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ECONOMIC AND SOCIAL IMPACT OF CARDIOVASCULAR EVENTS IN LITHUANIA

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Economic and Social Impact of Cardiovascular Events in Lithuania

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Signed

Teodors Muzis
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03.04.2023.

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Abbreviations

ACS – acute coronary syndrome
ASCVD – atherosclerotic cardiovascular disease
BMI – body mass index
CHD – coronary heart disease
CPRD – Clinical Practice Research Datalink
CV – cardiovascular
CVD – cardiovascular disease
DALYs – disability adjusted life years
DDD – defined daily dose
EAS – European Atherosclerosis Society
ESC – European Society of Cardiology
EU – European Union
FH – familial hypercholesterolemia
FOURIER – A phase 3, double-blind, randomised, placebo-controlled, multicentre study to evaluate the effect of additional LDL-C reduction on major cardiovascular events when evolocumab is used on top of statin therapy in patients with clinically evident CVD.
GDP – gross domestic product
HF – heart failure
HR – hazard ratio
IHD – ischemic heart disease
IS – ischemic stroke
LDL-C – low-density lipoprotein-cholesterol
LLT – lipid-lowering therapy
LPA – Lithuanian Pharmacoeconomic Analysis
LY – life years
MACE – major adverse cardiovascular event
MI – myocardial infarction
MTD – maximally tolerated dose
NF – non-fatal
NASCVD – nonatherosclerotic cardiovascular disease
oASCVD – other atherosclerotic cardiovascular disease comprises all CV disease other than IHD and IS, i.e., transient ischemic attack, atherosclerosis and other diseases of artrites, heart failure and haemorrhage stroke
OSP – Official Statistics Portal, Lithuania
PAD – peripheral arterial disease
PCSK9 – proprotein convertase subtilisin/kexin type 9
PCSK9i – proprotein convertase subtilisin/kexin type 9 inhibitors
PP – primary prevention
QALY – quality-adjusted life year(s)

RHD – rheumatic heart disease
RR – rate ratio
SoC – standard-of-care (treatment that is accepted by medical experts as the most appropriate for a certain type of disease in a particular setting).
SP – secondary prevention
UA – unstable angina
WHO – World Health Organization
YLD – years lived with disease
YLL – years life lost

Abstract

Cardiovascular diseases are the primary cause of death worldwide; in Lithuania, cardiovascular diseases account for almost half of the yearly deaths. In addition to the large mortality burden, non-fatal cardiovascular events decrease the quality of patients' life and productivity and increase the need for health care services as well as informal care.

In this research, we assess the burden of cardiovascular disease in Lithuania by employing a Markov cohort model with a time horizon of 30 years. We assess both direct (medical healthcare costs) and indirect (productivity loss due to absenteeism and presenteeism, unpaid work loss being replaceable by caregivers) costs. This holistic perspective enables us to understand the wide-scale economic and social consequences of cardiovascular diseases in Lithuania. The results show that the 74,324 cardiovascular events predicted for 2021 cost the Lithuanian economy around EUR 1.42 billion, equalling 2.53% of the GDP.

JEL codes: *H51, D61*

1. Introduction

WHO (2021) estimated around 17.9 million deaths were caused by cardiovascular diseases (CVD) worldwide in 2019, which accounted for 32% of all deaths. In addition to the enormous mortality burden, non-fatal cardiovascular events often cause permanent deterioration of a patient's quality of life. On the one hand, the productivity of the affected population decreases, which is associated with a significant economic output loss. On the other hand, the patient requires both direct medical care and informal care, which poses a high economic burden on society. Hence, it is vital to evaluate the impact of cardiovascular diseases by accounting for both direct medical costs, losses from decreased productivity, and the necessity for increased informal caregiving (Pemberton-Ross et al., 2019).

In general, a comprehensive assessment of the burden of cardiovascular disease is lacking; there are only a few studies assessing both the direct and indirect costs as well as the consequences and potential cost savings from novel medications. As noted by Pemberton-Ross et al. (2019), most studies focus on the direct impact and burden it places on the healthcare system. However, empirical evidence by Kotseva et al. (2019) suggests that indirect costs are as significant as direct healthcare costs. By disregarding indirect costs, the total disease burden related to CVD is significantly underestimated. One needs to account for productivity loss due to absenteeism, presenteeism, and unpaid work loss to assess CVD's economic and social consequences more accurately. Absenteeism is defined as absence from work during hospitalization and recovery after experiencing a non-fatal CV event. Presenteeism refers to lowered productivity due to reduced performance after returning to the workplace following a CV event. Unpaid caregiver time captures informal care provided to a CV patient by a relative or friend, which is lost working time to society (Kotseva et al., 2019). Hence, a more holistic approach is required to understand the economic and social consequences of CV disease.

In this study, we assess the burden of cardiovascular disease in Lithuania. According to OECD (2021), the population of Lithuania has the lowest life expectancy in the European Union, mainly driven by high mortality from cardiovascular diseases. CVD accounted for around 35% of deaths, the highest mortality in the EU (OECD, 2021). In addition, Urbonas et al. (2020) survey documents a dramatic health situation in Lithuania, with around 20% of surveyed patients facing an exceptionally high CVD risk. The low life expectancy, high mortality rate, and high proportion of patients with exceptionally high CVD risk highlight the importance of

comprehensively assessing the burden of cardiovascular disease in Lithuania – its full economic and social cost. Currently, there is a lack of research in this area.

In 2015, two proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) received marketing authorization in the European Union, offering potential treatment for high CVD-risk patients (Blind et al., 2021). End of 2020, The European Medicines Agency also authorized inclisiran which interferes with RNA (genetic material) to limit the production of PCSK9 (EMA, 2023). All these inhibitors reduce low-density lipoprotein-cholesterol (LDL-C) levels, one of the leading causes of CVDs (Laučytė-Cibulskienė et al., 2017). In addition to the currently marketed PCSK9 inhibitors, small molecule drugs and vaccines are also being researched and developed with the aim of optimizing pharmacotherapeutic lipid lowering strategies. Early treatment can prevent the risk of experiencing a CV event and lower the economic burden of the disease. According to Pemberton-Ross et al. (2019), the percentage of patients achieving the target LDL-C levels would rise from 36% to 79% if the current standard of treatment is replaced by PCSK9i treatment.

This research aims at assessing the impact of cardiovascular disease in Lithuania. In order to do so, we assess direct costs (healthcare costs) and indirect costs (productivity loss due to absenteeism and presenteeism and unpaid work loss being replaceable by caregivers) of cardiovascular disease in Lithuania. Hence, we set the following research question: **What is the economic burden of cardiovascular diseases in Lithuania?**

2. Literature review

A vast amount of research assesses the burden of CVD both globally and in Europe. In this section, we first define and classify CVD (Section 2.1). Afterwards, to understand the leading causes of the disease burden, we comprehensively assess the main CVD risk factors (Section 2.2). Section 2.3 describes guidelines and the most common therapies used to lower the level of low-density-lipoprotein cholesterol for patients with a risk of developing CVD: statins, ezetimibe, and PCSK9i inhibitors. Section 2.4 summarizes the most recent statistics about the burden of CVD in Europe. Finally, section 2.5 describes the burden of CVD in Lithuania; we investigate the mortality statistics, assess the clinical burden and risk factors, and elaborate on the economic implications.

2.1. Classification of cardiovascular diseases

According to WHO (2021), cardiovascular disease (CVD) is an aggregated term for disorders related to the heart and blood vessels. This disease group includes coronary heart, cerebrovascular, peripheral arterial, rheumatic heart, congenital heart diseases, deep vein thrombosis, and pulmonary embolism. The Institute of Health Metrics and Evaluation (IHME) classifies CVDs resulting from 11 cardiovascular causes: (*i*) rheumatic heart disease (RHD); (*ii*) ischemic heart disease (IHD); (*iii*) stroke; (*iv*) hypertensive heart disease (HHD); (*v*) cardiomyopathy and myocarditis; (*vi*) atrial fibrillation and flutter; (*vii*) aortic aneurysm; (*viii*) peripheral artery disease (PAD); (*ix*) endocarditis; (*x*) non-rheumatic valvular heart disease; (*xi*) other cardiovascular and circulatory diseases (IHME, 2022).

Both atherosclerotic (ASCVD) and nonatherosclerotic (NASCVD) cardiovascular diseases are incorporated into the classification, with ASCVD being the most prevalent disease and the leading cause of CV disease deaths worldwide (Barquera et al., 2015). Nevertheless, NASCVD can also be considered a significant cause of sudden cardiac death. Hill et al. (2010) report that although the non-atherosclerotic coronary disease is linked to sudden cardiac death in all age groups, it typically poses an increased risk in the younger male population. This highlights the importance of carefully investigating and identifying all cardiac symptoms to diagnose patients early and prevent the risk of experiencing a fatal CV event. Section 2.2 shall explore some of the main factors causing CVDs.

2.2. CVD risk factors

The four most important risk factors include sociodemographic factors, environmental factors, health behaviours, and clinical risk factors. Table 1 summarises the most common risk factors associated with developing CVD. In addition, the table shows the main components of the risk factors and the related literature.

Among others, older people generally have a higher risk of developing CVD (Ciumărnean et al., 2021). Rodgers et al. (2019) argue that while age is an independent CVD risk factor, the ageing process is often associated with developing conditions such as obesity, diabetes, frailty, which in turn increases the likelihood of cardiac complications.

Table 1. Risk factors associated with developing CVD.

