The case for investing in a healthier future for the European Union

Annex

Contents

Methodology

This investment case highlights the critical link between sustained resource allocation for health systems and the resultant improvements in patient and population health outcomes. It is designed to serve as a tool for outreach and advocacy at both EU and national levels, emphasizing the importance of long-term investments in health in Europe.

In consultation with the EFPIA Health Systems Working Group, we selected five NCDs and three countries for in-depth analysis:

1. Stroke
2. Ischaemic heart disease
3. type 2 diabetes mellitus
4. Chronic obstructive pulmonary disease (COPD)
5. Breast cancer

The analysis started with an estimation of the current and future burden of these diseases on health systems, economies and societies across the 27 EU Member States, followed by an examination of three countries—Sweden, Romania and Portugal. These countries were chosen to represent the diversity of health systems in Europe, reflecting a spectrum of health care challenges and opportunities. Additionally, we evaluated the costs and return on investment (ROI) associated with a set of intervention packages. To complement this analysis, we incorporated the country case studies, exploring the factors that contribute to the significant impact of these diseases in these specific countries.

The following disease selection was made by country:

1. Sweden: breast cancer
2. Romania: stroke and ischaemic heart disease
3. Portugal: type 2 diabetes mellitus and COPD

The economic analysis employs a cost-of-illness methodology that incorporates both direct health care expenditures and indirect costs, including lost productivity due to absenteeism, presenteeism and the costs of premature mortality. By systematically estimating these economic impacts in 27 countries, the analysis offers a detailed understanding of the economic burden that NCDs impose on European societies.

In addition, the economic analysis includes four ROI analyses that further demonstrate the value of investing in health in three different countries. For Portugal and Romania, these case studies estimate the health and economic benefits obtained after scaling up intervention strategies over 27 years. For Sweden, the analysis uses a different approach by investigating the benefits of providing comprehensive breast cancer against current scenarios. By comparing the costs of these intervention strategies and the economic benefits they provide, the return on investment analyses seek to demonstrate the long-term financial and societal gains of investing in health interventions. The One-health Tool was used in two out of the four case studies to model the cost of the interventions and their health impacts. The One-health Tool is a valid and widely recognized software developed by several international agencies, including the World Health Organization, to support policy-makers in evaluating the cost–effectiveness of health interventions and in planning resource allocation for health systems. The standard parameters of the tool were carefully reviewed

and updated to ensure they reflected as much as possible current guidelines, practices and costs in the selected countries and provided a valid basis for projecting the outcomes of health interventions.

The development of this investment case follows a structured approach comprising the following key components:

- **Trend analysis of health expenditure and cost drivers in Europe** conducted through a desk review of literature, data and policy documents and expert input from case study countries to reflect real-world challenges and policy options.
- **Recommendations for health financing decision-making** grounded in a rigorous economic analysis that evaluates the health system and societal benefits of implementing and scaling innovative health care interventions. To ensure the feasibility and relevance of these recommendations, they have been refined through an institutional context analysis in case study countries, which assessed relevant economic, social and political dimensions.
- **Stakeholder engagement and validation activities were conducted** to validate and refine our findings and recommendations. This included a series of key informant interviews to capture nuanced perspectives from individual national stakeholders. In addition, we facilitated two roundtable discussions with representatives from patient associations, clinicians, academics and decision-makers at national level. This collaborative and consultative process with the EFPIA Health Systems Working Group, the national associations in Sweden, Romania and Portugal, as well as with national stakeholders has been instrumental in ensuring that the investment case is both evidence-informed and actionable for sustained investment in health-care resources and innovation.

2.1 Economic burden of NCDs in the EU

2.1.1 Health burden

This analysis uses incidence, prevalence and mortality rates from the Institute of Health and Metrics Evaluation Global Burden of Disease 2019 (GBD 2019) to estimate the health burden of stroke, ischaemic heart disease, type 2 diabetes mellitus, COPD and breast cancer in the 27 countries of the European Union in 2023. Demographic projections from the United Nations Department of Economic and Social Affairs (United Nations, 2022) were used to estimate the future annual health burden until 2050. In these projections, the analysis assumes that incidence, prevalence and mortality rates will remain constant throughout the study period. Therefore, any observed changes in the annual number of new cases and deaths over time are attributable to demographic shifts rather than changes in epidemiological trends.

2.1.2 Economic burden structure

This study used a cost-of-illness approach to estimate the direct and indirect economic losses associated with the five selected NCDs in the EU between 2023 and 2050. The (a) direct costs refer to the costs incurred by the health system to treat and manage these diseases. The indirect costs include (b) the cost of premature mortality, (c) the foregone productivity due to absenteeism and (d)

the foregone productivity due to presenteeism. The costs of absenteeism, presenteeism and health care costs were estimated using a prevalence-based approach for all diseases except breast cancer. For breast cancer, the use of an incidence-based approach was preferred to avoid overestimating the health care costs and impact on productivity, which are usually more pronounced in the first year after diagnosis.

2.1.3 Direct health care costs

The direct costs represent the government and private health spending on drugs, medical staff salaries, supplies, and procedures for treating and managing the five selected diseases. These health expenditures were calculated by multiplying the average cost per patient by the estimated number of treated patients. The average cost per patient was sourced from the scientific literature [1] (Santos et al., 2023; Rehman et al., 2020; IDF, 2021). The number of treated patients was estimated using utilization rates reported by the Organization for Economic Cooperation and Development (Health at a Glance 2023: OECD Indicators, 2023). When country-specific data were unavailable, average values calculated for the geographical subgroup were used as proxy indicators.

2.1.4 Cost of absenteeism and presenteeism

Excess absenteeism was defined as the average additional days of work that employees missed due to NCDs. Conversely, presenteeism refers to lower on-the-job productivity when employees attend work but are less productive due to disease-related impairment and disability. A multistep approach was used to quantify these economic losses. First, the number of economically active individuals was determined by considering the age range 15–64, along with the sex-specific labour force participation rate and employment rate (ILOSTAT, 2024). Second, incidence rates from the IHME were applied to estimate the fraction of the workforce affected by the selected diseases. Third, disease-specific productivity reduction rates due to excess absenteeism and presenteeism were sourced from the scientific literature (Łyszczarz B, 2024; Breton et al., 2013; Dierick et al., 2021; Kotseva et al., 2019). Finally, the GDP per worker was used to approximate each worker's productive output in any given year. It was then multiplied by the number of affected workers and the productivity reduction rates to estimate the annual foregone productivity.

2.1.5 Cost of premature mortality

We employed the human capital approach to estimate the cost of premature mortality from the five selected NCDs. This approach quantifies the economic losses resulting from the deaths of economically active individuals and assumes that forgone economic output is equivalent to the total output that workers would have generated throughout their lives until retirement age. The foregone productivity due to premature mortality was estimated from the number of working years lost between the age at death and the age at, which the deceased employee would have reached the average retirement age. Economic losses

[1] Country-specific cost per patient for stroke, ischaemic heart disease and breast cancer were obtained from Santos et al. (2023). For diabetes, the average health expenditure per adult with diabetes in the WHO European Region was sourced from the IDF Diabetes Atlas 2021 (tenth Edition). For COPD, average annual direct costs per patient were obtained from eight countries from Rehman et al. (2020). For the 19 others, direct costs were approximated by using the average value within each geographical subgroup.

were calculated by multiplying the GDP per worker, used to approximate each worker's output, by the working years lost in each age group and considering the sex-specific labour force participation rate and employment rate. It is important to note that the human capital approach can only value economic losses due to deaths below the retirement age and does not take into consideration the economic losses due to deaths that occur after that age.

All future costs were discounted at 3%, which is the rate recommended by the WHO for investment cases (A Healthy return: WHO, 2022).

2.2 Return on investment analyses for Portugal and Romania

2.2.1 Portugal and Romania analyses

A six-step methodology was used to estimate the economic returns of implementing and scaling up clinical interventions to address cardiovascular diseases in Romania and diabetes and COPD in Portugal: *(1)* selecting the clinical interventions, *(2)* determining current and target coverage rates, *(3)* estimating the interventions' costs, *(4)* estimating the health benefits, *(5)* converting the health into economic benefits, *(6)* calculating the return-on-investment.

2.2.2 Selecting the clinical interventions

The clinical interventions were selected based on the following inclusion criteria: *(1)* the intervention directly or indirectly affects the quality of life, incidence and mortality and *(2)* the cost of implementing and scaling up the intervention can be determined. Once selected, the interventions and treatment regimens were updated to ensure they reflect, as much as possible, current guidelines and practices in the selected countries. A detailed description of the assumptions used is provided in the annexes.

2.2.3 Determining current and target coverage rates

The current coverage rates were determined from the scientific literature, national statistics and reports from international organizations. The target coverage rate was 100% by 2050, with a linear scale-up over the 27 years.

2.2.4 Estimating the interventions' costs

The incremental costs of scaling up the clinical interventions were calculated by multiplying the number of patients treated by the average cost per patient. The cost per patient is calculated using a cost ingredient method, considering *(1)* the intervention assumptions, *(2)* the cost of the diagnosis, procedures, drugs and supplies and *(3)* the cost of the labour force. The unit cost of the drugs used

for each intervention was carefully reviewed and updated to ensure they reflect actual costs in the selected countries.

2.2.5 Estimating the health and economic benefits

The health benefits of scaling up clinical interventions were assessed by modelling the number of disease cases averted and lives saved over the 27 years under study. The economic value of the benefits obtained from reducing mortality were estimated by using the human capital approach, as described in section 2.1.5. For the cases averted, the economic benefits were calculated as the value of the direct health care costs saved, the value of avoided absenteeism and the value of avoided presenteeism, as described in sections 2.1.3 and 2.1.4. As the human capital approach can only capture the economic benefits of providing the intervention to people below the retirement age, the age of retirement would alter the results. An increase in the retirement age by one year would increase the ROI.

In the analysis of diabetes interventions, the cost of unemployment was also incorporated to monetise the health benefits. To do so, we valued the number of working years lost due every year based on disease-adjusted unemployment rate.

2.2.6 Calculating the return on investment (ROI)

The ROI for each intervention package was calculated by comparing the economic benefits with the incremental costs of scaling up. All future costs and benefits were discounted at 3%.

2.3 Sweden Analysis

2.3.1 Study design

A state transition population model was developed to simulate the impact of comprehensive breast cancer treatment in a cohort of 48 092 girls in Sweden in 2003. In line with the WHO guidelines on cost–effectiveness analyses (WHO, 2003), the intervention was introduced for a period of ten years and its effectiveness was assessed compared with a no-intervention scenario. Five models were tested to determine the impact of the intervention when implemented at different moments of the lifetime (20–30, 30–40, 40–50, 50–60 and 60–70). While the intervention cost was calculated over ten years, the health benefits were assessed throughout the cohort's lifetime to capture both its short and long-term effects.

2.3.2 Intervention components and costs

In this model, comprehensive breast cancer treatment includes the provision of *(1)* initial diagnosis, *(2)* evaluation during the treatment, *(3)* chemotherapy, *(4)* radiotherapy, *(5)* surgical intervention, *(6)* endocrine therapy (Technical Briefing: WHO, 2022). The proportion of patients eligible for each of

these components depends on the stage of the disease and was determined from Zelle et al. (Zelle et al., 2012) as well as national data. The number of hospitalization days and outpatient visits required at each stage of disease was updated to integrate the latest assumptions from the One-health Tool. In addition, the study assumes that 20% of patients had HER2-positive breast cancer and were also treated with trastuzumab (Olofsson et al., 2016). An ingredient costing method was employed to estimate the cost of the treatment at each stage. The cost of hospitalization days and outpatient visits were obtained from the WHO-CHOICE database and adjusted to 2023 using annual inflation rates from the International Monetary Fund (International Monetary Fund, 2024). The cost of radiotherapy was derived from Defourny et al. (Defourny et al., 2019) . The cost of the drugs and supplies were extracted from the One-health Too (Avenir Health). Acknowledging a certain level of uncertainty regarding the cost of the drugs and supplies obtained from the One-health Tool, a one-way sensitivity analysis was performed to assess the impact of a 50%, 100% and 200% increase of these costs.

