular endothelial function and downregulation of NADPH oxidase. Am J Physiol Heart Circ Physiol. 2014;306(3):H299-308. https://doi.org/10.1152/ajpheart.00744.2013
26. Ungvari Z, Labinskyy N, Mukhopadhyay P, Pinto JT, Bagi Z, Ballabh P, et al. Resveratrol attenuates mitochondrial oxidative stress in coronary arterial

endothelial cells. Am J Physiol Heart Circ Physiol. 2009;297(5):H1876-81. https://doi.org/10.1152/ajpheart.00375.2009

27. Zhang H, Zhang J, Ungvari Z, Zhang C. Resveratrol improves endothelial function: role of TNF{alpha} and vascular oxidative stress. Arterioscler Thromb Vasc Biol. 2009;29(8):1164-71. https://doi.org/10.1161/ATVBAHA.109.187146
28. Price NL, Gomes AP, Ling AJ, Duarte FV, Martin-Montalvo A, North BJ, et al. SIRT1 is required for AMPK activation and the beneficial effects of resveratrol on mitochondrial function. Cell metabolism. 2012;15(5):675-90. https://doi.org/10.1016/j.cmet.2012.04.003
29. Csiszar A, Pinto JT, Gautam T, Kleusch C, Hoffmann B, Tucsek Z, et al. Resveratrol Encapsulated in Novel Fusogenic Liposomes Activates Nrf2 and Attenuates Oxidative Stress in Cerebromicrovascular Endothelial Cells From Aged Rats. J Gerontol A Biol Sci Med Sci. 2014. https://doi.org/10.1093/gerona/glu029
30. Ungvari Z, Bagi Z, Feher A, Recchia FA, Sonntag WE, Pearson K, et al. Resveratrol confers endothelial protection via activation of the antioxidant transcription factor Nrf2 Am J Physiol Heart Circ Physiol. 2010;299(1):H18-24. https://doi.org/10.1152/ajpheart.00260.2010
31. de Pablos RM, Espinosa-Oliva AM, Hornedo-Ortega R, Cano M, Arguelles S. Hydroxytyrosol protects from aging process via AMPK and autophagy; a review of its effects on cancer, metabolic syndrome, osteoporosis, immune-mediated and neurodegenerative diseases. Pharmacol Res. 2019;143:58-72. https://doi.org/10.1016/j.phrs.2019.03.005
32. Terracina S, Petrella C, Francati S, Lucarelli M, Barbato C, Minni A, et al. Antioxidant Intervention to Improve Cognition in the Aging Brain: The Example of Hydroxytyrosol and Resveratrol. Int J Mol Sci. 2022;23(24). https://doi.org/10.3390/ijms232415674
33. Boronat A, Mateus J, Soldevila-Domenech N, Guerra M, Rodriguez-Morato J, Varon C, et al. Cardiovascular benefits of tyrosol and its endogenous conversion into hydroxytyrosol in humans. A randomized, controlled trial. Free Radic Biol Med. 2019;143:471-81. https://doi.org/10.1016/j.freeradbiomed.2019.08.032
34. Ikonomidis I, Katogiannis K, Chania C, Iakovis N, Tsoumani M, Christodoulou A, et al. Association of hydroxytyrosol enriched olive oil with vascular function in

chronic coronary disease. Eur J Clin Invest. 2023:e13983. https://doi.org/10.1111/eci.13983