Risk factor	Component and comment	Related literature
Sociodemographic factors	**1)** *Age* (CVD risk usually increases with age) **2)** *Genetics* (family history can explain a higher risk of CVD at a young age) **3)** *Gender* (some CV causes are more prevalent in one gender) **4)** *Ethnicity* (higher CVD risk for black individuals and South Asian compared to white individuals)	**1)** Ciumărnean et al., 2021; Rodgers et al., 2019 **2)** Daniels & Hayman, 2011; Winham, de Andrade & Miller, 2015 **3)** Ritter et al., 2020; Gao, Chen, Sun & Deng, 2019; Perez-Lopez et al., 2010 **4)** Ho et al., 2022; Chaturvedi, 2003
Environmental risk factors	**5)** *Air pollution* (considered an integral CVD risk factor, causing up to 30% of total CVD mortality) **6)** *Environmental noise* (accounts for around 48,000 new IHD cases and 12,000 deaths per year in Europe) **7)** *Neighbourhood characteristics* (incidence and fatality rates are higher for people from deprived neighbourhoods) **8)** *Urbanisation* (overcrowding, social deprivation, and stress are some aspects impacting CV health)	**5)** Lelieveld et al., 2019; Chaulin & Duplyakov, 2021 **6)** WHO, 1999; Timmis et al., 2022 **7)** Winkleby, Sundquist & Cubbin, 2007; Bhatnagar, 2017 **8)** Timmis et al., 2022; Cosselman, Navas-Acien & Kaufman, 2015
Health behaviours	**9)** *Smoking* (increases mortality from all health causes, especially ASCVD; more than 30% of IHD mortality is related to active smoking) **10)** *Alcohol consumption* (positive association found between alcohol consumption and MI) **11)** *Exercising* (reduced risk of IHD and stroke incidence by 20-30% for males and 10-20% for females) **12)** *Diet* (strongly related to CV risks)	**9)** Lakier, 1992; Burns, 2003; Gallucci et al., 2020 **10)** Connor & Hall, 2018 **11)** Li & Siegrist, 2012 **12)** Jacobsen et al., 2009; Kromhout, 2001; Pan, Lin, Hemler, & Hu, 2018
Clinical risk factors	**13)** *Blood pressure* (the leading risk factor of CVD) **14)** *Cholesterol* (LDL-C is linked to high CVD exposure) **15)** *Obesity* (incidence of obesity-related cardiac dysfunction increases with the prevalence of obesity) **16)** *Diabetes* (diabetes doubles the risk of death, and almost half of the global deaths are driven by CVD)	**13)** Timmis et al., 2022; Vasan et al., 2001; Fuchs et al., 2020 **14)** Nelson, 2013; Ueda et al., 2018; Stone et al., 2014; Parums, 2021; Ference et al., 2017; Rikhi & Shapiro, 2022; Ferhatbegović et al., 2022; Nelson, 2013 **15)** Barquera, 2015; Bastien et al., 2014 **16)** Ma et al., 2022; Ortega et al. 2015; Van Gaal et al., 2006; Timmis et al., 2022

Sources for risk factor classification: Ada, 2022; Timmis et al., 2022

Clinical risk factors are of major importance. Most importantly, *high blood pressure* is the leading risk factor for CVD (e.g., Timmis et al., 2022; Vasan et al., 2001; Fuchs et al., 2020). *Cholesterol* is another key CVD risk factor, especially hypercholesterolemia – a lipid disorder that causes excessive elevation of cholesterol concentration in the blood. *Low-density lipoprotein*

cholesterol (LDL-C) is explicitly linked to high exposure to CVD (Nelson, 2013; Ueda et al., 2018). For example, Ueda et al. (2018) found that moderate LDL-C levels in the long-term bear similar coronary heart disease (CHD) risks as high LDL-C levels in the short term. Familial hypercholesterolemia (FM, clinical diagnosis) and LDL-C has become the primary target in many European CV health programs due to their modifiable nature and the promising results in preventing ASCVD (Stone et al., 2014; Parums, 2021). The causality of elevated LDL-C and ASCVD has been proven in many studies (e.g., Ference et al., 2017; Rikhi & Shapiro, 2022; Ferhatbegović et al., 2022).

2.3. Treatment of cardiovascular disease

Although the exact cause of CVD is unknown, several risk factors might increase the probability of developing CVD (NHS, 2022). If a patient has multiple risk factors, chances of developing CVD increase. One such risk factor is high cholesterol, a fatty substance in the blood. In the case of high cholesterol, the blood vessels might narrow and increase the risk of developing a blood clot resulting in CVD (NHS, 2022). If a patient has an exceptionally high risk of developing CVD a result of having elevated levels of cholesterol in their bloodstream, it is recommended to take medicines to reduce the risk (NHS, 2022).

2.3.1. Lipid-lowering guidelines

A vast amount of empirical evidence shows that low-density lipoprotein cholesterol (LDL-C) is explicitly linked to high exposure to CVD (e.g., Maher et al., 1995; Nelson, 2013; Penson et al., 2000; Silverman et al., 2016; Ueda et al., 2018). For example, in a meta-analysis covering 312 175 participants, Silverman et al. (2016) show that the relative risk of major vascular events (e.g., CV death, acute MI, IS) is associated with LDL-C level.

Several European guidelines emphasize the importance of lowering LDL-C levels based on patients' risk – the higher the risk, the lower the target LDL-C level shall be (Mach et al., 2020). According to the joint guidelines of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) for the management of dyslipidaemias (Mach et al., 2020), the first step is to identify the patient's risk: very high risk, high risk, intermediate risk or low risk, and set the targets:

- Very high risk - LDL-C reduction ≥ 50% from baseline and achieve LDL-C target <1.4 mmol/L.
- High risk - LDL-C reduction ≥ 50% from baseline and achieve LDL-C target <1.8 mmol/L.
- Moderate risk - LDL-C target <2.6 mmol/L.
- Low risk - LDL-C target <3.0 mmol/L.

Patients with confirmed ASCVD are classified as very high cardiovascular risk patients. In the first place, doctors prescribe statins to these patients in combination with lifestyle advice to correct LDL-C levels, but a significant proportion of them do not achieve their treatment goals, i.e., the set LDL-C targets. According to the 2019 guidelines of the ESC and EAS (Mach et al., 2020), if LDL-C targets are not reached, ezetimibe and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are added to statin therapy.

The NHS (2020) also provides detailed guidance for lipid management for primary and secondary prevention of CVD. In primary prevention, doctors shall consider *statin* therapy for adults with no established CVD but at risk of developing one. High-intensity statin treatment should reduce by a minimum of 40% the non-high-density lipoprotein cholesterol from baseline (NHS, 2020). If the maximum tolerated statin dose does not achieve this minimum reduction after three months, doctors should consider adding 10 mg of *ezetimibe* daily and refer the patient to a specialist.

In secondary prevention, if the maximum tolerated dose of statin does not control LDL-C sufficiently after three months, the doctor shall confirm statin adherence and consider the following two options: *i*) ezetimibe as monotherapy; *ii*) ezetimibe and bempedoic acid in combination when ezetimibe alone does not control LDL-C sufficiently (NHS, 2020). If LDL-C remains higher than 2.5 mmol/L despite treatment with ezetimibe alone or combined with bempedoic acid, the specialists shall consider *injectable therapies (*inclisiran or *PCSK9i*) (NICE 2016a,b; NICE, 2021). The guidelines of NHS (2020) are based on extensive empirical evidence and are in line with the suggestions of several scientific papers (e.g., Dayar & Pechanova, 2022).

2.3.2 Lipid lowering therapies in Lithuania

The primary lipid lowering therapies used in Lithuanian are statins. PCSK9 inhibitors are not reimbursed, while ezetimibe and its combination with statins is reimbursed only for a small proportion of patients (very high-risk patients with ICD-10 code E78). It should be noted that in Lithuania, from March 2023 the targets for ezetimibe and its combinations with statins in very high-risk patients are set in line with the 2019 guidelines of the ESC and EAS (Mach et al., 2020), i.e., an LDL-C target of <1.4 mmol/L.

2.3.3. Therapeutic advances in CVD management

In addition to the currently marketed PCSK9 inhibitors and other lipid modifying agents, small molecule drugs and vaccines are also being researched and developed with the aim of optimizing pharmacotherapeutic lipid lowering strategies. Although the binding interface of PCSK9 protein is rather flat and open, there is promising results in the area of small molecule drugs. BMS-962476 is a recently developed small molecule that blocks the biological activity of PCSK9 by preventing the binding of LDL receptor (Liu et al, 2022).

Finally, vaccine drugs are also under development. The short half-life *in vivo* of the widely used monoclonal antibodies is associated with frequent administration and high cost, which urged the need for vaccine inhibiting circulating PCSK9 activity. Recently, the L-IFPTA + vaccine showed a high IgG response to PCSK9, which induces the production of a PCSK9 antibody (Liu et al, 2022).

2.4. The burden of cardiovascular diseases in Europe

Cardiovascular diseases (CVD) have been Europe's primary cause of death and morbidity for many years (Timmis et al., 2022). Nevertheless, statistics by Timmis et al. (2022) show a decreasing trend of CVD incidence for the most recent years when compared to the beginning of the 21st century. However, prevalence rates remained the same in most European countries, while a slight increase can be observed in the Baltic states (ESC, 2019; Timmis et al., 2022).

The most recent ESC Atlas report on cardiovascular disease indicates that around 113 million people across ESC member countries[1] live with CVD (ESC, 2019). CVD is the reason for almost half of all deaths in Europe. The statistics suggest that CVD caused 2.2 million female and 1.9 million male deaths in 2021 in ESC countries, corresponding to 45% of all female and 39% of all male deaths (ESC, 2019). Ischemic heart disease (IHD), i.e., coronary heart disease and myocardial infarction, are the two most frequent causes of CVD deaths. Disability-adjusted life years (DALYs) is a widely used measure of disease burden. It reflects ill health, disability, or death effects on the cumulative number of years lost; it is a concise measure of health lost due to CVDs. The measure is the sum of years of life lost (YLL) from early deaths and years lived with the disease (YLD). Data suggest that CVDs accounted for 85 million all-age DALYs among ESC countries in 2019, from which 46 million are attributable to IHD, 23 million to stroke, and roughly 1% of DALYs are accountable to PAD (Timmis et al., 2022).