2.3.3 Main parameters

Age-specific incidence rates from the Global Cancer Observatory were used to estimate the number of new breast cancer cases (Global Cancer Observatory, 2024). The distribution per stage was sourced from Abdoli et al. (Abdoli et al., 2017). To simulate the natural progression of the disease and estimate the annual number of deaths in the absence of treatment, the model uses standard transition and case-fatality rates from the literature *(18.25,26)*. During the ten years of treatment, the model uses differential case-fatality rates, and the progression of the disease is stopped, except for stage IV (Zelle et al., 2012;Groot et al.,2006; Ralaidovy et al., 2018). The case fatality rates were adjusted to reflect the impact of using trastuzumab in HER2-positive patients. In a meta-analysis, trastuzumab was found to reduce breast cancer mortality by 33% in early stage breast cancer compared with chemotherapy alone (Trastuzumab for early stage, 2021). Finally, the model also accounts for mortality from other causes than breast cancer by using data from the Swedish National Board of Health and Welfare (Socialstyrelsen, 2024).

2.3.4 Economic valuation of the health benefits

The number of lives saved during the ten-year intervention period was calculated by comparing the deaths in the no-intervention scenario to those in the intervention scenarios. The lives saved were converted into monetary value using the human capital approach, as described in the annexes. As the human capital approach can only capture the economic benefits of providing the intervention to people below the retirement age, the current trend in Europe of delaying the age of retirement would alter the results. An increase in the retirement age by one year would increase the ROI.

2.3.5 Return on investment (ROI)

The ROI was calculated by comparing the health benefits with the costs of delivering comprehensive breast cancer treatment over ten years. The ROI was estimated for the five scenarios to determine to what extent the timing of the intervention influences the economic returns. All future costs and benefits were discounted at 3%.

The health and economic burden of chronic disease

As Europe's population ages, more people are living longer, often with disabilities or chronic conditions that require ongoing care. This shift places increased demand on health-care systems, particularly in managing long-term care and complex medical needs.

3.2.2.1 Population projections

According to the United Nations World Population Prospects, the total population of the EU in 2023 was 449 million, with 22% of the population over the age of 65. The total population was projected to reach 423 million in 2050, with 31% of the population over the age of 65. This signifies a 6% decrease in the total population and a 35% increase in the population above the age of 65 in the EU. Understanding these demographic shifts is crucial for interpreting the results of the economic burden analysis since they substantially influence incidence, prevalence and mortality indicators and associated costs over time.

3.2.2.2 Health burden in the EU (2023–2050)

In 2023 the cumulative burden of the five NCDs in the European Union was substantial, with over 6.4 million new cases and nearly 1.5 million deaths estimated, representing a total of 17.7 million years of life lost (YLLs). Assuming that incidence and mortality rates remain constant between 2023 and 2050, the annual number of new cases is expected to reach 7.4 million in 2050 (+16%), while the annual number of deaths will increase to 2.2 million (+50%) (Fig. 1).

In terms of diseases, IHD accounts for 30% of the new cases in 2023, followed by diabetes type 2 (27%) and COPD (26%). The main driver of mortality was IHD (11%). If the projections indicate that the number of deaths will increase in a constant way from 2023 to 2050, the most significant increase is expected in the number of deaths attributable to stroke (+61%).

Fig. 1A. Number of new cases between 2023 and 2050 in the EU

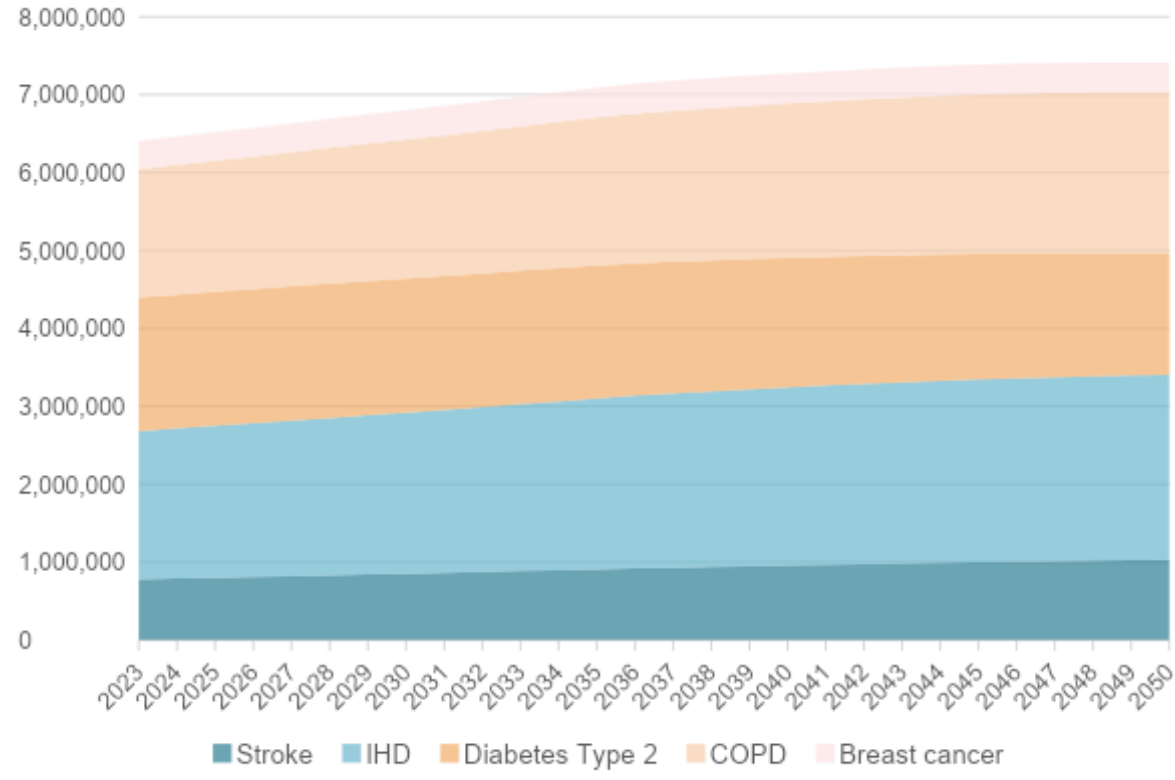
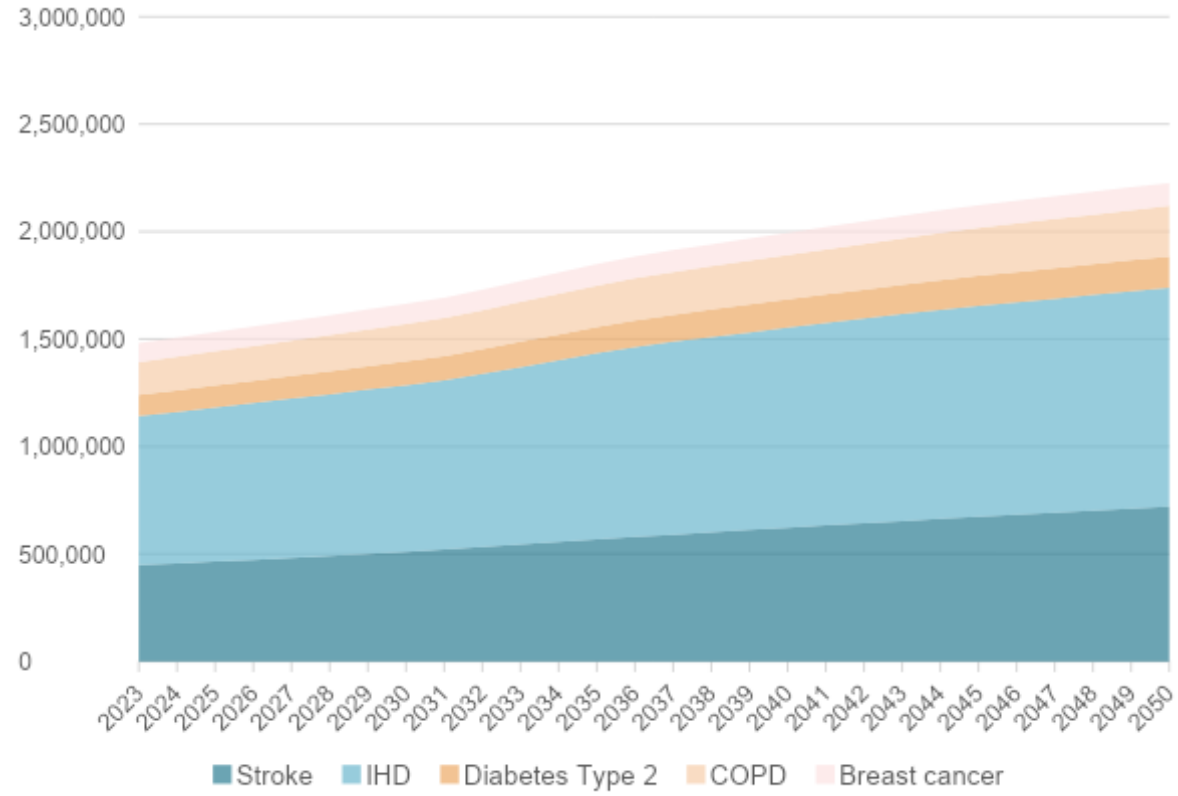
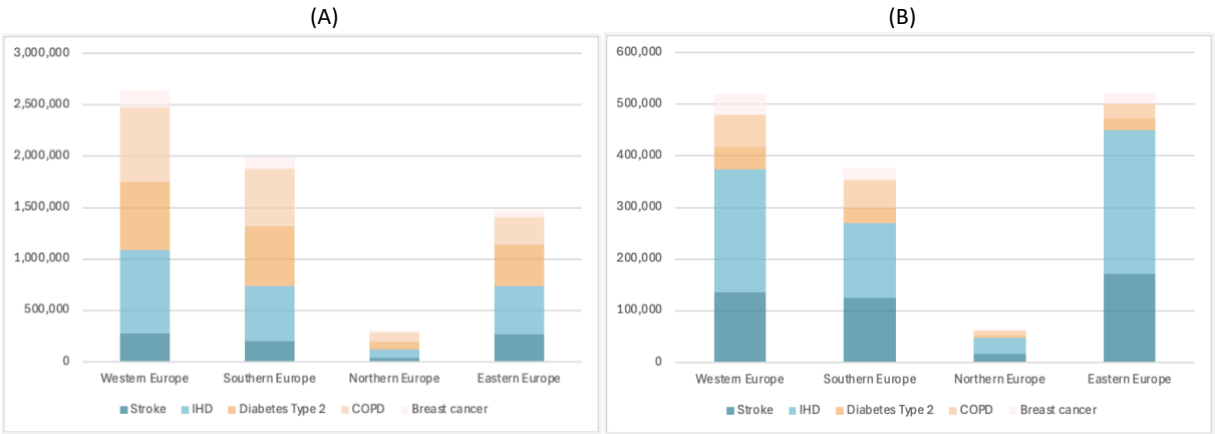


Fig. 1B. Number of deaths between 2023 and 2050 in the EU



Western Europe had the highest number of new cases of the five selected NCDs (2.64 million) among all four regions of the EU in 2023. However, considering their population sizes, the four regions show relatively similar rates, with new cases ranging from one per 65 inhabitants in Southern Europe to one per 73 in Western and Northern Europe. If the absolute number of deaths in Eastern and Western Europe were relatively similar, the mortality rate per capita was significantly higher in eastern Europe (1 per 204 inhabitants) compared with Western Europe (1 per 370 inhabitants). Northern and Western Europe experienced one death per 344 and one death per 341 deaths inhabitants, respectively (Fig. 2).