35. Kaindl U, Eyberg I, Rohr-Udilova N, Heinzle C, Marian B. The dietary antioxidants resveratrol and quercetin protect cells from exogenous pro-oxidative damage. Food Chem Toxicol. 2008;46(4):1320-6. https://doi.org/10.1016/j.fct.2007.09.002
36. Islam MT, Tuday E, Allen S, Kim J, Trott DW, Holland WL, et al. Senolytic drugs, dasatinib and quercetin, attenuate adipose tissue inflammation, and ameliorate metabolic function in old age. Aging Cell. 2023;22(2):e13767. https://doi.org/10.1111/acel.13767
37. Krzystyniak A, Wesierska M, Petrazzo G, Gadecka A, Dudkowska M, Bielak-Zmijewska A, et al. Combination of dasatinib and quercetin improves cognitive abilities in aged male Wistar rats, alleviates inflammation and changes hippocampal synaptic plasticity and histone H3 methylation profile. Aging (Albany NY). 2022;14(2):572-95. https://doi.org/10.18632/aging.203835
38. Official website of the European Union, Eurostat - Nutritional habits statistics [cited 2023 Apr 12] [Available from: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Nutritional_habits_statistics#Consumption_of_fruit_and_vegetables.
39. Goldman L. Three Stages of Health Encounters Over 8000 Human Generations and How They Inform Future Public Health. American journal of public health. 2018;108(1):60-2. https://doi.org/10.2105/ajph.2017.304164
40. Lancaster HO. Expectations of life: a study in the demography, statistics, and history of world mortality: Springer Science & Business Media; 2012.
41. Riley JC. Estimates of regional and global life expectancy, 1800–2001. Population development review. 2005;31(3):537-43. https://doi.org/10.1111/j.1728-4457.2005.00083.x
42. Benedictow OJ. The Black Death, 1346-1353: the complete history: Boydell & Brewer; 2004.
43. Braudel F. A mindennapi élet struktúrái: a lehetséges és a lehetetlen Anyagi kultúra, gazdaság és kapitalizmus, XV–XVIII. század. I. kötet: Gutta Kiadó; 2004. 602 p.

44. Sadeghi S, Ghaffari F, Heydarirad G, Alizadeh M. Galen's place in Avicenna's The Canon of Medicine: Respect, confirmation and criticism. Journal of Integrative Medicine. 2020;18(1):21-5. https://doi.org/10.1016/j.joim.2019.11.002
45. Toledo-Pereyra LH. Medical Renaissance. Journal of Investigative Surgery. 2015;28(3):127-30. https://www.doi.org/10.3109/08941939.2015.1054747
46. Madarász B, Forrai J. Számok és statisztikák szerepe az élettudományok fejlődésének történetében; az epidemiológia születése. Kaleidoscope history. 2021;11:95-107. https://doi.org/10.17107/kh.2021.23.95-107
47. Snow J. On the Mode of Communication of Cholera. Much enlarged. London: John Churchill, New Burlington St.; reprinted in Snow on Cholera: Being a Reprint of Two Papers by John Snow MD. New York: The Commonwealth Fund; London: Humphrey Milford. Oxford University Press; 1936.
48. Berridge V, Berridge V. 42Sanitation to education: 1800–1900s. Public Health: A Very Short Introduction: Oxford University Press; 2016. p. 0. http://doi.org/10.1093/actrade/9780199688463.003.0004
49. Riedel S. Edward Jenner and the history of smallpox and vaccination. Proceedings (Baylor University Medical Center). 2005;18(1):21-5. http://doi.org/10.1080/08998280.2005.11928028
50. Newsom SWB. Pioneers in infection control—Joseph Lister. Journal of Hospital Infection. 2003;55(4):246-53. https://doi.org/10.1016/j.jhin.2003.08.001
51. Mould RF. Röntgen and the discovery of X-rays. British Journal of Radiology. 1995;68(815):1145-76. http://doi.org/10.1259/0007-1285-68-815-1145
52. Bennett JW, Chung K-T. Alexander Fleming and the discovery of penicillin. Advances in Applied Microbiology. 49: Academic Press; 2001. p. 163-84. https://doi.org/10.1016/S0065-2164(01)49013-7
53. Willets RC, Gallop AP, Leandro PA, Lu JLC, Macdonald AS, Miller KA, et al. Longevity in the 21st Century. British Actuarial Journal. 2004;10(4):685-832. http://doi.org/10.1017/S1357321700002750
54. World Health Organizations (WHO) - Public health milestones through the years [cited 2024 Aug 06] [Available from: https://www.who.int/campaigns/75-years-of-improving-public-health/milestones#year-1980.