More than 12 million new CVD cases are estimated annually in ESC countries (Timmis et al., 2022). The financial burden of CVD on the EU economy has been estimated to cost around 210 billion EUR a year; the most prominent component is direct healthcare cost (53%), followed by indirect costs: productivity losses (26%) and informal care (21%). In general, the limited availability and the lack of the most recent up-to-date data from all countries prevent a more precise assessment of the economic burden of CVD (Timmis et al., 2022).

Table 2 summarises the reported deaths of all causes and CVD in Europe in 2019. Based on the cause-specific mortality database of WHO (2022), deaths of all causes amounted to 9.1 million in Europe, from which 4.6 million were males and 4.5 million were females (WHO, 2022). At the same time, deaths from CVD amounted to 3.9 million, of which 1.8 million were attributable to males and 2.1 million to females. Cardiovascular diseases amounted to 43% of total deaths in Europe. The burden of CVD is more common for older people; the highest mortality (48%) from CVD is observed in the 70+ age group. Mortality rates due to CVD are increasing by age; significant death rates have already been reported from 30 years of age, as seen in Table 2. This phenomenon is associated with reduced productivity, early retirement, and elevated healthcare costs.

[1] EU countries plus Albania, Algeria, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Egypt, Georgia, Iceland, Israel, Kosovo, Kazakhstan, Kyrgyzstan, Lebanon, Libya, Moldova, Montenegro, Morocco, North Macedonia, Norway, Russia, San Marino, Serbia, Switzerland, Syria, Tunisia, Turkey, Ukraine, United Kingdom, Uzbekistan

Table 2. Deaths of all causes and CVD in Europe by different age groups in 2019.

		0-4 years	5-14 years	15-29 years	30-49 years	50-59 years	60-69 years	70+ years	Total
All causes	Male	50 348	9 854	62 503	362 363	503 536	927 179	2 691 145	**4 606 928**
	Female	38 524	7 186	25 489	157 706	245 230	526 394	3 501 904	**4 502 433**
	Total	**88 872**	**17 040**	**87 992**	**520 069**	**748 766**	**1 453 573**	**6 193 049**	**9 109 361**
CVD	Male	337	299	4 917	92 852	176 384	365 468	1 146 495	**1 786 752**
	Female	284	275	2 320	29 480	62 178	186 816	1 806 713	**2 088 066**
	Total	**621**	**574**	**7 237**	**122 332**	**238 562**	**552 284**	**2 953 208**	**3 874 818**
% of CVD from all causes	Male	1%	3%	8%	26%	35%	39%	43%	**39%**
	Female	1%	4%	9%	19%	25%	35%	52%	**46%**
	Total	**1%**	**3%**	**8%**	**24%**	**32%**	**38%**	**48%**	**43%**

Source: WHO (2022)

2.5. The burden of cardiovascular diseases in Lithuania

2.5.1. Country overview

According to OECD (2021), life expectancy in Lithuania is the third lowest in the EU, 5.5 years below the average in the EU countries, based on 2020 data. The gender gap in life expectancy in Lithuania is the widest in the EU, indicating that women live approximately ten years longer than men, generally due to high male mortality from ischemic heart diseases (IHD) and alcohol consumption among Lithuanian males. Preventable mortality in Lithuania is twice as large as the EU average (OECD, 2021).

Data from OECD (2021) suggest that the mortality from IHD in Lithuania is the highest among other EU countries. Nearly half of the death events in Lithuania can be attributed to environmental and health behavioural risk factors. For instance, deaths related to dietary risks are 8 percentage points higher in Lithuania (25%) compared to the EU average (17%). Other risk factors such as smoking, alcohol consumption, low physical activity, and air pollution altogether accounted for 27% of all deaths in 2019 in Lithuania.

OECD Country Health Profile 2021 (OECD, 2021) unveiled that in 2019 the public health expenditure was lower in Lithuania (EUR 1,885 per capita) than the EU average (EUR 3,521). While 80% of health expenditure is publicly financed in the EU on average, only two-thirds of health spending in Lithuania is public, with the rest privately financed. Lastly, health spending, including both public and private funding, in Lithuania accounts for only 7% of the GDP, while it was 9.9% in the EU on average.

2.5.2. CVD incidence, prevalence and mortality in Lithuania

Lithuania is one of the exceptionally high-risk countries for CVD in Europe (Miglinas et al., 2022). The median annual incidence rate for CVD across EU member states was 747.6 per 100 000 inhabitants, meanwhile median prevalence was 6 963 per 100 000 inhabitants (Timmis et al., 2022). Both figures from Lithuania are higher, with incidence standing at 900 and prevalence at 7 170 per 100 000 inhabitants. Furthermore, according to Eurostat (2022), in 2019 Lithuania documented 731.7 total CVD-related deaths per 100 000 inhabitants, nearly twice as much as the EU average of 367.6 deaths. The difference is even more significant among males – 952.0 deaths per 100 000 inhabitants in Lithuania compared to 438.8 in the EU. Table 3 shows the number of total deaths by cardiovascular causes, based on the Centre of the Lithuanian Institute of Hygiene's newest data for 2021 (Higienos Institutas, 2022a).

Total ASCVD deaths accounted for approximately 38.5% of all deaths in Lithuania in 2021. The most common cause of ASCVD deaths was oASCVD being responsible for 82.29% of total ASCVD death. Ischemic stroke was responsible for 11.67% of the total ASCVD deaths, while myocardial infarction accounted for 6.03%.

Table 3. Causes of death related to ASCVD in Lithuania in 2021.

CV-related cause	The number of deaths (total)	% of total ASCVD deaths
MI	1,110	6.03%
IS	2,147	11.67%
oASCVD	15,137	82.29%
Total ASCVD deaths	**18,394**	
Total deaths	**47,746**	

Source: Higienos Institutas (2022a); Causes of Death Finder (2023)

According to the Global Burden of Disease Study 2019, CVDs accounted for 333 thousand all-age DALYs in Lithuania in 2019, from which 207 thousand were attributable to IHD and 96 thousand to stroke (Vos et al., 2020). Age-standardised DALYs for CVD per 100,000 individuals in Lithuania in 2019 for CVD amounted to 5,830, from which 3,490 were attributable to IHD and 1,430 to stroke. CVD is the main component for DALY counts in Lithuania, responsible for approximately one-third of total DALYs from all causes. Overall, 81%

of all-age CVD DALYs were attributable to IHD in Lithuania in 2019, while among ESC countries, IHD amounted to roughly 54% of all-age CVD DALYs (Timmis et al., 2022).

2.5.3. Risk factors associated with CVD in Lithuania

Laucevičius et al. (2019) analysed the results from the Lithuanian primary prevention program (LitHiR) implemented in 2006 to identify *clinical risk factors* causing CVDs. The authors documented that arterial hypertension instances gradually decrease, while dyslipidemia prevalence does not. Other cardiovascular disease risk factors show a slightly decreasing prevalence. Over the past ten years, the mortality rate from cardiovascular diseases among the middle-aged group has dropped by over one-third. The working age group (ages 45 to 65) had the highest prevalence and mortality from CVD.

Ischemic heart diseases (IHDs) are Lithuania's most prevalent CVD causes of incidence and death. A study by Wang et al. (2021) shows the ranking of the most common risk factors of IHD globally and concludes that *high blood pressure* is the most critical cause of the DALY rate of IHD in Eastern Europe. The second most significant risk factor is high LDL-C, followed by smoking, high body mass index (BMI), and diet.

In Lithuania, several important CVD-related clinical targets (*BMI*, *blood pressure*, *LDL-C*) are often not met. Urbonas et al. (2020) assessed whether the key clinical targets were met for 201 patients at high risk of developing CVD in Lithuania enrolled in the EUROASPIRE V survey. The authors reported that only 15.4% of the patients met the BMI targets. Burokienė et al. (2017) also showed on a volunteer sample that BMI was above targets for both men and women and was significantly higher for participants with CVD.

In the literature, two studies assessed whether the *target blood pressure* in Lithuania is met (Urbonas et al., 2020; Kotseva et al., 2016). Urbonas et al. (2020) documented that only 57.2% of the patients achieved target blood pressure. Kotseva et al. (2016) assessed lifestyle and risk factor management in people at high risk of CVD in several European countries, including Lithuania. The authors found that in Lithuania, the target blood pressure with no blood pressure-lowering medication was observed for 29% of the male patients (the lowest in the sample) and 58.8% of the female patients. At the same time, blood pressure targets for patients on blood pressure-lowering medication were achieved for 32.9% of male and 45.7% of female patients. Both figures were below the sample average of 35.0% and 48.4%, respectively.

Regarding the *target LDL-C levels,* five studies report reliable estimates for Lithuania (Burokienė et al., 2017; Kotseva et al., 2016; Laucevičius et al., 2019; Urbonas et al., 2020; Viigimaa et al., 2014). On the volunteer sample, Burokienė et al. (2017) document an LDL-C concentration of 4.1 mmol/L both for males and females, which is substantially higher than the LDL-C estimates in other European countries. Viigimaa et al. (2014) assessed statin-treated patients with a mean age of 66. They concluded that the Baltic states do not reach target lipid levels and have a very substantial risk of CVD. Of the 1,797 patients studied, 63.4% had cardiovascular disease, and 77.8% were at high risk for CV complications. The authors documented that the target LDL-C level was not reached for 80.7% of the enrolled patients. Laucevičius et al. (2019) concluded the same; the authors report that only 19.8% of middle-aged Lithuanian adults had LDL-C < 3 mmol/l and more women than men had LDL-C concentration higher than 3 mmol/l. When assessing only patients with a high risk of developing CVD, Urbonas et al. (2020) documented that only 4.5% reached the LDL-C targets. For patients treated with dyslipidaemia, Kotseva et al. (2016) documented that only 32.7% achieved the LDL-C target of <2.5 mmol/l. This target was among the lowest in Lithuania for patients with no lipid-lowering medication and the lowest for patients on lipid-lowering medication compared to the 13 European sample countries. Overall, based on the literature reviewed, we can conclude that there is a need for appropriate CVD-related health interventions in Lithuania, where risk prevention control is unsatisfactory for BMI, blood pressure, and LDL-C parameters.