Fig. 2. Number of new cases (A) and deaths (B) by region in 2023



3.2.2.3 Economic burden in the EU (2023)

In 2023 the economic burden of the five NCDs was estimated to be €530.1 billion. The direct health care costs were the largest contributor to the economic burden of the five NCDs, amounting to 60.5% of the burden. The cost of absenteeism and presenteeism made up 29.2% and 2.4% of the combined economic burden, respectively. With an economic cost of €41.9 billion, the costs due to premature mortality contributed to 7.9% of the burden (Table 1).

Table 1. Economic burden in the EU in 2023 (in billions €).

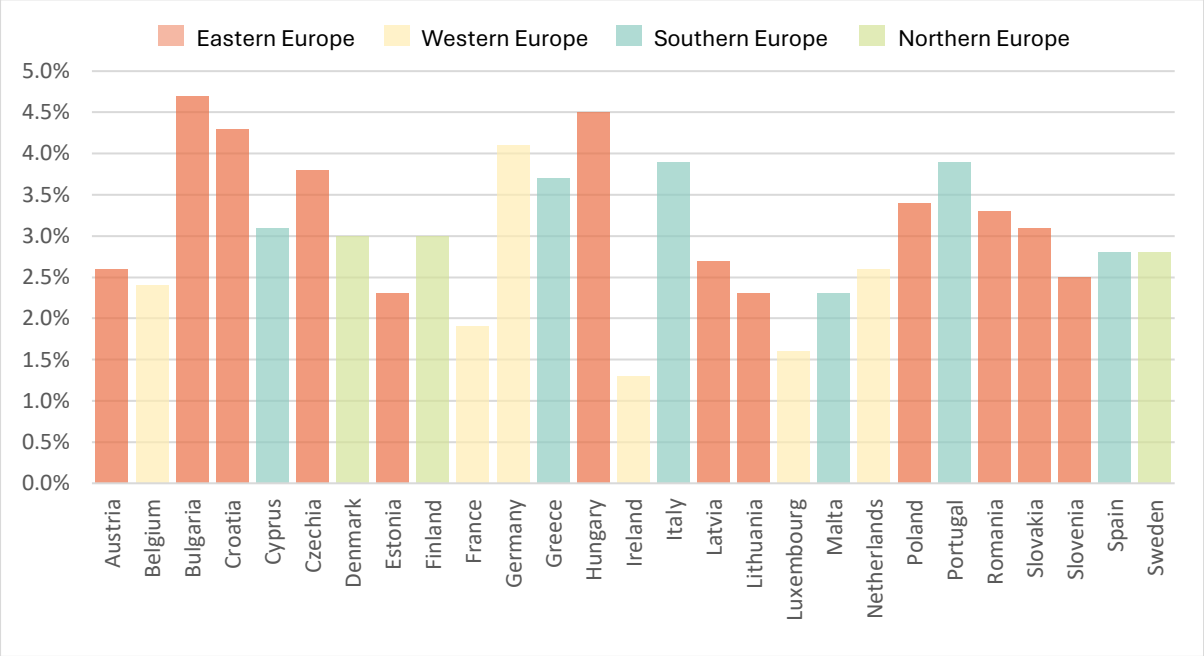
	Stroke	IHD	DM II	COPD	BC	Total	Total (%)
Direct health care costs	28.0	19.5	130.1	133.8	9.3	320.8	60.5
Absenteeism	21.6	54.3	20.9	57.3	0.7	154.9	29.2
Presenteeism	4.2	6.1	- x	- x	2.3	12.5	2.4
Premature mortality	8.0	19.7	3.3	3.1	7.8	41.9	7.9
Indirect costs	33.8	80.1	24.2	60.4	10.8	209.3	39.5
Total	**61.8**	**99.6**	**154.3**	**194.2**	**20.1**	**530.1**	**100.0**

x The cost of presenteeism due to diabetes type II and COPD could not be assessed due to lack of evidence in the scientific literature.

3.2.2.4.1 Comparative analysis

In 2023 the economic burden expressed as a percentage of the GDP ranged from 1.3% in Ireland to 4.7% in Bulgaria (Fig. 3). 12 countries, including seven countries of eastern Europe, had an economic burden higher than the average (3.03%).

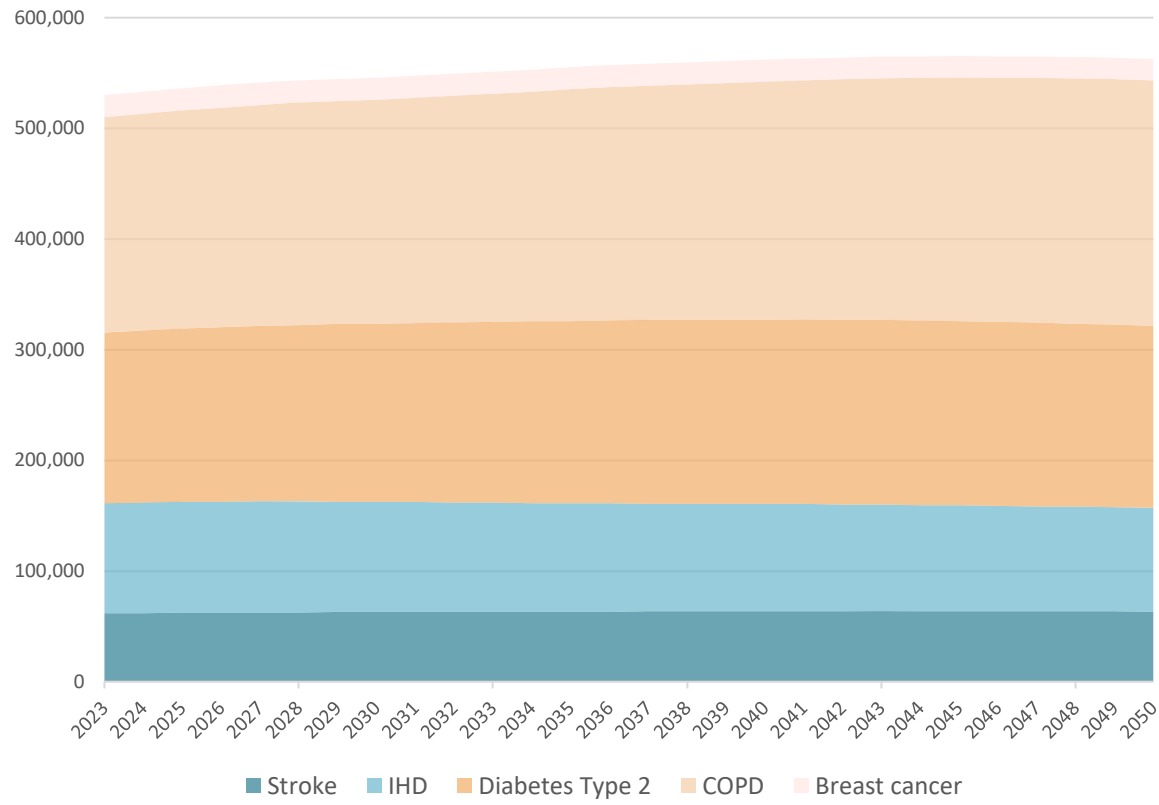
Fig. 3. Economic burden in the countries of the EU as % of 2023 GDP



3.2.2.4 Economic burden projection from 2023–2050

The economic burden was estimated at €530.1 billion in the EU in 2023. Assuming that incidence, prevalence and mortality rates remain constant between 2023 and 2050, the economic burden is expected to amount to €562.4 billion by 2050, representing a 6% increase (Fig. 4).

Fig. 4. Projected economic burden between 2023 and 2050 in the EU (in millions €)



Illustrating the value of investing in health: European case studies

This project examines the significant impact of NCDs through three case studies in Sweden, Portugal and Romania. Each case study is designed to build a strong investment case by analysing the country context in, which decisions about investing in health are made, assessing the economic burden that the case study diseases pose and evaluating targeted interventions aimed at addressing these challenges. Additionally, we present findings on the return on investment (ROI) for these interventions, highlighting the potential benefits of strategic health investments.

4.1 Portugal

4.1.1 Context

Health care and health status trends

In 2022 Portugal's life expectancy was 81.7 years, surpassing the EU average. However, older adults face higher disability rates despite lower preventable mortality. Mortality in Portugal has been driven by circulatory diseases and cancer, but life expectancy gains in the past decade are mainly due to reduced deaths from cardiovascular diseases, particularly stroke. Yet, 61% of people over 65 live with health-related limitations, particularly impacting women over 65, who spend only one third of their life disability-free.

Mortality rates from preventable and treatable causes were significantly lower than the EU average, with lung cancer being the top preventable cause and ischaemic heart disease and colorectal cancer accounting for a significant portion of treatable mortality. Portugal has fewer deaths from preventable and treatable causes and lower hospitalization rates for diabetes, asthma and COPD

than the EU average. **Robust primary care services contribute to low avoidable hospital admissions**. In 2019 hospitalization rates for these conditions were nearly 60% lower than the EU average. Despite declines in hospitalizations, Portugal has a high prevalence of diabetes, ranking fourth globally in 2021 with an age-adjusted prevalence of 9.1% and significant associated costs (Soares et al., 2023).

Portugal's success in reducing hospitalizations for chronic conditions is contrasted by significant **challenges in accessing medical care**. In 2022 nearly 3% of Portuguese residents reported unmet medical needs, exceeding the EU average and pre-pandemic rates. This issue is primarily due to cost constraints and high out-of-pocket expenses, particularly in outpatient care. Disparities based on gender, income and region persist, with lower-income individuals and women facing more barriers. Regions such as Alentejo, Algarve and the Centre Region have higher age-standardized mortality rates, which is often connected to inequities in health-care access and resource distribution, including for services as well as new technologies (Oliveira et al., 2022). Additionally, challenges in accessing health-care services are compounded by factors such as travel distance and increased wait times.

Portugal also has a slightly lower cancer incidence than the EU average, with cancer accounting for nearly one in four deaths in 2020. The lower prevalence of behavioural risk factors, such as smoking and dietary risks, contributes to this. However, ageing is expected to increase cancer cases and Portugal's ageing population faces significant disability and lifestyle-related health challenges, with obesity, inactivity and environmental risks being key concerns. Proactive measures, such as tax-based strategies, have successfully reduced smoking and alcohol intake, but challenges such as high obesity rates and physical inactivity persist. The National Cancer Control Strategy 2030 focuses on prevention through healthier lifestyles and reducing carcinogen exposure.

Health financing and governance

Portugal's National Health Service (NHS) is a tax-funded, universal health-care system that covers all residents, including asylum seekers and migrants (OECD, 2023). The Ministry of Health oversees planning and regulation at the national level. In 2023, the government in office initiated a reorganization of the NHS, replacing the Regional Health Administrations with 39 Local Health Units (ULS). These units integrate hospitals and health centres under a single management structure, aiming to improve accessibility and streamline patient movement between healthcare facilities. Municipalities manage primary care infrastructure and health promotion programmes. Primary care is delivered through the NHS's Network of Health Centres, including family health units and personalized health care units. Infarmed, a government agency, is responsible for medicine evaluation, authorization and regulation (Infarmed, web).

The NHS operates on a tax-financed model, ensuring universal access to health care at no cost. Healthcare is provided through a mix of public and private providers, with general practitioners serving as gatekeepers (OECD, 2023). Healthcare coverage in Portugal extends beyond the NHS through supplementary channels, including various insurance schemes for specific professional groups, such as those for the military, civil service and police and private voluntary health insurance.