55. Schindler S. Model, Theory, and Evidence in the Discovery of the DNA Structure. 2008;59(4):619-58. http://doi.org/10.1093/bjps/axn030
56. Seeram E. Nobel Prize for CT and MRI pioneers: historical article. The Radiographer: The Official Journal of the Australian Institute of Radiography. 2006;53(1):4-7.
57. Pérez-Lloréns JL, Acosta Y, Brun FG. Seafood in Mediterranean countries: A culinary journey through history. International Journal of Gastronomy and Food Science. 2021;26:100437. https://doi.org/10.1016/j.ijgfs.2021.100437
58. Watson AM. The Arab Agricultural Revolution and Its Diffusion, 700–1100. The Journal of Economic History. 1974;34(1):8-35. http://doi.org/10.1017/S0022050700079602
59. Morin GA, Unies N, l'agriculture OdNUplae. Long-term historical changes in the forest resource: UN; 1996.
60. Pearson KL. Nutrition and the Early-Medieval Diet. Speculum. 1997;72(1):1-32. https://doi.org/10.2307/2865862
61. Cosman MP. Fabulous feasts: Medieval cookery and ceremony1976.
62. Banegas López RA. Consumption of meat in Western European cities during the late middle ages: A comparative study. Food History. 2010;8(1):63-86. https://doi.org/10.1484/J.FOOD.1.100974
63. Eu Agricultural Outlook For Markets, Income And Environment 2021 - 2031, Luxembourg: Publications Office of the European Union, 2021.
64. Astill GG, Langdon J. Medieval farming and technology: The impact of agricultural change in Northwest Europe: Brill; 1997.
65. Wall C. George Washington: Country Gentleman. Agricultural History. 1969;43(1):5.
66. Sicking L, Abreu-Ferreira D. Beyond the catch: fisheries of the North Atlantic, the North Sea and the Baltic, 900-1850: Brill; 2008.
67. Inderhaug T. Stockfish Production, Cultural and Culinary Values. Food Ethics. 2020;5(1):6. https://doi.org/10.1007/s41055-019-00060-6
68. Sweeney D. Agriculture in the middle ages: technology, practice, and representation: University of Pennsylvania Press; 2016.

69. Schmitt T. Biogeographical and evolutionary importance of the European high mountain systems. Frontiers in zoology. 2009;6:1-10. https://doi.org/10.1186/1742-9994-6-9
70. Zvelebil M, Dolukhanov P. The Transition to Farming in Eastern and Northern Europe. Journal of World Prehistory. 1991;5(3):233-78. https://doi.org/10.1007/BF00974991
71. Samojlik T, Rotherham ID, Jędrzejewska B. The Cultural Landscape of Royal Hunting Gardens from the Fifteenth to the Eighteenth Century in Białowieża Primeval Forest. In: Rotherham ID, editor. Cultural Severance and the Environment: The Ending of Traditional and Customary Practice on Commons and Landscapes Managed in Common. Dordrecht: Springer Netherlands; 2013. p. 191-204. https://doi.org/10.1007/978-94-007-6159-9_13
72. Eriksson O. Origin and development of managed meadows in Sweden: A review. Rural Landscapes: Society, Environment, History. 2020;7(1):1-23. https://doi.org/10.16993/rl.51
73. Katz J. Tradition and crisis: Jewish society at the end of the Middle Ages: Syracuse University Press; 2000.
74. Dembinska M. Food and drink in medieval Poland: rediscovering a cuisine of the past: University of Pennsylvania Press; 1999.
75. Huizinga J. A középkor alkonya. ford. Szerb Antal, Athenaeum, 1938.
76. Dickie J. Delizia!: The epic history of the Italians and their food: Simon and Schuster; 2008.
77. De Vooght D. Royal taste: food, power and status at the European Courts after 1789: Routledge; 2016.
78. Veneziano A. Libro di cucina del sec. XIV a curoe di Ludovico Frati. Livorno1899.
79. Montanari M. Food is culture: Columbia University Press; 2006.
80. Spooner F. régimes alimentaires d'autrefois. Annales. 1961:568-74.
81. Dénesi T. Szerzetesi élet a 18. századi Bakonybélben. In: Vallis sanctorum. Fejezetek a bakonybéli monostor ezeréves történetéből. Dénesi T, editor. Bakonybél-Pannonhalma2020.
82. Pannonhalmi Főapátsági Levéltár - BAL GL Perceptio et erogatio 1739-1748, 9-14.