2.5.4. Economic burden of CVD in Lithuania

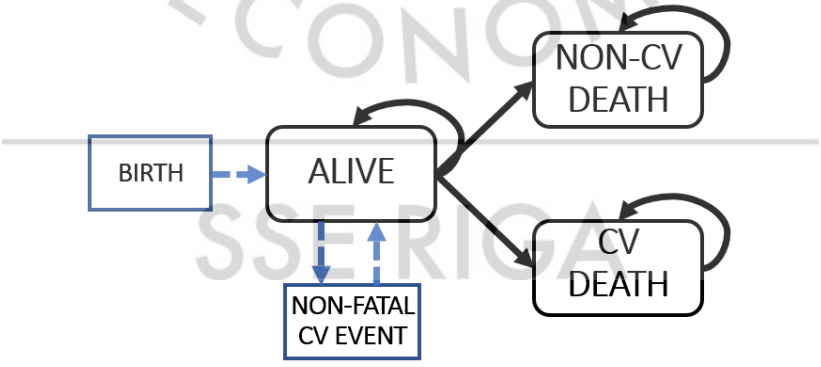
A report by Eurostat on Health Expenditures by Diseases and Conditions documents that expenditure on circulatory disease as a percentage of total health expenditure in Lithuania accounts for the largest share of allocated current healthcare spending, estimated at 23.5% (Eurostat, 2016). The corresponding figure for the other ten countries assessed by the Eurostat ranges from 10.4% in Finland to 22.5% in Bulgaria. A study by Nedzinskienė et al. (2021) assessed the healthcare costs in Lithuania for patients with multimorbidity, including several cardiovascular diseases (IHD, HF, stroke). The authors found that for patients with multimorbidity, 51.5% of total expenditure was allocated to inpatient treatment and 30.9% to reimbursed medications. The highest share of expenditure (60%) across age groups was attributable to patients aged 65-84.

3. Methodology

We follow the methodology developed by Pemberton-Ross et al. (2019) and employ a population-based Markov cohort model. We distinguish a country's population into three discrete health states: *alive*, *CV death*, and *non-CV death* (Figure 1). The model assumes a one-year-long cycle, a widely used time frame for the economic evaluations of LLTs (Wei et al., 2017). During each cycle, a person can transition from the *alive* health state to the other two states. There is no limit on the number of CV events a person can experience during his/her life. The health states and the transformations between them can be summarised as follows:

- *Alive*: this health state includes the total population of a country in the year when the model starts and adds the projected number of births in the future years. The population classified in this group can either experience: (*i*) a non-fatal CV event and remain in the alive health state; in this case, no change in health state is observed as there is no deviation from the initial CV event risk; (*ii*) a fatal CV event and move to the CV death health state; or (*iii*) a fatal non-CV event and move to a non-CV death health state.
- *CV death*: a person moves to this health state from the alive state after undergoing a fatal CV event.
- *Non-CV death*: a person moves to this health state from the alive state after undergoing a fatal non-CV event.

Figure 1. Structure of the Markov Model.



Source: Figure reproduced from Pemberton-Ross et al. (2019)

The Markov cohort model delivers the epidemiological component of the research. The model predicts the number of CV events in the population by age for every year, which can then be separated into different disease types. These include two most prevalent CV event types:

myocardial infarction (MI) and ischemic stroke (IS). All other non-fatal ASCVD conditions are grouped together and labelled as other atherosclerotic CV diseases (oASCVD). In addition, there is also the CV death event. Relying on Lithuanian healthcare data, specific event rates (probabilities) can be estimated for the different types of diseases, which are needed to estimate direct healthcare costs. Augmenting the model with information on time lost per CV event, the model estimates the indirect costs stemming from productivity and unpaid work loss. Information on time lost (absenteeism, presenteeism, and caregiver time) is derived from the study of Kotseva et al. (2019).

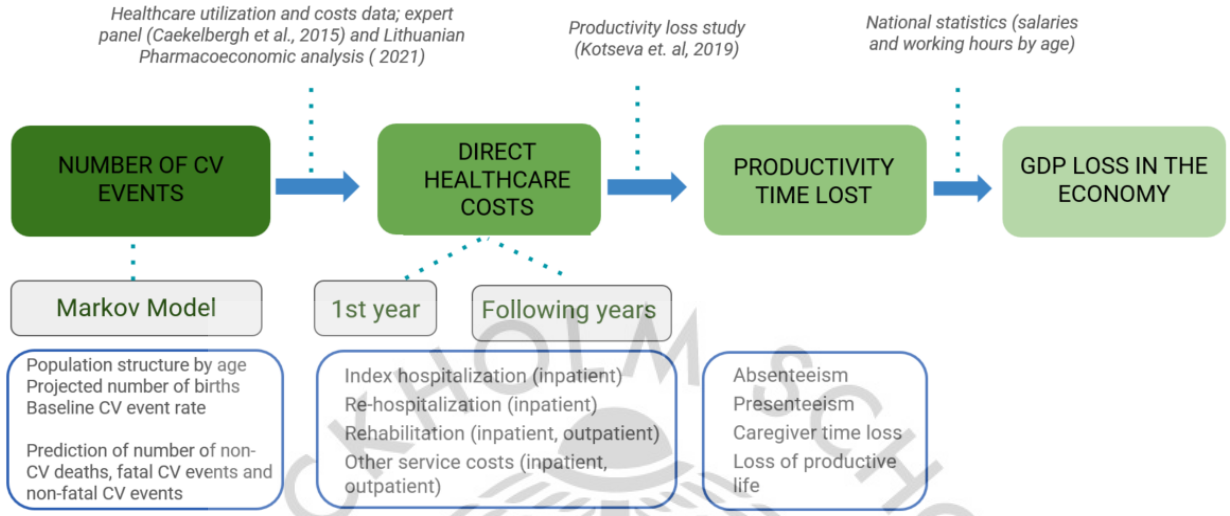
We estimate the productivity loss from time spent away from work and unpaid caregiver work loss using the human capital approach. While being a predominant method in healthcare studies, it has often been criticised for overestimation of productivity losses (Pike et al., 2018). Hence, two adjustments are made in our approach compared to Pemberton-Ross et al. (2019). First, our study uses the average daily income instead of the GVA approach employed by Pemberton-Ross et al. (2019). The human capital approach consists of two major steps:

- estimating the economic loss related to patients with CVD in the year of the CV event;
- estimating the economic loss related to patients with CVD in the years following the CV event.

Second, we include a conservative estimate for the unpaid work loss. Unpaid work is a vital component of indirect costs, and it consists of several elements, such as caregiver time and voluntary work in society. In this research, we only assess the unpaid work loss linked to caregiving. We aim to assess the unpaid work of informal caregivers helping the patient after a non-fatal CV event which would be replaceable by caregivers. Goods and services not sold on the market (e.g., household work) or volunteer work in society (non-profit organisation, church) are not considered even if they are socially or culturally valuable activities. They are assumed to be replaced by other volunteers without additional cost to society; this approach allows us to arrive at a conservative estimate typically preferred by national health insurance funds. Figure 2 shows the general structure of the model as described previously. A full index of the model sheets and their contents can be found in Appendix 1.

The model predicts the number of CV events by type, including MI, IS, oASCVD, and CV death, as well as the associated direct healthcare costs incurred in Lithuania.

Figure 2. The general structure of the model.



Source: Created by the authors

The model is set up with a flexible time horizon of up to 30 years (from 2021 to 2051) to fully explore and understand the long-term impact of CVD on patients, the healthcare system, the economy, and society. Since it is important to model the impact of CV events (deaths and long-term consequences) in an ageing society to fully capture the burden of CVD in Lithuania, we use Lithuanian life tables up to the age of 120. Exploring the impact of the condition over a patient's lifetime has been widely used in similar disease and treatment settings (e.g., Wei et al., 2017).

4. Model inputs

4.1. Epidemiological inputs

4.1.1. General population

The current population at the beginning of 2021 constituted the initial population for the model. According to data from the Official Statistics Portal (OSP), the population in Lithuania was 2.81 million (Official Statistics Portal, 2023a). The general population is displayed by age to allow age-specific estimations of the baseline risk and the impact of CV events. This is necessary to account for the increased risk of CV events for older people and the different economic or social impacts CVD causes at different stages of life. The model includes estimates for the predicted number of births, non-CV, and CV deaths in the following years.

4.1.2. Baseline cardiovascular event rate

In the general population, the annual baseline CV event rate is the number of ASCVD events per year that patients are expected to suffer. The baseline CV event rate in the model is calibrated to predict the CV incidence in Lithuania. Observed CV events (deaths, incidence, prevalence) by ASCVD type in Lithuania for 2021 are presented in Table 4. The data was retrieved from the Lithuanian Institute of Hygiene (Higienos Institutas, 2022b). Incidence is defined as the number of people with at least one disease registered for the first time in a given period of time, and prevalence is the number of people with at least one illness previously registered in a given period (Higienos Institutas, 2022c). The total number of deaths caused by ASCVD in Lithuania in 2021 was 18,394, and the incidence – 93,683.

Table 4. Observed number of CVD events (deaths, incidence, prevalence) in Lithuania in 2021.

Disease type	Deaths	Incidence (new events)	Prevalence (all events)
MI	1,110	6,782	10,530
IS	2,147	12,872	19,234
oASCVD	15,137	74,029	190,995
Total ASCVD	18,394	93,683	220,759

Sources: Higienos Institutas (2022a); Higienos Institutas (2022b); Causes of Death Finder (2023)

We divided the total number of CV events by event type related to ASCVD based on the ICD-10 classification codes following the Strategies for Chronic Care guidelines (Strategies for Chronic Care, 2023) supplemented by expert opinion. ASCVD includes MI, IS, and oASCVD. The category of oASCVD includes diagnoses for patients at very high risk of cardiovascular disease: unstable angina, chronic coronary syndrome (stable angina), arterial revascularization, transient cerebral ischemic attack, aortic aneurysm, and peripheral arterial disease. The classification by disease types with the corresponding ICD-10 codes is summarised in Table 5.