Over the past four decades, Portugal's NHS has initiated decentralization, established Regional Health Administrations and delegated primary health care responsibilities to municipalities since 2018 (Nunes and Ferreira, 2022). Despite this, planning and resource allocation remain highly centralized. The gradual decentralization process has mainly focused on primary health care, aiming to bring services closer to citizens and address their specific needs (Mahmood et al., 2024). Centralized control of resources and decision-making in the hospital sector is remaining to avoid the potential drawbacks of full decentralization.

Public and private sector roles

While the public sector dominates health service provision, particularly hospital care, the private sector's role has grown significantly over the last 20 years. Private hospitals now feature technology comparable to public facilities and employ people full-time, a major shift from two decades ago (KII). Despite the NHS expanding services over the past five years (pre-COVID), escalating demand has outpaced resources, leading to longer waiting lists and limited treatment options for those without private care access (KII). Addressing these disparities is crucial for equitable health-care access.

Increasing numbers of individuals are using private hospitals for both hospital and primary care, reflecting a shift towards private settings (KII). In 2023 private hospitals invested €170 million, driven by foreign-backed firms as well as Portuguese market bonds and shares (KII). Portugal's population is concentrated along the coastline, with two-thirds of private hospitals also in these areas (KII). Reliance on the private sector, without parallel public sector investment, risks exacerbating regional inequalities, as rural and less densely populated areas rely on the public sector for their access to care.

Portugal has prioritized improving equitable access to health care by implementing measures to reduce financial barriers (OECD, 2023). Government initiatives, such as wide exemptions from cost-sharing and the elimination of user charges for primary care and NHS-prescribed services in 2020, followed by the complete abolition of charges within the NHS in 2022 (except for certain emergency care), aim to increase access for over 50% of the population. Although the full impact of these reforms is yet to be seen in the latest available data, they are expected to enhance public financing for both inpatient and outpatient medical care.

Health workforce

Despite substantial investments and strategic initiatives, Portugal faces challenges with the distribution of health-care professionals. The density of nurses in 2021 lagged 13% behind the EU average. The country also lacks various specialties, such as psychiatrists and paediatricians, due to limited training programmes. Although the number of active nurses has increased, 70% of health professionals are concentrated in Lisbon and the North Regions, which only account for 62% of the population. To address these imbalances, the government launched the More Doctors programme in 2024, offering incentives for medical professionals to practise in less densely populated areas (OECD, 2023).

Financial constraints and sustainability

Financial constraints contribute to this challenge. In 2021 health spending per capita accounted for 11% of GDP at €2630, over one third lower than the EU average. Public funding covers a smaller share of health expenditure, with private sources contributing nearly double the EU average (37% vs. 19%) (OECD, 2023). This disparity is driven by higher out-of-pocket expenses and private health insurance (29% and 8% of total health expenditure, respectively). Most out-of-pocket spending goes towards outpatient care and pharmaceuticals, which are less covered than the EU average.

High out-of-pocket payments, long waiting lists and difficulties in retaining health-care professionals undermine the sustainability and resilience of the Portuguese health system (Oliveira et al., 2022). Additionally, the system struggles with persistent debt and under-budgeting, resulting in minimal investments in infrastructure, equipment and facilities.

Despite financial constraints, Portugal prioritizes outpatient care, directing over 44% of health expenditure to this sector in 2021, the highest among EU countries. This focus results in a smaller hospital capacity but efficient acute hospital services, with an 82% occupancy rate in 2019, exceeding the EU average of 72% (OECD, 2023).

Portugal's spending on retail pharmaceuticals and medical devices slightly surpasses the EU average at 19% of the health budget. However, investment in prevention and long-term care is notably lower, as is spending on medical equipment maintenance, hindering disease screening and diagnosis capabilities. Limited expenditure in long-term care reflects a historical reliance on informal care arrangements (OECD, 2023). Efforts to address this gap have increased formal long-term care services, with the National Network for Long-term Care expanding inpatient capacity by 40% between 2014 and 2021. However, the continuous care system for elderly people (National Network for Long-term Care), created in 2007, remains only partly implemented due to low political priority and decreasing sensitivity among politicians (KII).

Elderly care falls under the Ministry of Social Security, not the Ministry of Health, leading to inefficiencies due to separate provider networks. This **fragmentation complicates ensuring continuity of care**. The private non-profit-making organization sector plays a significant role in chronic disease and elderly care but remains undercompensated, with the state in arrears and tariffs low and unadjusted to actual needs. Chronic and elderly care relies heavily on this sector, adding complexity to the situation (KII).

Looking forward: Planning to address health priorities

Approved in 2023, Portugal's National Health Plan (NHP) 2021–2030 prioritizes sustainability in the health sector by addressing health inequalities, behavioural risk factors and prevalent diseases (Direção-General da Saúde, 2022). It targets emerging health risks such as the impacts of climate change on disease patterns and antimicrobial resistance. Key priorities include addressing circulatory system diseases, cancers, chronic noncommunicable diseases and reducing maternal and infant mortality. The plan emphasizes partnerships, an integrated health information system, health human resources planning and infrastructure improvements. In alignment with the priorities of the NHP, the Portugal Recovery and Resilience Plan will allocate €1.38 billion by 2026 to enhance accessibility, efficiency and sustainability in the health-care system. Over 30% of this budget will be directed towards expanding primary care services, approximately 25% will focus on improving digital infrastructure and 20% will be invested in integration across care levels and modernizing the mental health and long-term care sectors.

The NHP faces challenges in implementation due to a lack of multiannual budgeting. Addressing these challenges will be critical to ensuring Portugal's preparedness to make the long-term investments needed to address chronic diseases and other health priorities and take up innovation in the health sector.

4.1.2 Burden of disease

In 2023 the cumulative burden of the five NCDs in Portugal included 143 509 new cases and 34 757 deaths, representing a total of over 393 090 years of life lost (YLLs). Assuming that incidence and mortality rates remain constant between 2023 and 2050, the annual number of new cases is expected to reach 158 265 in 2050 (+10%), while the annual number of deaths will increase to 51 997 (+50%). This represents a total economic burden of €9.96 billion in 2023, which is 3.9% of Portugal's 2023 GDP.

In 2023 type 2 diabetes mellitus accounted for 52 911 new cases and 3471 deaths. By 2050, the annual number of new cases was expected to be 44 980 (-15%), while the annual number of deaths would rise to 4976 (+43%).

Regarding COPD, the disease accounted for 46 401 new cases and 4612 deaths in 2023. By 2050, the annual number of new cases was expected to reach 59 089 (+27%), while the annual number of deaths would rise to 7037 (+53%).

4.1.3 The case for investing in health

4.1.3.1 Economic returns of diabetes intervention in Portugal

4.1.3.1.1 Description of the selected interventions

Intensive glycaemic control was the intervention included in the cost–benefit analysis (Table 2). This intervention was aligned with the national treatment guidelines in Portugal (Duarte et al., 2018). The national treatment guidelines are based on the HbA1C levels of patients. The recommendations employ an evidence-informed approach to manage diabetes and its complications such as cardiovascular diseases, renal failure, retinopathy and neuropathy using newer drugs and treatment regimens.

Table 2. Selected interventions, target population and associated drugs and supplies.

Intervention	Target population	Drugs and supplies
Intensive glycaemic control	People with diabetes	HbA1c test
	Diabetic patients with HbA1C < 7.5%	Metformin 850 mg
	Diabetic patients with HbA1C < 7.5% + High cholesterol	Metformin 850 mg; Sitagliptin 100 mg
	Diabetic patients with HbA1C < 7.5% + Obesity	Metformin 850 mg; Dulaglutide 0.75 mg
	Diabetic patients with HbA1C between 7.5% and 9%	Metformin 850 mg; Sitagliptin 100 mg
	Diabetic patients with HbA1C between 7.5% and 9% + Obesity	Metformin 850 mg; Dulaglutide 0.75 mg
	Diabetic patients with HbA1C > 9%	Metformin 850 mg; Sitagliptin 100 mg; Insulin
	Diabetic patients with HbA1C > 9% + Obesity	Metformin 850 mg; Dulaglutide 0.75 mg; Insulin

4.1.3.1.2 Coverage rates and scale-up pattern

Baseline parameters such as the coverage rates for intensive glycaemic control was derived from the Portuguese Society of Diabetology (Diabetes Factos e Numeros, 2023). A target coverage rate of 100% was used, with a linear increase throughout the 27 years (Table 3). The impact of intensive glycaemic control on the various complications of diabetes such as stroke, ischaemic heart disease, end-stage renal disease, diabetic retinopathy and lower extremity amputation was estimated using effect sizes from published literature. Details are provided in Annex 3.

Table 3. Estimated current coverage rate and target coverage rate by 2030, 2040, 2050 (%).

	2023	2030	2040	2050
Intensive glycaemic control	55.9	67.3	83.7	100.0

4.1.3.1.3 Intervention cost assessment

The net present value (NPV) of the incremental cost of the intervention package is estimated at €188.1 million in 2030, €871.9 million in 2040 and €1.8 billion in 2050. This sum represents the additional investment required to reach the coverage rate targets after seven years, 17 years and 27 years. (Table 4).

Table 4. NPV of incremental cost (in millions €).

	2023–2030	2023–2040	2023–2050
Intensive glycaemic control	188.1	871.9	1802.8

4.1.3.1.4 Health benefits

Scaling up this intervention package significantly reduces the number of diabetes complications (Table 5). Over 27 years, 4953 cases of stroke, 2415 cases of IHD, 10 565 cases of end-stage renal disease, 215 488 cases of diabetic retinopathy and 5670 cases of lower extremity amputations will be prevented. This translates to approximately 183 cases of stroke, 89 cases of ischaemic heart disease, 391 cases of end-stage renal disease, 7981 cases of diabetic retinopathy and 210 lower extremity amputations annually. In total, the package of interventions will save more than 8700 lives between 2023 and 2050. The reduction in mortality is primarily attributed to the reduction in diabetes complications.

Table 5. Health benefits of the diabetes interventions package in Portugal.

	New cases averted		Deaths averted	
	2023–2050	Per year (avg)	2023–2050	Per year (avg)
Stroke	4953	183	1551	57
Ischaemic heart disease	2415	89	1565	58
Lower extremity amputation	5670	210	2136	79
End-stage renal disease	10 565	391	3497	130
Diabetic retinopathy	215 488	7981	-	-

4.1.3.1.5 Economic benefits

Implementing this intervention package will yield significant economic benefits, with a net present value of €2.6 billion over 27 years. The largest contribution comes from the productivity gains from reduction of absenteeism and presenteeism associated with the complications of diabetes. (Table 6).

Table 6. NPV of the health benefits (in millions €).

	PV (2023) of the economic benefits (€)	Distribution of the benefits
Direct Healthcare Savings	477.7	19%
Absenteeism/Presenteeism Reduction	1106	43%
Unemployment/Job Loss Reduction	545.3	21%
Mortality Reduction	448.8	17%
Total	**2577.8**	**100%**

4.1.3.1.6 Return on investment (ROI)

The diabetes intervention is estimated to provide an ROI of €1.4 per €1 invested after 27 years. (Table 7).

Table 7. ROI of scaling up the diabetes interventions package.

	2023–2050
NPV of the intervention's cost (in millions €)	1802.7
NPV of the health benefits (in millions €)	2577.8
ROI	1.43

4.1.3.2 Economic returns of COPD interventions in Portugal

4.1.3.2.1 Description of the selected interventions

Six interventions were selected from the One-health Tool and included in the cost–benefit analysis (Table 8). These were modified to align with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2024 guidelines for the treatment of COPD (Agustí et al., 2024). These guidelines are revised annually and provide evidence-informed management strategies for COPD, including diagnosis, treatment and prevention. GOLD classifies COPD on the basis of airflow limitation and national recommendations from Portugal stratify treatment based on the GOLD classification scheme (GOLD A, B, E) for COPD (Miravitlles et al., 2016).