83. Pannonhalmi Főaptsági Lévéltár - BAL AA 8.22 327.
84. Erdélyi Ls, Sörös Pc. A Pannonhalmi Szent-Benedek-Rend története: a Magyar kereszténység, királyság és Benczés-Rend fönnállásának kilenczszázados emlékére. Budapest: Stephaneum; 1902. 12 v. in 4 p.
85. Erdélyi, L., Sörös, P. A Pannonhalmi Szent-Benedek-Rend története: a Magyar kereszténység, királyság és Benczés-Rend fönnállásának kilenczszázados emlékére. Kilenczedik kötet. Budapest: Stephaneum. 1902-1916 650 p.
86. Pannonhalmi Főaptsági Lévéltár - PFL BAL GL Perceptio et erogatio 1739-1748, 31.
87. Pannonhalmi Főapátsági Levéltár - PFL BAL GL Perceptio et erogatio 1739–1748, 10., 13., 16–17., 23–24., 27., 38., 43., 47., .
88. Pannonhalmi Főapátsági Levéltár - BAL GL Registrum proventus et erogationis 1764–1765, 25.
89. Madarász B, Fazekas-Pongor V, Szarvas Z, Fekete M, Varga JT, Tarantini S, et al. Survival and longevity of European rulers: geographical influences and exploring potential factors, including the Mediterranean diet — a historical analysis from 1354 to the twentieth century. GeroScience. 2023. https://doi.org/10.1007/s11357-023-00957-5
90. Encyclopedia Britannica [Internet]. Accesed: 2021-2023. Available from: https://www.britannica.com/ [
91. Morby JE. Dynasties of the world. Oxford: Oxford University Press; 2002.
92. Publications Office of the European Union - Geographical division of Europe [cited 2022 Oct 10] [Available from: https://eur-lex.europa.eu/browse/eurovoc.html?params=72,7206,5781#arrow_5781.
93. Légányi N. BP. Pannonhalmi Szent Benedek-Rend Névtára 1802-19861987.
94. Gustafsson H. A state that failed? Scandinavian Journal of History. 2006;31(3-4):205-20. https://doi.org/10.1080/03468750600930720
95. Rohleder N. Chronic stress and disease. Insights to neuroimmune biology: Elsevier; 2016. p. 201-14. https://doi.org/10.1016/B978-0-12-801770-8.00009-4
96. Boualam MA, Pradines B, Drancourt M, Barbieri R. Malaria in Europe: a historical perspective. Frontiers in Medicine. 2021;8:691095. https://doi.org/10.3389/fmed.2021.691095

97. Ryan SJ, Lippi CA, Villena OC, Singh A, Murdock CC, Johnson LR. Mapping current and future thermal limits to suitability for malaria transmission by the invasive mosquito Anopheles stephensi. Malaria Journal. 2023;22(1):104. https://doi.org/10.1186/s12936-023-04531-4
98. Jedwab R, Johnson ND, Koyama M. The economic impact of the Black Death. Journal of Economic Literature. 2022;60(1):132-78. https://doi.org/10.1257/jel.20201639
99. Plundrich M. Killer high: a history of war in six drugs. Mezinárodní vztahy. 2021;56:103-8. https://doi.org/10.32422/mv-cjir.1773
100. Mann ME. Little ice age. Encyclopedia of global environmental change. 2002;1:504-9.
101. Jutikkala E. The great finnish famine in 1696–97. Scandinavian Economic History Review. 1955;3(1):48-63. https://doi.org/10.1080/03585522.1955.10411468
102. Messisbugo C. Banchetti compositioni di vivande 1549.
103. Mason DS. A concise history of modern Europe: liberty, equality, solidarity: Rowman & Littlefield; 2022.
104. Headrick DR. The tools of empire : technology and European imperialism in the nineteenth century. New York Oxford: Oxford University Press; 1981. 229 p.
105. Encyclopaedia Britannica, Kenny Chmielewski, A map depicting the spread of the Industrial Revolution through Europe in the 19th century. [cited 2023 Mar 7] [Available from: https://www.britannica.com/summary/Industrial-Revolution-Key-Facts.
106. Robinson DH, Toledo AH. Historical Development of Modern Anesthesia. Journal of Investigative Surgery. 2012;25(3):141-9. https://doi.org/10.3109/08941939.2012.690328
107. Smith KA. Louis pasteur, the father of immunology? Frontiers in immunology. 2012;3:68. https://doi.org/10.3389/fimmu.2012.00068
108. Madarász B. Megment vagy elpusztít: a higany és arzén gyógyászati karrierje I. rész higany. Kaleidoscope history. 2019;10(18):210-41. https://doi.org/10.17107/kh.2019.18.210-240
109. Cilliers L, Retief F. Poisons, poisoning and the drug trade in ancient Rome. Akroterion. 2000;45(1):88-100. https://doi.org/10.7445/45-0-166