Considering the classification by ICD-10 codes, the number of ASCVD deaths was estimated at 18,394 (see Table 4). The highest number of deaths (15,137) and incidence (74,029) resulted from oASCVD. Both the number of deaths and incidence were included in the model to predict the events up to 2051.

Table 5. The classification of ASCVD by disease types based on ICD-10 codes.

ASCVD diagnosis	ICD-10 codes	Classification in the model
Acute and subsequent myocardial infarction	I21-I23	MI
Cerebral infarction	I63	IS
Stroke, not specified as haemorrhage or infarction	I64	
Aortic aneurysm	I71	oASCVD
Elective coronary revascularization	Z95	
Peripheral artery disease	I73	
Stable/unstable angina	I20	

Sources: Higienos Institutas (2022b); Strategies for Chronic Care (2023)

As age is a major driver of CV event risk, it is crucial to distribute the predicted events over the population by age. The total number of events is distributed over the population so that the event rate increases with age in the same way as the model used by Pemberton-Ross et al. (2019), who use prediction by the regression model reported by D'Agostino et al. (2008). This specifies an equation determining how the CV event rate increases for each year of age by gender. The average rate weight *R(j)* for the male and female is taken as specified in Equation 1:

$$R(j) = \frac{1}{2}(exp(3.06117)^{ln(j)} + exp(2.32888)^{ln(j)}) \quad (1)$$

where *j* denotes age. This is then scaled uniformly to match the observed number of events and combined with the distribution of the total population by age to specify the event rate at each age in the model as seen in Equation 2:

$$E(j) = TE \cdot \frac{R(j)}{\{\Sigma_n R(n) \cdot P(n)\}} \quad (2)$$

where *E(j)* is the event rate at age *j*, *TE* is the total number of CV events, *P(n)* is the population at age *n*. The denominator is summed over all ages, *n*, in the model from 0 to 120.

A summary of the baseline CV rates in the general population is reported in Table 6.

Table 6. Summary of baseline CV rate.

	Baseline rate (per 100 patient-years)	Age	Source
General population	1.45	43[1]	Fit to OSP (2023) data

CV events include all the events: MI, IS, oASCVD, and CV death.
[1] CV event rate at the mean age of the population is given for illustration.

4.1.3. Event distribution

The estimated baseline CV event rates represent a composite CV event rate that includes all types of CV events. Therefore, the baseline rate is disaggregated to CV event-specific annual rates for MI, IS, other atherosclerotic CV events (oASCVD), and CV death using the distribution of events taken from Higienos Institutas (2022a,b) and Causes of Death Finder (2023) data exhibited in Table 7.

Table 7. Distribution of fatal and non-fatal CV events.

CV event	Event distribution
Non-fatal MI	7.66%
Non-fatal IS	14.49%
oASCVD	53.00%
ASCVD death	24.85%

Source: Higienos Institutas (2022a,b); Causes of Death Finder (2023)

The resulting CVD event-specific annual rates are converted into annual event risks that constitute the transition probabilities of the model. These probabilities determine the chances of transitioning between different health states during each cycle of the model.

4.1.4. Time-dependent transition probabilities

Patients face a risk of both CV events and non-CV death concurrently. Because these risks are based on separate sources of data, it is possible that the sum of all risks can exceed one. Such cases could lead to negative transition probabilities in a state transition model in extreme circumstances and give inaccurate results. To avoid this, a competing risk adjustment was implemented in the model similar to the approach of Maruszczak, Villa & Lothgren (2017),

whereby the probability of non-CV death in each cycle is computed first, and CV event-specific transition probabilities are then applied given that the individual remains alive.

Mortality rates from non-CV causes were obtained from national life tables that predict the changes in annual mortality rates over the years (Eurostat, 2021). Since the transition probabilities are subject to being alive and thus dependent on the mortality rates, time-dependent transition probabilities were incorporated into the model capturing the changes in mortality.

4.1.5. Mortality

Data from Higienos Institutas (2023a) show that 38.5% of deaths in Lithuania are due to CVD causes, while 61.5% are related to non-CVD causes. Mortality from non-CV causes is estimated by taking 61.5% of the mortality rates of the general population displayed in Lithuanian national life tables (Eurostat, 2021). As data was only available for each gender separately, the weighted average mortality rate by age was calculated based on the proportion of males and females in the total population in 2021. The same proportion was applied for the mortality rate prediction up to 2051. Mortality due to CVD is modelled separately; the estimation is based on CV events predicted by the model based on the baseline CV event rates and distribution of fatal events, as described in Section 4.1.4.

4.1.6. Resource use and costs

4.1.6.1. Direct healthcare costs. In this section, we report direct ASCVD-related medical costs from a healthcare payer perspective; costs of all healthcare services (inpatient and outpatient) covered by the Lithuanian National Sickness Fund, irrespective of the actual payer.

The direct medical costs of MI, IS, and oASCVD relevant to the national healthcare system were calculated based on index hospitalization, re-hospitalization, and other service costs by prior cardiovascular events (Vanagas, 2022). The frequency of services was estimated based on the assessment of healthcare utilisation and costs associated with cardiovascular events in Belgium using hospital disease database and expert panel data (Caekelbergh, Chevalier & Lamotte, 2015). Costs for respective services were estimated based on prices paid in 2021 for hospital services by the Lithuanian National Sickness Fund according to the DRG system (National Health Insurance Fund, 2023; IPHA, 2015). The unit costs in the Lithuanian Pharmacoeconomic Analysis (LPA) by Vanagas (2022) were calculated as DRG weighted

average for the DRGs corresponding to the disease type. Re-hospitalization costs in the LPA cover the recurred CV events and inpatient follow-up costs for the first year. Since re-hospitalization risk is by far the highest in the first year, all re-hospitalization costs were counted under the 1st year costs in our model.

The follow-up costs in the following years are considered for a period of 20 years, with discounting applied as described in Section 4.1.7.3. In the scenario analysis section, the application of follow-up costs over the expected remaining lifespan and during a reduced time period of 10 years is applied. Patients who suffer multiple events will incur multiple sets of long-term costs. However, this may not scale linearly with the number of events. Due to synergies of care and medication, the long-term costs from two events may not be twice the long-term cost of the first event. To avoid this sort of double counting, in the model, we adjust the long-term cost by a factor that estimates the probability that an event is the first event, which then, in effect, only applies long-term direct health costs to the first event. This factor is calculated by taking the product of the probabilities of not having an event in each year up to that age.

Appendices 2-4 depict the calculated cost estimates. A summary of the components of direct costs in year 1 and the following years is described in Table 8. The chosen proxy of unstable angina (UA) for estimating the total costs of oASCVD may not be entirely accurate due to heterogeneity of oASCVD events. However, it is a good approximation because UA incidence represents 69% of all oASCVD incidence in 2021.

Table 8. Components of direct healthcare costs.

	Frequency of events, methodological considerations	**Data source**
Year 1 costs		
Index hospitalization: MI, IS, and oASCVD	Calculated as DRG weighted average values: - MI (F41A, F41B) - IS (B70A, B70B, B70C) - oASCVD proxied by unstable angina (F72A, F72B) The prices are taken from the LPA. Obtained unit costs (Appendix 2) are then incorporated into the model by multiplying the unit costs with CV event rate by event type, age, and year.	Vanagas (2022)
Re-hospitalization and inpatient follow-up care	Frequency of re-hospitalization events within one year by prior cardiovascular event (Appendix 3). Frequencies were given for MI and IS events. We proxy oASCVD with the frequency of unstable angina (UA). Frequencies are then multiplied by unit costs.	Caekelbergh, Chevalier & Lamotte (2015)

Outpatient care (cardiologist, neurologist, etc., and other costs from services like nuclear scan, MRI, etc.)	The two-year cost from the LPA is split between year 1 and year 2, based on the frequency of visits in each year. Year 1 frequencies are taken and multiplied by unit costs (Appendix 4).	Caekelbergh, Chevalier & Lamotte (2015)
Rehabilitation	Rehabilitation costs over 24 months were split into year 1 and year 2 costs based on the proportion of the total number of rehabilitation sessions in years 1 and 2. Year 1 cost proportion is applied (Appendix 4).	Caekelbergh, Chevalier & Lamotte (2015)
Costs in the following years		
Outpatient care (cardiologist, neurologist, etc., and other costs from services like nuclear scan, MRI, etc.)	The two-year cost from the LPA is split between year 1 and year 2, based on the frequency of visits in each year. Year 2 frequencies are taken and multiplied by unit costs (Appendix 4).	Caekelbergh, Chevalier & Lamotte (2015)
Rehabilitation	Rehabilitation costs over 24 months were split into year 1 and year 2 costs based on the proportion of the total number of rehabilitation sessions in years 1 and 2. Year 2 cost proportion is applied (Appendix 4).	Caekelbergh, Chevalier & Lamotte (2015)

The cost of CV death in the model was taken from LPA, calculated as DRG weighted average of Z63A (other follow-up care after surgical or therapeutic treatment – condition is complex) and Z63B (other follow-up care after surgical or therapeutic treatment – condition is uncomplicated). As the LPA contained prices for 2021 and our model starts from 2021, there was no need to increase the cost by inflation. Direct healthcare costs are summarised in Table 9.

Table 9. Direct healthcare costs (EUR).

CV event	1st Year	Following years
MI	2,610.13	282.27
IS	3,054.43	1067.40
oASCVD	1,293.37	569.12
CV death	915.30	

Source: Vanagas (2022); Caekelbergh, Chevalier & Lamotte (2015); National Health Insurance Fund (2023); IPHA (2015).