Table 8. Selected interventions, target population and associated drugs and supplies.

Intervention	Target population	Drugs and supplies
Bronchodilator	People with COPD (GOLD A)	Inhaled salmeterol, 25-50 mcg
LABA + LAMA*	People with COPD (GOLD B)	Formoterol 12 mcg; Aclidinium 340 mcg
LABA + LAMA + ICS*	People with COPD (GOLD E)	Umeclidinium 62.5 mcg + Vilanterol 25 mcg + Fluticasone 100 mcg
Exacerbation treatment with antibiotics	People with COPD (GOLD E)	Amoxicillin 875 mg + Clavulanic acid 125 mg
Exacerbation treatment with anti-inflammatory	People with COPD (GOLD E)	Roflumilast 500 mcg
Exacerbation treatment with oxygen	People with COPD (GOLD E)	Oxygen, 1000 liters, primarily with oxygen cylinders

LABA: Long-Acting Beta 2 Agonist, LAMA: Long-Acting Muscarinic Antagonist, ICS: Inhaled Corticosteroids

4.1.3.2.2 Coverage rates and scale-up pattern

Due to the lack of country-specific information in the scientific and grey literature, average estimates from the European Federation of Allergy and Airways Diseases Patients' Associations were used to approximate the current coverage rates of the selected interventions in Portugal (Active Patients Access Care, 2019). A target coverage rate of 100% was used for all interventions, with a linear increase throughout the 27 years (Table 9).

Table 9. Estimated current coverage rate and target coverage rate by 2030, 2040, 2050 (%).

	2023	2030	2040	2050
Bronchodilator	96	97.2	98.7	100.0
LABA + LAMA	96	97.2	98.7	100.0
LABA + LAMA + ICS	96	97.2	98.7	100.0
Exacerbation treatment with antibiotics	96	97.2	98.7	100.0
Exacerbation treatment with anti-inflammatory	96	97.2	98.7	100.0
Exacerbation treatment with oxygen	96	97.2	98.7	100.0

LABA: Long-Acting Beta 2 Agonist, LAMA: Long-Acting Muscarinic Antagonist, ICS: Inhaled Corticosteroids

4.1.3.2.3 Intervention cost assessment

The net present value (NPV) of the incremental cost of the intervention package is estimated at €25.4 million in 2030, €119.6 million in 2040 and €252.0 million in 2050. This sum represents the

additional investment required to reach the coverage rate targets after seven years, 17 years and 27 years. (Table 10).

Table 10. NPV of incremental cost (in millions €).

	2023-2030	2023-2040	2023-2050
Bronchodilator / LABA + LAMA / LABA + LAMA + ICS	19.4	91.1	191.9
Exacerbation treatment with antibiotics	1.0	4.6	9.8
Exacerbation treatment with anti-inflammatory	2.7	12.7	26.8
Exacerbation treatment with oxygen	2.4	11.1	23.4
Total	**25.4**	**119.6**	**252.0**

4.1.3.2.4 Health benefits

In total, scaling up the package of interventions will save 1328 lives between 2023 and 2050, which equates to 49 deaths per year. In addition to the deaths prevented, 12 031 healthy life years will be gained over the next 27 years, equating to approximately 446 healthy life years gained annually (Table 11). The package is also estimated to avert a total of 6768 years lived with disability or 251 years lived with disability annually, reflecting a significant improvement in the overall quality of life for individuals with COPD.

It is important to note that controlling COPD results in other health benefits that were not captured by this analysis, such as a reduction in emergency room visits, consultations and long-term care services, as well as reductions in comorbidities associated with COPD.

Table 11. Health benefits of the COPD interventions package in Portugal.

	2023-2030	2023-2040	2023-2050	Per year
Deaths averted	96	513	1,328	49
Healthy year lives gained	715	4,484	12,031	446
Years lived with disability averted	518	2,789	6,768	251

4.1.3.2.5 Economic benefits

Scaling up this intervention package will generate economic benefits estimated at a net present value of €48.3 million over 27 years, (Table 12). As mentioned above, the One-health Tool is primarily designed to measure the impact of interventions on mortality. Since the reduction in COPD symptoms could not be obtained, savings in health care costs and reduced absenteeism and presenteeism were not measured.

Table 12. NPV of the health benefits (in millions €).

	2023–2030	2023–2040	2023–2050
Productivity recovered from reduced mortality	5.1	24.3	48.3

4.1.3.2.6 Return on investment (ROI)

The package of COPD interventions is estimated to provide an ROI of 30 cents per €1 invested after 27 years (Table 13).

Table 13. ROI of scaling up the COPD interventions package.

	2023–2030	2023–2040	2023–2050
NPV of the intervention's cost (in millions €)	17	82	172
NPV of the health benefits (in millions €)	5	24	48
ROI	**0.3**	**0.3**	**0.3**

4.2 Romania

4.2.1 Context

Health status and health care trends

In 2022 Romania's life expectancy was 75.3 years, among the lowest in the EU, with significant gender disparities—men at 71.5 years and women at 79.3 years (OECD, 2023). Despite a slightly faster increase in life expectancy compared with the EU average from 2010 to 2019, Romania continues to face significant public health challenges, particularly related to NCDs and health-care access (OECD, 2023).

Cardiovascular diseases remain the leading cause of death, accounting for over 55% of all deaths in 2020, with ischaemic heart diseases (18.8%) and stroke (13.9%) as major contributors. Romania also grapples with high mortality rates from preventable and treatable causes, the highest in the EU as of 2020. Key drivers include ischaemic heart diseases, pneumonia and stroke (OECD, 2021). Although 30-day mortality rates for stroke and heart attack patients in hospitals are relatively low—indicative of good-quality inpatient care—access to outpatient services and essential pharmaceuticals remains a critical issue (OECD, 2023).

Several risk factors significantly contribute to Romania's mortality rates, including poor diet, tobacco and alcohol use and air pollution. However, adult obesity rates in Romania are the lowest in the EU (OECD, 2023). The country's cancer mortality rate slightly exceeds the EU average, despite a lower incidence, which points to challenges in early diagnosis and treatment. Screening services in Romania are notably underutilized, with only 9% of women aged 50–69 participating in breast cancer screening, far below the EU average of 66%. (OECD, 2023) Similarly, cervical cancer screening rates are low, with only 25% of women aged 20–69 participating and just 4% of people aged 50–74 undergoing colorectal cancer screening, compared with the EU averages of 60% and 33%, respectively (OECD, 2023). Efforts to improve screening rates have included new pilot programmes

for breast, cervical and colorectal cancer, funded by EU Structural Funds, the World Bank and national sources, although challenges in staffing and quality assurance persist (OECD, 2021).

Romania's ageing population presents additional health challenges. The proportion of individuals aged 65 and over increased from 13% in 2000 to 19% in 2020, yet they experience shorter lifespans and fewer healthy years compared with the EU average (OECD, 2023). In 2021 20% of Romanians over 16 years old reported suffering from chronic diseases or long-term health issues, with conditions such as hypertension, low back disease, diabetes mellitus and cervical disease being prevalent (Petre et al., 2023). A higher proportion of women with multiple chronic conditions also experience limitations in daily activities compared with the EU average (Petre et al., 2023).

Health financing and governance

Romania's health-care system is primarily financed through a centralized social health insurance system, managed by the National Health Insurance House (NHIH). This public, autonomous institution ensures the unified operation of the system, offering comprehensive benefits to most of the population. The Ministry of Health oversees policy-making, planning and regulation, finances public health programmes (like mother and child health, for example) and priority actions (stroke units, for example) while local implementation is managed by district public health authorities and district health insurance houses. Coverage includes a broad range of health-care services, pharmaceuticals and medical devices. Decisions on the health benefits package are made collaboratively by the Ministry of Health and NHIH, with the National Agency for Medicines and Medical Devices proposing a positive list for medicine reimbursement, although some high-performance medical services and rehabilitation procedures are not fully covered.

Public sources fund nearly 80% of Romania's health care, with Social Health Insurance contributing 65% and State and Local Authorities adding 15% (Petre et al., 2023).

Inequalities and barriers to health-care access

Out-of-pocket payments remain high, particularly for outpatient pharmaceuticals, where patients cover 10–80% of drug costs depending on the medication's reimbursed price. While ambulatory care is free, the cost-sharing burden for outpatient pharmaceuticals is significant. To address underfunding, the private sector's role has expanded, particularly in specialized services like dialysis, ophthalmology, gynaecology and oncology. However, this shift, without equivalent public investment, risks worsening health-care access inequalities, particularly in rural and less populated areas. Urban centres dominate health care infrastructure, with over 90% of hospitals, specialist outpatient clinics and specialist medical centres located in cities (Petre et al., 2023). Vulnerable groups, including the Roma and homeless individuals, face substantial barriers to accessing health-care services and educational resources (OECD, 2021). Inequalities are also evident in cancer screening, where higher-income Romanians are significantly more likely to participate than their lower-income counterparts, particularly in cervical cancer screening (OECD, 2023).

Romania faces significant barriers to accessing medicines, due to reimbursement procedures, bureaucratic processes, inadequate financing and supply limitations. Although there has been progress in the reimbursement of innovative medicines, access delays persist (EFPIA Patients WAIT Indicator 2023 Survey). Price control mechanisms, designed to keep prices low compared with other EU countries, have inadvertently led to parallel trade exports, threatening the sustainability of the pharmaceutical supply chain and contributing to stock outs and shortages (OECD, 2021). In response, Romania implemented time-limited export restrictions on certain cancer drugs in 2019

and COVID-19-related medicines and consumables in 2020 (OECD, 2021). These challenges exacerbate existing inequalities in health-care access, particularly affecting vulnerable populations who already face significant barriers. Addressing these issues is critical to improving equity and ensuring consistent access to essential health-care services across Romania.

Health spending and risks to sustainability

Despite recent increases, Romania allocates only 6.5% of its GDP to health care, one of the lowest levels in the EU (OECD, 2023). Overall health spending stands at 13%, compared with the EU average of 15% (KII). This underfunding contributes to poorer health outcomes compared with EU averages. The ongoing financial challenges, coupled with structural inefficiencies and workforce shortages, pose a substantial risk to the sustainability and resilience of Romania's health-care system (KII).

Romania's health-care system relies heavily on public funding, which accounts for nearly 80% of total health expenditure. However, the social health insurance system, funded by contributions from employees and employers, is under significant pressure due to limited contributions from certain segments, such as pensioners. This shortfall is often addressed with unpredictable government subsidies, undermining financial predictability and strategic planning (KII). Implementing a more predictable, formula-based approach to funding could enhance the system's sustainability and allow for more effective long-term planning.

In Romania, health care funding is collected into a central budget before being allocated to the health-care sector, making the process indirect and subject to influence by political decisions. Although the percentage of GDP allocated to health care remains the same, as GDP grows, this results in more funds each year. However, this has led to a perception of inefficiency among politicians, who see the increased funding as not yielding proportional improvements, making them reluctant to further increase health care spending (KII). This uncertainty and underfunding have led to an expanded role for the private sector, particularly in outpatient care and specialized services like dialysis, ophthalmology, gynaecology and oncology, where public funding has fallen short (KII).

Significant barriers to accessing medicines persist due to reimbursement procedures, bureaucratic processes, inadequate financing, and supply limitations.