110. Dash M. Chapter 6 - Aqua Tofana. In: Wexler P, editor. Toxicology in the Middle Ages and Renaissance: Academic Press; 2017. p. 63-9. https://doi.org/10.1016/B978-0-12-809554-6.00006-8
111. Karamanou M, Androutsos G, Hayes AW, Tsatsakis A. Toxicology in the Borgias period: The mystery of Cantarella poison. Toxicology Research Application. 2018;2. https://doi.org/10.1177/2397847318771126
112. Jain N, Chandramani S. Arsenic poisoning- An overview. Indian Journal of Medical Specialities. 2018;9(3):143-5. https://doi.org/10.1016/j.injms.2018.04.006
113. Madarász B. Megment vagy elpusztít: a higany és arzén gyógyászati karrierje. II. rész arzén. Kaleidoscope history. 2019;2019/19:137-46. https://doi.org/10.17107/KH.2019.19.137-146
114. Frankenberger J. Environmental chemistry of arsenic: CRC Press; 2001.
115. Alfani G. Plague in seventeenth-century Europe and the decline of Italy: an epidemiological hypothesis. European Review of Economic History. 2013;17(4):408-30. https://doi.org/10.1093/ereh/het013
116. Conti AA. Quarantine Through History. In: Heggenhougen HK, editor. International Encyclopedia of Public Health. Oxford: Academic Press; 2008. p. 454-62. https://doi.org/10.1016/B978-012373960-5.00380-4
117. Boccaccio G, Witte K. Das Dekameron: Anaconda; 2013.
118. Nursiai Szent Benedek, Szent Benedek regulája. Pannonhalma: Bencés Kiadó; 1995. 143 p. [
119. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. Ageing Research Reviews. 2017;39:46-58. https://doi.org/10.1016/j.arr.2016.10.005
120. Weber SR, Pargament KI. The role of religion and spirituality in mental health. Current opinion in psychiatry. 2014;27(5):358-63. https://doi.org/10.1097/yco.0000000000000080
121. Yadav K, Lewis RJ. Immortal Time Bias in Observational Studies. JAMA. 2021;325(7):686-7. https://doi.org/10.1001/jama.2020.9151
122. Alvarez G, Ceballos FC, Quinteiro C. The role of inbreeding in the extinction of a European royal dynasty. PloS one. 2009;4(4):e5174. https://doi.org/10.1371/journal.pone.0005174

9 Bibliography of the candidate's publications

9.1 Publications directly related to this thesis

1. **Madarász Bálint**, Fazekas-Pongor Vince, Szarvas Zsófia, Fekete Mónika, Varga János Tamás, Tarantini Stefano, Csiszar Anna, Lionetti Vincenzo, Tabák Adam G, Ungvari Zoltan, Forrai Judit. Survival and longevity of European rulers: geographical influences and exploring potential factors, including the Mediterranean diet — a historical analysis from 1354 to the twentieth century. **GEROSCIENCE: OFFICIAL JOURNAL OF THE AMERICAN AGING ASSOCIATION (AGE)** 2023 Paper: DOI: 10.1007/s11357-023-00957-5, 18 p. (2023)

2. **Madarász Bálint**, Forrai Judit. Számok és statisztikák szerepe az élettudományok fejlődésének történetében; az epidemiológia születése. **KALEIDOSCOPE: MŰVELŐDÉS- TUDOMÁNY- ÉS ORVOSTÖRTÉNETI FOLYÓIRAT** 11: 23 pp. 95-107. (2021)

3. **Madarász Bálint** Megment vagy elpusztít: a higany és arzén gyógyászati karrierje I. rész higany **KALEIDOSCOPE: MŰVELŐDÉS- TUDOMÁNY- ÉS ORVOSTÖRTÉNETI FOLYÓIRAT** 10: 18 pp. 210-241. (2019)

4. **Madarász Bálint.** Megment vagy elpusztít: a higany és arzén gyógyászati karrierje. II. rész arzén. **KALEIDOSCOPE: MŰVELŐDÉS- TUDOMÁNY- ÉS ORVOSTÖRTÉNETI FOLYÓIRAT** 10: 19 pp. 137-146. (2019)