4.1.6.2. Discounting. In the model, the time value of money is considered, and costs are discounted using Equation 3 and assuming a discount rate of 3.5% which is consistent with the respective national regulation (Seimas of the Republic of Lithuania, 2023). Other plausible discount rates are explored as part of the scenario analysis.

$$Discounted\ total\ = \frac{Total_t}{(1+r)^t} \quad (3)$$

where *r* is the discount rate per annum, *t* is time in years, and $Total_t$ is the total cost at time t.

4.2. Inputs for assessing the broader economic and social impact of CVD

4.2.1. Measuring productivity time loss

Three components are assessed that contribute to productivity time loss in society due to CV events. The first two components include productivity time loss incurred through absenteeism and presenteeism. The third component is unpaid caregiver time. A cross-sectional study conducted on patients following acute coronary syndrome (ACS) or stroke in Europe (Kotseva et al., 2019) was used to estimate the number of working hours per year that patients would lose after suffering a non-fatal CV event. The study involved 394 patients across 7 European countries and provides a more holistic view than other similar studies in the field, which often focus on a single country, fail to include data on presenteeism (Kigozi et al., 2017) and unpaid time loss (Oliva-Moreno et al., 2017). As Lithuania is not included in the country sample, the mean workdays lost during the first year after a non-fatal CV event in Lithuania are estimated using the average European values from the study, which are summarised in Table 10.

Table 10. Productivity time loss due to non-fatal CV events (mean workdays per year).

Event	MI	IS
Absenteeism	53	47.1
Presenteeism	6.3	8.8
Total	59.3	55.9

Source: Average values in Europe, as reported by Kotseva et al. (2019).

Mean workdays are then converted to mean working hours lost per year, assuming 8 hours per workday. As we use the average European estimate from the study by Kotseva et al. (2019) instead of values for Lithuania, the robustness of these values is further explored in the scenario analysis. Due to the heterogeneity of possible events in the oASCVD group and the lack of available data regarding time loss, the model takes a conservative approach by assuming that there are no productivity losses associated with these events. Thus, the model only considers losses due to MACE events.

4.2.2. Monetizing the value of paid working time

For estimating productivity loss, we follow the human capital approach. In particular, we estimate productivity loss by calculating the salary lost by patients due to experiencing a CV event. Three main components constitute productivity loss. The first component captures the loss stemming from lowered participation in the workforce following a fatal CV event. Using remaining life expectancy before retirement age and weighing it by the employment rate, we predict the years of working life lost at the time of CV death, which is then multiplied by the annual median salary to estimate the total GDP loss. The second component captures productivity loss from absenteeism, while the third component captures productivity loss from presenteeism. We use days missed from work estimated by Kotseva et al. (2019); this figure is multiplied by daily salary.

Annual gross wages and salaries for employees were obtained from the Official Statistics Portal (2023b); for 2021, it was EUR 18,952 (salaried employees receive a fixed amount of pay in each pay period regardless of the number of hours worked, while wage workers are paid by the hour). The daily and hourly salaries are calculated by assuming 8 hours in each workday and 252 working days in 2021 in Lithuania (European Central Bank, 2022). Additionally, the working day before public holiday is shortened by 1 hour according to Labour code in Lithuania. With 7 such public holidays, there were 2009 working hours in total, resulting in an average hourly salary of 9.43 EUR. Labour productivity growth, increase in the minimum wage, and tight labour market have contributed to rapid wage growth in Lithuania in the last decade (3.9% annually between 2011-2015 and 9.3% annually between 2016-2022; Bank of Lithuania, 2022a). We assume that the wage growth in Lithuania during the next 30 years is in line with the average wage growth observed in the past 12 years, during the period of 2011-2022. As a result, we increase salary each year at a rate of 7.02%.

4.2.3. Measuring and monetizing unpaid time loss

Unpaid activities can be defined as the production of goods and services that are not sold on the market, such as household work, taking care of someone, or volunteer work. They play a crucial role in estimating the societal burden of disease and the value of new therapies because people dedicate a substantial amount of their time to such socially and culturally valuable activities. As described in section 3, in this study we take a conservative approach and focus only

on the unpaid activities of patients, which are replaceable by caregivers. The study by Kotseva et al. (2019) assesses the time devoted by informal caregivers to help patients after a non-fatal CV event and estimates that on average 10.9 workdays are lost during the first year after a non-fatal MI and 11.7 workdays after a non-fatal stroke. The unpaid workdays are then multiplied by the average daily salary in Lithuania to estimate the economic costs.

4.2.4. Estimating productivity loss

This analysis aims to estimate the country's economic and social burden of disease by calculating the total monetized value of paid and unpaid activities lost each year in the population. The number of *non-fatal CV events* predicted in the epidemiological part of the model each year is distributed by age and multiplied by the number of paid working hours lost per year due to each type of event (as reported in Table 10) to estimate the total working hours lost per year. The time and productivity loss from non-fatal events occurs in the year the event occurs. Total working hours lost are monetized by multiplying the hours lost by age per year by the average hourly salary. The total number of *unpaid caregiver hours* due to non-fatal events is estimated and multiplied by the average hourly salary.

The impact of *fatal events* is calculated for the years up to retirement, based on the human capital approach, and adjusted for unemployment by age. Currently, the retirement age is 64 years in Lithuania. In the model, we use the current retirement age for years 1-10. For years 11-30, we introduce the highest retirement age observed in Europe as of 31 December 2022. In Europe, the highest retirement age is currently 67, which has been either introduced already (e.g., France, Greece Italy, the Netherlands), or being gradually introduced in the near future (e.g., Croatia, Germany, Spain) (Hinrichs et al., 2021).

4.3. Validation and verification

The model takes the data from 2021 as observed in Lithuania, and then calibrates the age-dependent CV event rate distribution that matches this data, as presented in Table 11. The model's ability to recreate historical trends in CV event occurrence at the population level was not explored.

The predicted values for each CV event are close to the input values from Higienos Institutas (2022b) and Causes of Death Finder (2023), with a relative difference below 2%. This

means that our model can replicate 2021 values accurately and give reliable death and incidence estimates to predict event numbers in future years.

Table 11. Validation of predicted CV events in the model.

CV event	Values from Higienos Institutas	Values predicted in the model	Relative difference (%)
non-fatal MI	5,672	5,747	1.33%
non-fatal IS	10,725	10,844	1.11%
oASCVD	39,238	39,196	0.11%
ASCVD Death	18,394	18,537	0.78%
Total ASCVD events	74,029	74,324	0.40%

Source: Higienos Institutas (2022a); Higienos Institutas (2022b); Strategies for Chronic Care (2023)

5. Results and discussion

Our findings are summarized in several sections. Section 5.1. presents the economic and social burden of CV disease that Lithuania faces now and is projected to experience over a 30-years' horizon. Section 5.2. tests the sensitivity of the economic and social burden estimates to various model inputs. At the end of this section, we also discuss the limitations of our modelling exercise.

5.1. Burden of disease

5.1.1. Impact of CVD on health and healthcare costs

The model predicts 74,324 fatal and non-fatal CV events to occur in Lithuania in 2021, costing the healthcare system EUR 443 million in total, as summarised in Table 12.

Table 12. Predicted health impact of CVD in Lithuania in 2021.

CV event	Number of CV events	Direct healthcare costs (EUR in million)
non-fatal MI	5,747	29.91
non-fatal IS	10,844	139.54
oASCVD	39,196	256.53
ASCVD Death	18,537	16.97
Total ASCVD events	74,324	442.95
Life years lost	263,446	

Over a 30-year horizon, the model estimates more than 2.3 million CV events in total, among them 578,710 (25.0%) being fatal events. The model prediction of the number of events and the total population being close (2.3 million vs 2.8 million) is plausible: with the ageing society, more people would experience first-time events, and many would suffer multiple CV events in a row in 30 years.

The predicted number of CV events and associated direct healthcare costs over a 1, 15- and 30 years' time horizon are summarised in Table 13. The resulting healthcare costs exceed EUR 5.2 billion and EUR 8.1 billion over a 15- and 30-years' time horizon, respectively.

Table 13. Predicted health impact of CVD in Lithuania over 30 years.

Time Horizon	Total CV events	Direct healthcare costs (EUR in million)
1 year	74,324	442.95
15 years	1,154,304	5,229.39
30 years	2,319,078	8,116.56

5.1.2. Broader economic and social impact of CVD

The CV events experienced by the Lithuanian society would also create an economic loss through missed working hours and reduced productivity. The model estimates more than 2.7 million lost working hours per year due to non-fatal MIs and strokes alone and over 102 million

working hours lost in total from all CV events, representing a loss of over EUR 965 million in 2021 alone, as shown in Table 14.

Table 14. Economic loss in paid-work settings of CV events in year 1, and over 15 and 30 years.

CV event	Working hours lost in year 1 (in million)	Salary losses in year 1 (EUR in million)	Salary losses in 15 years (EUR in million)	Salary losses in 30 years (EUR in million)
non-fatal MI	1.00	9.41	175.51	450.14
non-fatal IS	1.78	16.74	312.41	801.17
ASCVD Death	99.58	939.43	17,518.63	44,935.13
Total ASCVD events	102.36	965.58	18,006.55	46,186.44

Over a 15-year and 30-year horizon, the productivity losses reach EUR 18.0 billion and 46.2 billion EUR, respectively. More than 97% of the loss stems from CV deaths because every fatal event results in losing the remaining productive life entirely. At the same time, every non-fatal event is only associated with a temporary absence from work during hospitalization and lowered productivity in the year of the event.

Lastly, we estimate an economic loss of EUR 12.72 million from more than 1.3 million unpaid hours of caregiver activity in 2021 due to non-fatal MI and IS as shown in Table 15. Over a 15- and 30-years' horizon, the losses amount to EUR 243.18 million and EUR 621.66 million, respectively.

Table 15. Predicted caregiver unpaid time loss in year 1, and over 15 and 30 years.