Romania's health-care system is overly reliant on hospital-based care, with insufficient investment in outpatient and primary care (KII). Shifting more resources towards outpatient services and primary care could reduce unnecessary hospital admissions and improve cost–effectiveness. Romania exhibits some of the highest rates of avoidable hospital admissions for conditions like diabetes in the EU, reflecting this hospital-centric model, which is rooted in historical investment patterns. The pandemic also revealed the potential overuse of hospital care, as hospitalizations dropped significantly, underscoring the need to strengthen primary care and reduce unnecessary admissions (OECD, 2023; Jullien et al., 2023).

Despite Romania's strong medical education system, the country faces a significant health-care workforce deficit due to substantial migration, with over 10 000 physicians emigrating between 2008 and 2019, leading to over €650 million spent on medical services procured within the EU (Petre et al., 2023). The COVID-19 pandemic further exposed these workforce shortages, particularly in intensive care, resulting in compromised service provision despite efforts to hire and train additional staff and provide incentives (OECD, Romania, 2021). Preexisting shortages persist, causing understaffing, increased workloads for physicians—particularly general practitioners—and subsequent burnout (OECD, 2023). To address these challenges, Romania has developed a Human Resources Strategy with WHO support and published sectoral Action Plans (OECD, 2023). Efforts to

retain medical professionals, particularly in underserved and rural areas, are essential for ensuring the sustainability of the health-care system.

Spending on reimbursed medications has increased, although not as quickly as wage growth. Investments have improved outpatient laboratory and imaging services, reducing waiting lists. However, the health-care system remains underfunded, particularly in outpatient care, which is among the lowest in the EU.

Priorities, reforms and areas of focus

Romania's health-care system has long faced challenges such as underfunding, medical personnel shortages, inadequate infrastructure and ineffective service delivery, particularly in remote areas. These issues have exacerbated regional disparities in health-care access and quality. To address these deep-rooted problems, the country has prioritized key areas such as primary care, hospital modernization and enhanced screening programmes (RR).

One of the most significant shifts in Romania's health care strategy has been the increased emphasis on primary care. Historically, the country has over-relied on hospital-based care, leading to a disproportionate allocation of resources towards inpatient services at the expense of primary and ambulatory care. This imbalance has weakened the primary care system, resulting in frequent bypassing of general practitioners in favour of emergency departments and specialist services, even for non-urgent cases (KII; OECD, 2023). However, with significant investments being directed towards expanding services, improving infrastructure and ensuring better coverage, particularly in underserved regions, primary health care is now receiving the attention it deserves (KII). The ratification of Law No. 1/2021, which supports the Results-Based Programme in the Health Sector, marks a crucial step in Romania's commitment to primary health care reform (KII). Despite these positive changes, a key informant interview (KII) highlighted concerns that transitioning back to a performance-based funding model, after the increased hospital budgets during COVID-19, could financially strain hospitals, potentially leading to bankruptcies (KII).

In parallel, Romania has undertaken efforts to modernize hospital infrastructure. A substantial portion of funds from the EU's Recovery and Resilience Plan and the EU Cohesion Policy is being allocated to upgrade hospital facilities. These investments aim to enhance patient safety, reduce care-related infections and improve the overall resilience of the health-care system. However, there is a growing recognition of the need to balance hospital investments with the development of outpatient services and primary care to better manage the growing burden of NCDs (OECD, 2023).

In addition to infrastructure improvements, the health-care system is undergoing a comprehensive overhaul of its cancer care services. The National Plan for Beating Cancer, adopted in 2022, introduces an integrated, multidisciplinary approach to treatment. This plan includes a revamped patient pathway, the creation of an Innovation Fund for faster reimbursement of innovative medicines and programmes to provide psychological, palliative and nutritional counselling. Prevention strategies are also a focal point, with initiatives like mobile health units being deployed to underserved regions to increase cancer screening uptake. These efforts, largely financed through EU funds, highlight the critical role of external support in advancing Romania's health care goals. Regarding cardio- and cerebrovascular diseases, a National Strategy was published in October 2024, providing an integrated approach to prevention, early diagnosis, treatment, palliative care, research and development, and more.

Advancements in data use and digitalization are also central to Romania's health care transformation. The COVID-19 pandemic accelerated the adoption of electronic information systems, which are crucial for optimizing health-care delivery, particularly in resource-scarce settings. The National Health Insurance House has launched a project with a budget of approximately €100 million to develop an improved data platform that supports evidence-informed decision-making in health policies and reimbursement. Additionally, the development of national registers for cardiology and the digitization of clinical data are expected to enhance the quality and efficiency of health-care services, particularly in the management of chronic conditions.

Finally, telemedicine has emerged as a vital component of Romania's health care strategy, particularly for improving access to care in rural areas. The amendment of the primary health care law in 2020 laid the groundwork for the development and utilization of telemedicine, enabling the remote monitoring of chronic diseases and offering a potential solution to the challenges of health-care delivery in underserved regions.

4.2.2 Burden of disease

In 2023 the cumulative burden of the five NCDs in Romania included 275 071 new cases and 116 762 deaths, representing a total of over 1.3 million years of life lost (YLLs). Assuming that incidence and mortality rates remain constant between 2023 and 2050, the annual number of new cases is expected to reach 317 028 in 2050 (+15%), while the annual number of deaths will increase to 165 779 (+42%). This represents a total economic burden of €10.59 billion in 2023, which is 3.3% of Romania's 2023 GDP.

In 2023 there were 64 664 new cases due to stroke and 97 239 cases due to IHD in Romania. Deaths were estimated to be 48 401 due to stroke and 56 212 due to IHD. By 2050, new cases would increase to 82 543 for stroke (+28%) and 122 401 for IHD (+26%). Deaths would rise to 72 007 for stroke (+49%) and 78 089 for IHD (+39%).

4.2.3 The case for investing in health

4.2.3.1 Description of the selected interventions

Four interventions were selected from the One-health Tool and included in the return-on-investment analysis (Table 14). These were modified to align with the 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice (Visseren et al., 2021). These regional guidelines provide recommendations for health-care professionals to diagnose and manage cardiovascular diseases and risk factors. The guidelines focus on both primary and secondary prevention of cardiovascular diseases using novel therapies and evidence-informed targets. It considers recent advances in cardiovascular risk assessment and treatment, including major risk factors such as obesity, hypertension, diabetes and dyslipidaemias. The class of drugs used and treatment regimens were adapted from the ESC guidelines.

Table 14. Selected interventions, target population and associated drugs and supplies.

Intervention	Target population	Drugs and supplies
Treatment for those with an absolute risk of CVD/Diabetes	People with a 20-30% chance of developing CVD or diabetes	Simvastatin 15 mg; Hydrochlorothiazide 25 mg; Enalapril 20 mg; Atenolol 50 mg; Amlodipine 10 mg; Colchicine 0.5 mg
Treatment for new cases of AMI	People with acute strokes or IHD <4.5 hr duration	Intravenous thrombolysis with alteplase
	People with acute strokes or IHD ≥4.5 hr duration	Mechanical thrombectomy
Treatment of cases of established IHD	People with post-acute IHD	Acetyl salicylic acid (aspirin) 75 mg; Ticagrelor 90 mg; Prasugrel 10 mg; Enalapril 20 mg; Atenolol 50 mg; Simvastatin, 15 mg; Colchicine 0.5 mg; Blood glucose level test; Cholesterol test; Urine analysis
Treatment for those with established cerebrovascular disease	People with post-acute strokes or both post-acute strokes and IHD	Acetyl salicylic acid (aspirin) 75 mg; Clopidogrel 75 mg; Enalapril 20 mg; Atenolol 50 mg; Colchicine 0.5 mg; Blood glucose level test; Cholesterol test; Urine analysis

4.2.3.2 Coverage rates and scale-up pattern

The baseline coverage rate of the selected interventions was derived from academic studies and reports from international organizations (Self-reported screening, 2020; Berbecar et al., 2021; Worldwide trends in hypertension, 2021; Tatu-Chiţoiu et al., 2012). Due to the lack of data available regarding the coverage rate of the treatment of established ischaemic heart disease and cerebrovascular disease, the OECD population coverage calculated for a set of health services was applied as a proxy indicator (OECD, 2023). A target coverage rate of 100% was used for all interventions, with a linear increase throughout the 27 years under study (Table 15).

Table 15. Estimated current coverage rate and target coverage rate by 2030, 2040, 2050 (%).

	2023	2030	2040	2050
Treatment for those with an absolute risk of CVD/Diabetes	60	70	85	100.0
Treatment for new cases of AMI	49	62	81	100.0
Treatment of cases of established IHD	86	90	95	100.0
Treatment for those with established cerebrovascular disease	86	90	95	100.0

4.2.3.3 Annual Intervention cost assessment

The net present value (NPV) of the incremental cost of the intervention package is estimated at €543.1 million in 2030, €2.4 billion in 2040 and €4.8 billion in 2050. This sum represents the additional investment required to reach the coverage rate targets after seven years, 17 years and

27 years (Table 16). Treating individuals with absolute risk of cardiovascular diseases and/or diabetes produces the highest cost throughout the scale-up period.

Table 16. NPV of incremental cost (in millions €).

	2023–2030	2023–2040	2023–2050
Treatment for those with an absolute risk of CVD/Diabetes	340.6	1508.4	3038.1
Treatment for new cases of AMI	186.1	811.5	1637.4
Treatment of cases of established IHD	15.5	68.2	138.5
Treatment for those with established cerebrovascular disease	0.9	4.0	8.2
Total	**543.1**	**2392.0**	**4822.2**

4.2.3.4 Health benefits

Scaling up this package of intervention over 27 years prevents 74 815 new cases of stroke and 54 673 new cases of ischaemic heart disease (Table 17). This translates to 2771 fewer cases of stroke and 2205 fewer cases of ischaemic heart disease yearly. In total, the package of interventions will save 107 177 lives between 2023 and 2050.

By scaling up this intervention package, a total of 796 413 healthy life years will be gained over the next 27 years. This equates to approximately 29 497 healthy life years gained annually. 244 026 YLDs will be averted between 2023 and 2050, which equates to 9045 YLDs annually, reflecting a significant improvement in the overall quality of life for the population.

Table 17. Health benefits of cardiovascular interventions package in Romania.

	2023-2030	2023-2040	2023-2050	Per year
Deaths averted	7,070	41,697	107,177	3,970
Stroke averted	6,121	31,920	74,815	2,771
IHD averted	4,987	24,639	54,673	2,025
Healthy year lives gained	21,719	230,299	796,413	29,497
Years lived with disability (YLDs) averted	9,104	83,630	244,206	9,045

4.2.3.5 Economic benefits

Implementing this intervention package will yield significant economic benefits, of, which the net present value is estimated at €4.28 billion over 27 years. These benefits include productivity gains of €308.2 million and costs saved from reduced mortality of €3.98 billion (Table 18). It is important to note that scaling up the preventive treatment for at-risk individuals reduces the incidence of strokes and IHDs, which in turn lowers the resources required for the three other interventions. As a result, the savings in health care costs are inherently accounted for through this mechanism.

Table 18. NPV of the health benefits (in millions €).

	2023–2030	2023–2040	2023–2050
Productivity gains from reduced absenteeism	31.9	138.6	267.3
Productivity gains from reduced presenteeism	4.8	21.1	40.9
Productivity gains from reduced mortality	334.4	1848.8	3978.3
Total	**371.1**	**2008.5**	**4286.4**

4.2.3.6 Return on investment (ROI)

The package of cardiovascular interventions is estimated to provide an ROI of €1.1 per €1 invested after 27 years (Table 19).

Table 19. ROI of scaling up the cardiovascular interventions package in Romania.