9.2 Publications not related to this thesis

1. Fekete Mónika, Csípő Tamás, Fazekas-Pongor Vince, **Madarász Bálint**, Csizmadia Zoltán, Tarantini Stefano, Varga János T. The Possible Role of Food and Diet in the Quality of Life in Patients with COPD: A State-of-the-Art Review. **NUTRIENTS** 15: 18 Paper: 3902, 20 p. (2023)

2. Fekete Mónika, Balazs Péter, Lehoczki Andrea, Forrai Judit, Dosa Norbert, Fazekas-Pongor Vince, Feher Agnes, **Madarasz Bálint**, Varga János T. The role of gut microbiome and its modification while regulating the defence mechanisms,particularly in severe COVID-19 cases. **MEDICINA INTERNACIA REVUO** 30: 2 pp. 154-166. (2023)

3. **Madarász Bálint.** Paradigmaváltás az orvoslásban - Paracelsus: A iatrokémia megjelenése a medicinában**.** Paradigmaváltás a tudományok, a technika és az orvoslás körében. Magyar Természettudományi Társulat (2022) pp. 108-120.

4. **Madarász Bálint.** Paracelsus - A iatrokémia megjelenése az orvoslásban és a paracelán medicina alapjai. **KALEIDOSCOPE: MŰVELŐDÉS- TUDOMÁNY- ÉS ORVOSTÖRTÉNETI FOLYÓIRAT** 10: 20 pp. 17-29. (2020)

5. Árva Dorottya, Mészáros Ágota, Szarvas Zsófia, **Madarász Bálint**, Fazekas-Pongor Vince, Fehér Ágnes, Ungvári Zoltán. A magyarországi koronavírus-járvány alakulása és a meghozott intézkedések időbeliségének és hatékonyságának összehasonlítása más európai országokkal. **ORVOSKÉPZÉS** 95: 3 pp. 450-459. (2020)

10 Acknowledgement

The 3.5 version of ChatGPT, developed by OpenAI, was used as a language tool to refine our writing and enhancing the clarity of our work.

I would like to express my deep gratitude to my supervisor and mentor, Prof. Dr. Judit, to whom I am profoundly thankful for her assistance and patronage. I am deeply grateful for her guidance throughout my academic journey, her trust from the very beginning, and for granting me a great degree of freedom and flexibility. I appreciate her invaluable advices, guidance, and the many lessons she has taught me.

I am very grateful to my co-supervisor, Dr. Vince Fazekas-Pongor, for his professional and statistical guidance, assistance, patience, tolerance, flexibility, and understanding. Without his support, this work could not have been realized

I would like thank to Prof. Dr. Zoltán Ungvári, who provided professional support and for the basic idea of the research topic, as well as the one who established the research framework for me. I also extend special thanks for granting me significant freedom and for his valuable advices.

I am grateful to Prof. Dr. Adam G. Tabak, whose professional advices and supervision were essential for the completion of this work just as our conversations.

I would like to thank to all my colleagues from the Institute of Preventive Medicine and Public Health especially to Dr. Mónika Fekete, Dr. Zsófia Szarvas, Dr. Stefano Tarantini, Hajnal Szentgyörgyi and Nikoletta Horváth.

I would also like to express my gratitude to Dr. Dénesi Tamás for his help and support, as well as to Andrea Basso for his assistance and help.

I would like to extend a special thanks to all the staff at Semmelweis Medical History Library and Archives for their assistance, particularly to Dr. Katalin Kapronczay. Especially I am grateful to Dr. László András and to Dr. Károly Kapronczay who is unfortunately no longer with us.

I would like to thank everyone for their support, especially Professor Hilmi Orhan, Professor Isik Özgüney, Professor Tatiana da Ros, Nóra Seres, Esra Aydemir, Beatrice Perisutti, Jawad , Professor Lénárt Imre, Professor Dr. Magdolna Dank, Dr. Mate A. Balázs, Sayam Ghosal, the Arkis and Neconini families, Lidia, Irene, and Karakan, Mr. Fogg, Mr. Jinn, Mr. Lucas, Miss Mitsi, Mr. and Mr. Barillé, Mr Phill, Miss Marigold, and Samson, to all my friends and to the Fellowship of Room 215, and the H. L. P. G. Group.

Finally, I would like to express my deepest gratitude and love to my parents and family for their unwavering support and for always standing by my side.

List of tables and figures

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