CV event	Working hours lost in year 1 (in million)	Monetary losses in year 1 (EUR in million)	Monetary losses in 15 years (EUR in million)	Monetary losses in 30 years (EUR in million)
non-fatal MI	0.45	4.20	80.37	205.47
non-fatal IS	0.90	8.52	162.81	416.19
Total ASCVD events	1.35	12.72	243.18	621.66

5.1.3. Total disease burden

CV disease is the leading cause of death in Lithuania, and the burden continues to rise, causing a significant health and economic impact on patients and society. To design appropriate

public health strategies, it is crucial to have a comprehensive understanding of the humanistic, economic, and social consequences of CV disease and the impact of possible interventions.

While the health impacts of CV disease are well-documented (e.g., patient burden, mortality), the economic and social consequences are less well-understood. Our research has addressed this gap by extending the scope of analysis to include a more thorough evaluation of the anticipated costs and effects of CV disease. In addition to direct healthcare costs of fatal and non-fatal CV events, the analysis also includes indirect costs and their economic value estimation in terms of the number of hours of paid work loss and time loss of unpaid caregiver activities. Although data on all aspects of social value are currently unavailable, the study by Kotseva et al. (2019) represents an important advancement in this area. It provides a complete perspective compared to a narrower healthcare payer view.

The total economic and social consequences of CVD in Lithuania for year 1, years 15 and 30 are summarized in Table 16. Using our model, we estimate that the 74,324 cardiovascular events which were predicted to occur in Lithuania in just one year (2021) cost the healthcare system EUR 443 million and the economy EUR 965.6 million in lost workplace productivity, meanwhile EUR 12.7 million in additional social value was lost due to lost caregiver time. In total, the total economic and social impact of disease reached EUR 1.42 billion in 2021, which accounts for 2.53% of the total GDP of the country (Official Statistics Portal, 2023c).

Table 16. Total disease burden.

Time Horizon	Direct healthcare costs (EUR in million)	Salary losses (EUR in million)	Monetary loss due to unpaid caregiver activity (EUR in million)	Total disease burden (economic and societal consequences) (EUR in billion)
1 year	442.95	965.58	12.72	1.42
15 years	5,229.39	18,006.55	243.18	23.48
30 years	8,116.56	46,186.44	621.66	54.92

Over a 15- and 30-year time horizon, the model predicted that 1,154,304 and 2,319,078 cardiovascular (CV) events would occur in Lithuania, respectively, resulting in direct healthcare costs of EUR 5.23 billion and EUR 8.12 billion in present value (PV) terms. Additionally, the Lithuanian economy would experience a significant loss of productive hours (salary losses) and unpaid productive activities (unpaid caregiver activities), valued at EUR 18.01 billion and EUR

243 million over 15 years, as well as EUR 46.19 billion and EUR 622 million over 30 years, respectively. In PV terms, the total economic and social burden of CV disease would amount to a staggering EUR 23.48 billion over 15 years and EUR 54.92 billion over 30 years. In year one (2021), direct healthcare costs accounted for 31% of the total monetary burden of the disease, while indirect costs in the paid-work setting accounted for 68% of the total monetary burden. Indirect costs in the paid-work setting remain the most significant element of monetary loss over a 15- and 30-year time horizon, representing 77% and 84% of the total monetary burden of the disease, respectively. This emphasizes the importance of adopting a more comprehensive perspective when assessing the economic and social consequences of CV disease, rather than simply focusing on direct healthcare costs from a narrow healthcare payer perspective.

5.2. Sensitivity and scenario analysis

We present a scenario analysis for 2021 based on the variation of the following parameters: *i*) epidemiological inputs; *ii*) direct healthcare costs; *iii*) productivity inputs; *iv*) unpaid activities; and v) paid activities. The outcome variables of interest are direct health costs and indirect costs. Results from the scenario analysis are presented in Table 17.

When modifying the inputs for direct healthcare costs, the most notable impact on the results is observed when employing costs adjusted to 2023 prices. This modification yields a 31% increase in the economic burden of CVD, the costs surging from EUR 442.95 million in the base-case to over EUR 579.24 million in 2021. Given the high inflation rate experienced by Lithuania in 2022 and predicted for 2023, it is reasonable that the burden of CVD on direct healthcare costs is currently greater than the base-case scenario in 2021. The most notable impact on the indirect cost estimation is observed when no discount is applied to costs in the future years. This would result in increased costs of EUR 1,285.30 million instead of EUR 978.30 million when compared to the base-case.

Table 17. Scenario analysis.

	Burden of CV disease, direct health costs (EUR in million)	**Burden of CV disease, indirect costs (loss in paid-work setting and caregiver unpaid monetary losses)** (EUR in million)
Base-case scenario	442.95	978.30
Epidemiological inputs		
Change in age distribution of CV events using HR of 1.03 from original REACH equation (Danese et al., 2018)	No change	No change
Direct healthcare costs of CV events		
20% reduction of all healthcare costs	354.36	No change
20% increase of all healthcare costs	531.54	No change
Costs inflated to 2023 values (multiplier of 1.3077 by comparing GDP deflator in 2023 and 2021; Bank of Lithuania, 2022b)	579.24	No change
No costs assigned to oASCVD events	186.42	No change
Long-term costs applied during predicted life expectancy, i.e., no time cap applied	478.75	No change
Long-term costs applied for 10 years	352.70	No change
No discount (0%) applied for costs in future years	531.51	1,285.30
5% discount applied to costs in future years	414.67	888.10
Productivity inputs		
20% productivity time loss reduction	No change	973.07
20% productivity time loss increase	No change	983.53
Unpaid activities		
20% unpaid hours reduction	No change	975.75
20% unpaid hours increase	No change	980.84
Paid activities		
20% gross annual salary reduction	No change	782.64
20% gross annual salary increase	No change	1,173.96

Employing an HR of 1.03 instead of 1.06 in the age distribution of CV events does not result in any variation in the disease burden. However, it is worth noting that if no costs were assigned to oASCVD events, direct healthcare costs would decline by around 58%. This indicates that oASCVD events have a significant impact on the CV disease burden in Lithuania, as supported by the high event distribution of oASCVD events observed in Table 7.

There is a minor impact on indirect costs when modifying assumptions related to productivity inputs and unpaid activities, which indicates the robustness of the base-case scenario. However, for paid activities, a 20% increase or decrease in the gross annual salary would increase or decrease the indirect costs linearly by 20%. Since Lithuania has been experiencing rapid wage growth for several years, which is expected to continue, an increase in indirect costs is a plausible scenario.

Table 17 emphasises the model's conservative approach to data inputs and assumptions in the base-case scenario, ensuring that the results represent an underestimation rather than an overestimation of the health and economic impact of CVD.

5.3. Limitations and future research directions

Due to a lack of data on both direct (e.g., statin usage and adherence) and indirect (e.g., productivity loss) aspects related to CV events in Lithuania, several assumptions have been made in the model that relies on data from other European countries. While the sensitivity analysis confirms the reliability and robustness of the baseline scenario, we recognize the need for more thorough research in areas such as productivity loss following a CV event (this study takes the average European values from the study by Kotseva et al., 2019) and the frequencies of re-hospitalization, rehabilitation, and outpatient services (all taken from the Belgium study) for Lithuania in the future.

The analysis does not provide a full holistic societal view. For instance, patients treated with innovative medications live longer and are likely to incur more non-related medical costs throughout the remaining lifetime; however, this impact on the healthcare system is not captured in our study due to a lack of data. At the same time, the prevention of CV events can significantly improve the patients' well-being and societal engagement through volunteer activity and household work. As our study focuses on estimating the productive life lost, it neglects both the positive impact on society from unpaid work beyond caregiving and the value of life.

6. Conclusions

Cardiovascular diseases are the leading cause of death in Lithuania, where the majority of the total deaths can be attributed to CVD. Our study provides a comprehensive assessment of the burden of cardiovascular diseases in Lithuania from economic and social perspectives.

Our model predicted 74,324 CV for 2021, corresponding to EUR 443 million in costs incurred by the healthcare system and EUR 978 million in economic losses from reduced workplace productivity and unpaid caregiver time. This accounts for 2.53% of Lithuania's total GDP. Moreover, our model predicts the provisional situation in the long run: in 30 years' time, with current trends, the number of CV events will increase up to 2.3 million events by 2051, which amounts to EUR 8.1 billion in direct healthcare costs and EUR 46.8 billion in indirect costs. Thus, cardiovascular diseases put a significant burden on Lithuania's economy.