	2023–2030	2023–2040	2023–2050
NPV of the intervention's cost (in millions €)	543	2392	4822
NPV of the health benefits (in millions €)	429	2439	5324
ROI	0.8	1.0	1.1

4.3 Sweden

4.3.1 Context

Health status and health care trends

Sweden consistently ranks among the top performers in health outcomes within the European Union, boasting the second-highest life expectancy in the EU at 83.1 years in 2022 (OECD, Sweden 2023). The country has made significant strides in reducing mortality from circulatory diseases and cancer, although these remain the leading causes of death, alongside COVID-19-related fatalities during the pandemic (OECD, Sweden 2023). Swedish seniors enjoy longer, healthier lives post-65 compared with the EU average, reflecting the effectiveness of Sweden's health-care system in managing ageing populations (OECD, Sweden 2023). Moreover, Sweden has the lowest three-year average of excess mortality among EU nations, underscoring its resilience and strong public health infrastructure (OECD, Sweden 2023).

However, despite these impressive health indicators, Sweden faces substantial challenges due to behavioural risk factors. In 2019 approximately one third of all deaths in Sweden were attributed to such factors, including obesity, heavy alcohol consumption and smoking, although smoking rates are relatively low (OECD, Sweden 2023). The country has implemented robust public health policies that contribute to low preventable mortality rates, particularly for lung cancer, alcohol-related causes and traffic accidents, but these behavioural risks still pose a significant threat to public health (OECD, Sweden 2023).

Sweden's ageing population and the increasing prevalence of chronic diseases present further challenges. As of 2021, 82% of those aged 65 and older had at least one chronic condition, contributing significantly to health care costs and service demand (OECD, Sweden 2023). Sweden's demographic shifts, influenced by higher birth rates and significant immigration, present opportunities and challenges for the health-care system. While the influx of younger immigrants positively contributes to the workforce, the health-care system must adapt to meet the needs of a diverse population. This includes addressing language barriers, enhancing cultural competence and ensuring equitable access to health-care services. The health-care system's ability to effectively integrate these populations is crucial for maintaining the overall health and resilience of the nation (KII).

Swedish health care is renowned for its medical quality, with hospital admissions for chronic diseases decreasing since 2008 (Janlöv et al., 2023). However, challenges in delivering person-centred care persist, likely due to a comparatively weaker primary care system, which affects equity and outcomes across different socioeconomic groups and regions (Janlöv et al., 2023). Despite these challenges, Sweden has demonstrated resilience by increasing public spending on health during the pandemic, including allocating €452 million to address issues in the long-term care sector (OECD, Sweden 2023).

Sweden also excels in preventive care, with nationwide cancer screening programmes for breast, cervical and colorectal cancers achieving high participation rates, surpassing EU averages. These programmes are crucial for early detection and prevention, significantly improving health outcomes (OECD, Sweden 2023; Janlöv et al., 2023).

Health financing and governance

Sweden's health system is characterized by a decentralized structure, where health-care services are primarily provided by 21 regions and 290 municipalities, with national oversight ensuring equitable coverage for all residents (OECD, Sweden 2023). The national government plays a crucial role in regulating and supervising health care, while regions are responsible for financing, purchasing and service provision. This decentralized approach allows regions to levy income taxes and manage health-care delivery, tailored to the specific needs of their populations (KII).

The ongoing debate about centralization highlights the challenges of Sweden's current system. A government inquiry is currently evaluating the potential benefits and drawbacks of centralizing health care to improve efficiency, equity and reduce waiting times. However, the lack of political consensus at both national and local levels suggests that any changes may be incremental rather than sweeping (OECD, Sweden 2023). The inquiry aims to propose politically viable solutions that balance the need for centralized coordination with the benefits of localized decision-making.

In terms of health financing, Sweden's health spending slightly exceeds the EU average, with expenditures reaching €4200 per capita in 2021. Public funding covers 86% of health expenses, reflecting Sweden's commitment to maintaining a robust publicly funded health-care system (OECD, Sweden 2023). The country allocates 11.2% of its GDP to health spending, a figure that has risen due to pandemic-related costs (OECD, Sweden 2023). Despite the decentralized system, the central government provides a lump sum transfer to regions and municipalities, designed to equalize disparities across different regions, considering factors like education, age and health care needs (KII). Small patient fees apply to most services, with exceptions made for vulnerable groups, ensuring broad access to care (OECD, Sweden 2023).

Sweden's approach to drug reimbursement reflects the complexity of its decentralized system. The reimbursement process is overseen by the Dental and Pharmaceuticals Benefits Agency (TLV) and the Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU), which evaluate the cost–effectiveness of drugs to determine state reimbursement eligibility (Janlöv et al., 2023). Regions collaborate on drug introduction through a national initiative aimed at ensuring

equal and cost-effective health-care delivery across Sweden. However, the varying levels of cooperation among regions can lead to disparities in access to new treatments, particularly for rare diseases and cancers (KII). This has prompted discussions about centralizing pharmaceutical coverage recommendations to streamline processes and enhance equity (Ekdahl et al., 2019).

Despite the strengths of Sweden's health-care system, challenges remain in managing resources and ensuring equitable access across regions. The shortage of general practitioners and specialist nurses, combined with staffing challenges, has led to overcrowding in hospitals, particularly as the number of hospital beds has decreased over the decades (Janlöv et al., 2023). The shift towards outpatient care and the prioritization of home-based long-term care over institutionalized care reflect national policy trends, but these shifts also underscore the need for continued investment in comprehensive care systems.

Health Workforce: Outpatient and Inpatient care

Sweden's health-care system is marked by a relatively high density of doctors and nurses compared with EU averages, yet it faces significant challenges, particularly in primary care. While Sweden boasts one of the highest numbers of doctors and nurses per capita among OECD countries, the distribution of this workforce is heavily skewed towards hospital-based care. This hospital-centric approach drives up health care costs due to the high expense associated with hospital care (OECD, Sweden 2023; KII).

Despite the country's abundant health-care workforce, Sweden struggles with shortages of general practitioners (GPs) and specialist nurses, particularly in primary care settings. The health-care system's reliance on hospitals, where most doctors and nurses prefer to work, exacerbates these shortages. The preference for hospital work is driven by more attractive working conditions, such as better incentives and work environments, even although hospital roles often require night and weekend shifts (KII). In contrast, primary care positions are perceived as less desirable due to high patient-to-doctor ratios and other challenging working conditions (KII).

Efforts to shift focus from hospitals to primary care have been slow to progress. The central government has provided funding to regions to reduce hospital reliance, but a lack of strong governance and political will at regional level has hindered effective implementation (KII). Making primary care more attractive—by improving working conditions and reducing patient-to-doctor ratios—remains a critical challenge that must be addressed to successfully transition towards a more balanced health-care system (KII).

Insufficient bed capacity in hospitals, leading to overcrowding, is another pressing issue. Despite efforts to expand outpatient and day care services, hospitals continue to experience high demand, partly due to staffing challenges that prevent efficient resource management (Janlöv et al., 2023). Municipalities have prioritized home-based long-term care services over institutionalized care, but further investment in these areas is needed to alleviate the burden on hospitals (Janlöv et al., 2023).

Looking forward: Planning to address health priorities

Sweden's health-care system is focusing on key priorities, including enhancing patient choice, strengthening primary care, emphasizing prevention and improving efficiency through the concentration of specialized care.

Reforms like the 2010 mandatory choice in primary care and the 2015 Patient Act have expanded patient options, leading to the rise of private digital health-care providers. While these developments have improved access, they have also raised concerns about increased costs and alignment with needs-based care. Despite generally good access, waiting times remain above the EU average.

The ongoing shift from hospital-centric care to a stronger primary care system is crucial but faces challenges due to unattractive working conditions and high patient-to-doctor ratios. Making primary care more appealing to health-care professionals is essential for successful transition.

Since 2012, Sweden has concentrated specialized care in fewer units to improve quality and efficiency. National initiatives like cancer centres and standardized clinical pathways are designed to ensure equitable access to high-quality care.

While Sweden performs well in process measures, such as hospital stay duration, challenges like high health care costs, staff turnover and the rise of digital health-care providers need to be addressed. Recent efforts to centralize pharmaceutical pricing and subsidies are intended to support innovation, particularly in advanced therapies, while ensuring affordability and access.

4.3.2 Burden of disease

In 2023 the cumulative burden of the five NCDs in Sweden included 136 356 new cases and 28 035 deaths, representing a total of 318 839 years of life lost (YLLs). Assuming that incidence and mortality rates remain constant between 2023 and 2050, the annual number of new cases is expected to reach 178 098 in 2050 (+31%), while the annual number of deaths will increase to 44 247 (+58%). This represents a total economic burden of €15.43 billion in 2023, which is 2.8% of Sweden's 2023 GDP.

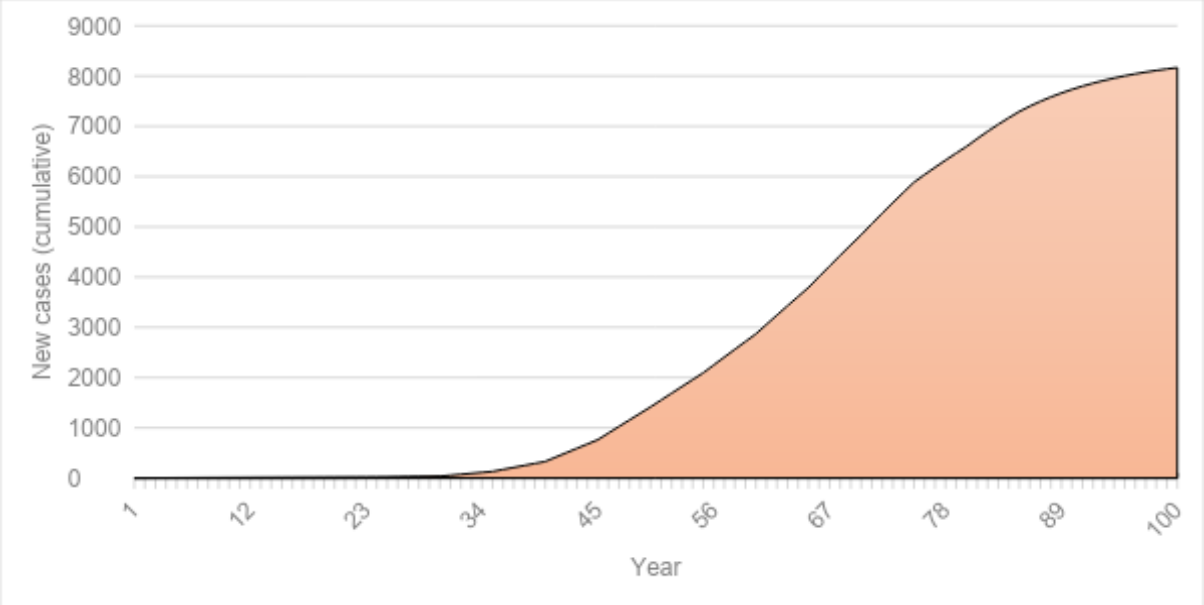
Breast cancer accounts for 7257 of the new cases and 1456 deaths in 2023. It is expected to reach 8702 new cases (+20%) and 1887 deaths (+30%) in 2050.

4.3.3 The case for investing in health

4.3.3.1 Lifetime's incidence

In the birth cohort of 48 092 girls, the model predicts that 8167 will be affected by breast cancer over a 100-year period (Fig. 5). This represents one woman out of seven before the age of 85, which is coherent with global estimates (Institute of M, 2005. The first incident cases are observed after 25, after, which incidence increases significantly as the cohort ages.