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8. Appendices

Appendix 1. Model worksheet contents and purpose

WORKSHEET NAME	**CONTENTS AND PURPOSE** (contents in **boldface** denote inputs)
SUMMARY RESULTS	- Predictions from the model of the impact of CV disease on the economy as a whole (top, in black) – in terms of direct health costs incurred, paid work time lost, unpaid and caregiver time lost
Epidemiological parameters	- **Estimates of the case-fatality ratio for CV disease, and the proportion of all mortality which is CV mortality** - **Estimate of the rate of CV events at a given age. This is fit numerically to the input data on counts of CV events** - **Estimate of the effect of age on CV event rate (used to distribute the total number of events over the population by age)** - **Time horizon** - **Time discounting rate for costs**
Local event data	- **Observed numbers of CV events (all types), MI, IS, oASCVD (fatal and non-fatal) and CV deaths** - Predicted estimates of the number of non-fatal events, and the observed ratios of event types
Population by age	- **Numbers of people by age in total population**
Direct health costs	- **Cost to the health system of MI, IS, oASCVD and CV death (both short term and long term)** - **Support sheet** *Calculations for direct healthcare costs*

Predicted births	- **Predictions of the number of births by year**
Life table	- **Observed and predicted life tables (probability of death before age *n+1*, conditional on being alive at age *n*)** - **Support sheet** *Population men vs women in 2021*
Event rates	- Calculated rate of CV events by year of age - These rates are then distributed by event type
Unadjusted TPs	- Conversion of the event rates into transition probabilities at each annual cycle. These are not yet adjusted for the competing risk of non-CV mortality - Calculation of the probability of PP status by age (i.e., probability no CV event has yet been experienced) - Calculation of remaining life expectancy (based on 2021 life table)
• TP Non-CV death • TP CV death • TP NF MI • TP NF IS • TP oASCVD	- Transition probabilities with competing risk adjustment at each annual cycle by age, for non-CV death, CV death, non-fatal MI, non-fatal IS and other atherosclerotic CV events.
• Trace ALIVE • Trace CV DEATH • Trace non-CV DEATH	- Records the number of people alive, dead of CV causes and dead of non-CV causes at each age and year
• MI counter • IS counter • oASCVD counter • WYLL counter • DWYLL counter • All CV counter	- Records the number of MI, IS and oASCVD predicted at each year and age. - WYLL records the predicted years of working life lost due to a CV death, using remaining life expectancy before retirement weighted by the employment rate by age. DWYLL records discounted working life years.
Direct health cost counter	- Records the expected costs to the health system of CV disease by year and age - Long term costs are calculated by applying the long-term costs for the remaining expected lifespan, conservatively weighted by the probability that this is the first CV event to avoid double counting in the event of multiple events
Productivity and fiscal inputs	- **Retirement age** - **Estimates of caregiver and unpaid work time lost per MI and IS (from productivity loss study)** - **Estimates of paid work lost per MI and IS (from productivity loss study)** - **Adjustment factor to allow friction costing adjustment. Currently set to 1, corresponding to human capital approach**
Unpaid work inputs	- In our study unpaid activities not linked to caregiving are disregarded
Employment inputs	- Total working hours per year - Employment rate, by age - Average salary - Estimated salary increase per year
• Employment calculations	- On these sheets, the median salary of worker is calculated considering the

2021-2030 • Employment calculations 2031-2051	average salary in Lithuania, the number of working hours per year and the retirement age for the first 10 years (2021-2030) or from year 10 (2031-2051)
• Paid hours lost MI • Paid hours lost IS • Paid hours lost CV Death • Paid hours lost TOTAL • Salary loss MI • Salary loss IS • Salary loss oASCVD • Salary loss TOTAL	- Estimates the productive time lost in paid work settings by each type of event, age and the year - For each type of event the respective salary loss is calculated and lastly the total monetary value of loss from all events is obtained
• CGUWT loss MI • CGUWT loss IS • CGUWT loss CV death	- Predicted loss of caregiver and unpaid work time (CGUWT), by event type, age and year

Appendix 2. Direct healthcare costs: Index hospitalization unit costs

Year 1		
States/events	Unit costs (EUR)	DRG codes (LT)
MI	1533.12	F41A, F41B
UA	543.47	F72A, F72B
IS	1225.40	B70A, B70B, B70C
HF	1140.58	F62A, F62B, F62C

Appendix 3. Direct healthcare costs: Re-hospitalization frequencies and costs by prior cardiovascular events

Year 1: After MI				
States/events	Frequency	Unit costs (EUR)	Costs (EUR)	DRG codes (LT)
MI	0.1128	1533.12	172.89	F41A, F41B
UA	0.0053	543.47	2.86	F72A, F72B
IS	0.0019	1225.4	2.34	B70A, B70B, B70C
HS	0.0006	1225.4	0.7	B70A, B70B, B70C
CABG	0.0077	8410.38	64.87	F05A, F05B
PCI	0.0565	2400.46	135.63	F10A, F10B
HF	0.0262	1140.58	29.87	F62A, F62B, F62C
TIA	0.0017	870.38	1.44	B70C
TOTAL:			410.59	

Year 1: After IS				
States/events	Frequency	Unit costs (EUR)	Costs (EUR)	DRG codes (LT)
MI	0.004	1533.12	6.13	F41A, F41B
UA	0.0008	543.47	0.43	F72A, F72B
IS	0.0381	1225.4	46.69	B70A, B70B, B70C
HS	0.0016	1225.4	1.96	B70A, B70B, B70C
CABG	0.0012	8410.38	10.09	F05A, F05B
PCI	0.0032	2400.46	7.68	F10A, F10B
HF	0.0087	1140.58	9.92	F62A, F62B, F62C
TIA	0.0147	870.38	12.79	B70C
TOTAL:			95.71	

Year 1: After oASCVD (proxied by HF)				
States/events	Frequency	Unit costs (EUR)	Costs (EUR)	DRG codes (LT)
MI	0.0135	1533.12	20.70	F41A, F41B
UA	0.0014	543.47	0.76	F72A, F72B
IS	0.0025	1225.4	3.06	B70A, B70B, B70C
HS	0.0014	1225.4	1.72	B70A, B70B, B70C
CABG	0.0043	8410.38	36.16	F05A, F05B
PCI	0.0071	2400.46	17.04	F10A, F10B
HF	0.1872	1140.58	213.52	F62A, F62B, F62C
TIA	0.0046	870.38	4.00	B70C
TOTAL:			296.97	

Appendix 4. Direct healthcare costs: Other service use frequencies and costs by prior cardiovascular events

Year 1: After MI				
States/service	Frequency	Unit costs (EUR)	Costs (EUR)	
Rehabilitation (24 months)	0.407	1188.4	483.68	401.94 (year 1)
Cardiologist	2.9	45.2	131.08	
Neurologist	0.05	34.23	1.71	
Endocrinologist	0.58	45.2	26.22	
Vascular surgeon	0.26	34.23	8.90	

Year 2: After MI				
States/service	Frequency	Unit costs (EUR)	Costs (EUR)	
Rehabilitation (24 months)	0.407	1188.4	483.68	81.74 (year 2)
Cardiologist	2	45.2	90.4	
Neurologist	0.05	34.23	1.71	
Endocrinologist	0.59	45.2	26.67	
Vascular surgeon	0.11	34.23	3.76	

Cardiac surgeon	0.51	34.23	17.46
Geriatrician	0.42	20.01	8.4
Nuclear scan	0.3	129.48	38.84
MRI	0.06	254.51	15.27
SPECT scan	0.01	253.07	2.53
PET scan heart	0.01	1406.27	14.10
TOTAL:			666.42

Cardiac surgeon	0.3	34.23	10.27
Geriatrician	0.43	20.01	8.6
Nuclear scan	0.23	129.48	29.78
MRI	0.06	254.51	15.27
SPECT scan	0	253.07	0
PET scan heart	0.01	1406.27	14.10
TOTAL:			282.27

Year 1: After IS

States/service	Frequency	Unit costs (EUR)	Costs (EUR)	
Rehabilitation (24 months)	0.8	1188.4	950.72	656.59 (year 1)
Neurologist	2.67	34.23	91.39	
Cardiologist	1.5	45.2	67.8	
Endocrinologist	0.33	45.2	14.92	
Ophthalmologist	0.92	34.23	31.5	
Vascular surgeon	1	34.23	34.23	
Cardiac surgeon	0.07	34.23	2.4	
Geriatrician	0.67	20.01	13.41	
CT heart	0.08	71.47	5.72	
Nuclear scan	0.43	129.48	55.68	
CT brain	0.83	71.47	59.32	
MRI	0.91	254.51	231.60	
Carotid angiography	0.52	253.07	131.60	
CT angiography brain	0.41	253.07	103.76	
SPECT scan	0.2	253.07	50.6	
PET scan brain	0.13	1406.27	182.8	
TOTAL:			1733.32	

Year 2: After IS

States/service	Frequency	Unit costs (EUR)	Costs (EUR)	
Rehabilitation (24 months)	0.8	1188.4	950.72	294.13 (year 2)
Neurologist	1.33	34.23	45.53	
Cardiologist	1	45.2	45.2	
Endocrinologist	0.29	45.2	13.11	
Ophthalmologist	0.92	34.23	31.5	
Vascular surgeon	1	34.23	34.23	
Cardiac surgeon	0.07	34.23	2.4	
Geriatrician	0.78	20.01	15.61	
CT heart	0.03	71.47	2.14	
Nuclear scan	0.53	129.48	68.62	
CT brain	0.62	71.47	44.31	
MRI	0.5	254.51	127.26	
Carotid angiography	0.27	253.07	68.33	
CT angiography brain	0.29	253.07	73.39	
SPECT scan	0.13	253.07	32.90	
PET scan brain	0.12	1406.27	168.75	
TOTAL:			1067.40	

Year 1: After oASCVD (proxied by HF)				
States/service	Frequency	Unit costs (EUR)	Costs (EUR)	
Rehabilitation (24 months)	0.42	1188.4	499.13	389.71 (year 1)
Cardiologist	4.6	45.2	207.92	
Neurologist	0.3	34.23	10.27	
Endocrinologist	0.65	45.2	29.38	
Vascular surgeon	0.41	34.23	14.03	
Cardiac surgeon	0.25	34.23	8.56	
Geriatrician	0.9	20.01	18.01	
CT heart	0	71.47	0.00	
Nuclear scan	0.78	129.48	100.99	
MRI	0.65	254.51	165.43	
SPECT scan heart	0.08	253.07	20.25	
PET scan heart	0.14	1406.27	196.88	
TOTAL:			1216.14	

Year 2: After oASCVD (proxied by HF)				
States/service	Frequency	Unit costs (EUR)	Costs (EUR)	
Rehabilitation (24 months)	0.42	1188.4	499.13	109.41 (year 2)
Cardiologist	4	45.2	180.80	
Neurologist	0.29	34.23	9.93	
Endocrinologist	0.51	45.2	23.05	
Vascular surgeon	0.25	34.23	8.56	
Cardiac surgeon	0.15	34.23	5.13	
Geriatrician	0.9	20.01	18.01	
CT heart	0	71.47	0.00	
Nuclear scan	0.62	129.48	80.28	
MRI	0.46	254.51	117.07	
SPECT scan heart	0.08	253.07	20.25	
PET scan heart	0.04	1406.27	56.25	
TOTAL:			628.74	

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