Fig. 5. Cumulative number of new breast cancer cases over 100 years



4.3.3.2 Treatment cost

The analysis of treatment costs reveals significant variation depending on the timing of the intervention (Table 20). The number of treated patients ranges from 36 when the intervention is delivered between 20 and 30, to 3162 when delivered between 60–70. Correspondingly, the total treatment costs increase from €0.7 million to €61.4 million. The average cost per patient treated remains relatively stable, with a slight increase when implementation is delayed. This increase reflects the accumulation of more advanced breast cancer cases due to the natural progression of the disease before implementation, resulting in higher treatment costs.

Table 20. Patients treated and treatment costs per ten-year **implementation period.**

	10-year implementation period				
	20-30	**30-40**	**40-50**	**50-60**	**60-70**
Patients treated*	36	339	1,377	2,321	3,162
Treatment costs (in million €)	0.65	6.3	26.2	45.3	61.4
Treatment cost per patient (€)	17,895	18,719	19,060	19,519	19,406

*Includes the prevalent cases in the first year of implementation and all new cases during the 10-year implementation period.

4.3.3.3 Health benefits

The health benefits of comprehensive breast cancer treatment were assessed by comparing the outcomes in the five intervention scenarios to those in the non-intervention scenario (Table 21). While the costs were captured over a ten-year period, the benefits were evaluated over the cohort's lifetime to capture both the short and long-term effects of the intervention.

The number of deaths averted ranges from 0 when the intervention is implemented between 20 and 30, to 201 when implemented between ages 60 and 70. Similarly, the QALYs gained range from 67 to 9814, with a weighted average of 770 QALYs gained annually. QALYs measure the additional years of healthy life gained from the intervention, reflecting both extended survival and improved quality of life. The greater impact observed when the intervention is implemented later is due to the significant increase in incidence and the accumulation of prevalent cases as the cohort ages.

Table 21. Health benefits per ten-year implementation period.

	10-year implementation period				
	20-30	**30-40**	**40-50**	**50-60**	**60-70**
Deaths averted	0	1	12	60	201
QALYs gained	67	911	4,152	8,018	9,814

QALY: Quality-adjusted life year

Health benefits (deaths averted, QALYs gained) are compared to the no-intervention scenario.

4.3.3.4 Economic valuation of health benefits

The economic valuation of health benefits was conducted by estimating the productivity gains resulting from reducing and delaying mortality from breast cancer (Table 22). While the highest productivity gains are obtained when the intervention is implemented between 40 and 50 (€147 million) and 50 and 60 (€129 million), the analysis of the economic benefits per patient treated presents a different perspective. Implementing the intervention between 30 and 40 produces the highest productivity gains per patient treated (€157 003), significantly outpacing the benefits from other ten-year implementation periods. Implementation between 60 and 70 generates a benefit of €3140 per patient treated.

These differences can be explained by two reasons. First, the economic benefits presented below represent the net present value discounted from 2023 onwards, reflecting the principle of the time value of money. Second, the economic benefits were estimated using the human capital approach, which calculates the potential gains from reduced and delayed mortality among economically active individuals up to retirement. As the cohort approaches retirement, which was defined at 64, the overall number of remaining productive years diminishes, thereby reducing the potential health benefits for each death avoided.

Table 22. NPV of the health benefits per ten-year implementation period.

	10-year implementation period				
	20-30	**30-40**	**40-50**	**50-60**	**60-70**
NPV of the productivity gains (in million €)	4	53	147	129	10
NPV of the productivity gains per patient treated (€)	96,754	157,003	106,999	55,576	3,140

4.3.3.5 Return on investment (ROI)

The model indicates that delivering comprehensive treatment to women affected by breast cancer provides an ROI from €0.6 to €13.0 per €1 invested, depending on the timing of the intervention. The average ROI weighted by the number of treated patients is positive at €4.9 per €1 invested.

Table 15. ROI of comprehensive breast cancer treatment per ten-year implementation period.

	10-year implementation period				
	20-30	**30-40**	**40-50**	**50-60**	**60-70**
NPV of the treatment cost (in millions €)	0.5	4.1	12.8	16.9	17.0
NPV of the health benefits (in millions €)	3.5	53.2	147.3	129.0	9.9
ROI	**6.5**	**13.0**	**11.5**	**7.6**	**0.6**

4.3.3.6 Sensitivity analysis

Table 16 shows the average ROI when increasing the drugs and supplies costs by 50%, 100% and 200%. The ROI decreases progressively from 4.9 to 3.0 when these costs are increased, but it remains positive even under the costliest scenario.

Table 16. Average ROI with a 50%, 100% and 200% increase in the cost of the drugs and supplies.

	Base Scenario	**+50%**	**+100%**	**+200%**
Average ROI*	4.9	4.2	3.7	3.0

*Weighted by the number of patients treated in each 10-year implementation period

Limitations of the Economic Burden and ROI Analyses

- Estimates from the Institute of Health Metrics and Evaluation Global Burden of Disease 2019 were used to estimate current incidence, prevalence and mortality in the 27 European countries. These estimates may vary from official health statistics.
- The scope of this study is limited to five NCDs posing substantial health and economic burden in the EU. While other conditions, such as obesity, chronic kidney disease or mental health disorders, also generate significant economic losses, they were not included in the present analysis due to the need for a focused approach.
- The analysis only captured the economic burden through absenteeism, presenteeism, health care costs and the societal cost of mortality. However, NCDs produce economic impacts through other pathways, such as early retirement, caregivers' loss of productivity, medical transport or social assistance. Similarly, complex interactions between the selected NCDs and other health issues, such as mental health disorders or infectious diseases, can further exacerbate the overall health and economic burden, which was not fully accounted for in our analysis.
- Due to challenges in measuring and projecting future epidemiological trends over the next 27 years, our projections only accounted for demographic shifts. Yet, available evidence indicates a substantial increase in the number of cases and deaths in the future, driven by

other factors such as lifestyle changes, the rising incidence of risk factors like obesity and physical inactivity or the impact of climate change.

- An incidence-based approach was used for breast cancer to avoid double-counting the high health care costs at the initiation of the treatment. This approach is conservative and may have underestimated the economic burden of the disease.
- In calculating absenteeism and presenteeism costs, the study assumes that the incidence and prevalence of the selected diseases are the same in the working and non-working populations. This may overlook the impact of the selected diseases on individuals' ability to obtain and maintain employment.
- Due to data limitations, average measures were used to approximate the cost of treating diabetes and COPD. This may not reflect variations in per-patient costs across the 27 countries.
- The selection of interventions included in the case studies for Portugal and Romania is limited to interventions available in the One-health Tool or Annex 3 of the WHO Global NCD Action Plan 2013–2030. The treatment regimen assumptions and impact sizes were adjusted as much as possible to align with current guidelines and practices in the two countries. However, due to technical limitations, some degree of variation may still be present.
- We could not model the impact of three major interventions in the treatment of COPD, smoking cessation, vaccination and pulmonary rehabilitation, due to technical limitations and a lack of exploitable data related to these interventions. Additionally, the model used was mainly parameterised to estimate the impact on mortality and, to a lesser extent, quality of life. It does not allow capturing further benefits that can be obtained from controlling the disease, such as the reduction in emergency room visits, consultations or comorbidities.
- Standard values from the One-health Tool were used to determine the unit cost of the non-recurring items (syringes, gloves, etc.). However, the cost of drugs and health-care providers was adjusted to reflect, at best, actual costs in the selected countries.
- The study used a simplified model to simulate the impact of providing comprehensive treatment on breast cancer mortality in Sweden. The model does not account for relapse over time, which would have required more advanced techniques and data.
- The model developed to assess the costs and benefits of providing comprehensive breast cancer treatment in Sweden relied who receive treatment regimen assumptions derived from the scientific literature, which may differ from current practices and guidelines in Sweden.
- The drugs and supplies' costs used in the treatment of breast cancer were extracted from different sources, including the One-health Tool. Since the tool provides cost estimates that are usually more suited for low and middle-income countries, the values used in the study may differ from real prices in Sweden. Acknowledging this limitation, a sensitivity analysis was conducted to assess the impact of increasing these estimates by up to 200%.
- In all analyses, the model does not account for future changes in productivity indicators due to the considerable uncertainty surrounding these variables. Introducing assumptions with such a level of uncertainty could have compromised the results.

Technical Annexes

Annex 1. Formulae used to estimate the economic burden of the five NCDs in the European Union.

Annex 2. Parameters and assumptions used to estimate the economic burden of the five NCDs in the European Union.

Annex 3. Assumptions used to model the impact of diabetes interventions in Portugal

Annex 3. Assumptions used to model the impact of COPD interventions in Portugal

Annex 4. Assumptions used to model the impact of COPD interventions in Romania.

Annex 5. Parameters and assumptions used to convert the health benefits from scaling up diabetes interventions in Portugal into economic benefits.

Annex 6. Parameters and assumptions used to convert the health benefits from scaling up COPD interventions in Portugal into economic benefits.

Annex 7. Parameters and assumptions used to convert the health benefits from scaling up cardiovascular interventions in Romania into economic benefits.

Annex 8. Parameters used to estimate the costs and benefits of comprehensive breast cancer treatment in Sweden.

Annex 9. Treatment assumptions (A) and cost of the ingredients (B) of comprehensive breast cancer treatment

Annex 1. Formulae used to estimate the economic burden of the five NCDs in the European Union

Annual direct health care costs:

$$\sum_{i=1}^{5} (PIN_i \times CR_i \times AC_i)$$

Where PIN is the population in need of an intervention (i), CR is the coverage rate for an intervention (i) and AC is the average per-patient treatment cost for an intervention (i).

Annual cost of absenteeism:

$$\sum_{s,d} \left(C_{s,d} \times LFPR_s \times ER_s \times GDPW \times ARF_d\right)$$

Where $C_{s,d}$ is the number of prevalent or incident cases aged 15–64 by sex (s) for a disease (d), $LFPR_s$ is the sex-specific labour force participation rate, ER_s is the sex-specific employment rate, GDPW is the GDP per worker and ARF_d is the absenteeism-related productivity reduction factor for a disease (d).

Annual cost of presenteeism:

$$\sum_{s,d} \left(C_{s,d} \times LFPR_s \times ER_s \times GDPW \times PRF_d\right)$$

Where $C_{s,d}$ is the number of cases aged 15–64 by sex (s) for a disease (d), $LFPR_s$ is the sex-specific labour force participation rate, ER_s is the sex-specific employment rate, GDPW is the GDP per worker and PRF_d is the presenteeism-related productivity reduction factor for a disease (d).

Cost of premature mortality (Human Capital Approach):

$$\sum_{a,s,d} \left\{D_{a,s,d} \times LFPR_s \times ER_s \times \left[\sum_{t=0}^{R-a} GDPW \,/\, (1+r)^t\right]\right\}$$

Where $D_{a,s,d}$ is the number of deaths attributable to a disease *(d)*, by age group (a) and sex (s), $LFPR_s$ is the sex-specific labour force participation rate, ER_s is the sex-specific employment rate, a is the age at death, R is the retirement age, GDPW is the GDP per worker and r is the discount rate.

Annex 2. Parameters and assumptions used to estimate the economic burden of the five NCDs in the European Union

Parameters	Source
Population by sex and five-year age group (2023–2050)	United Nations World Population Prospects (*1)*
Life expectancy by five-year age group	World Health Organization (*2)*
Incidence rate of stroke, IHD, DMII and COPD by sex and five-year age group	Institute of Health Metrics and Evaluation (*3)*
Prevalence rate of stroke, IHD, DMII and COPD by sex and five-year age group	Institute of Health Metrics and Evaluation (*3)*
Mortality rate of stroke, IHD, DM II and COPD by sex and five-year age group	Institute of Health Metrics and Evaluation (*3)*
Incidence rate of breast cancer by sex and five-year age group	Global Cancer Observatory (*4)*
Mortality rate of breast cancer by sex and five-year age group	Global Cancer Observatory (*4)*
Treatment coverage rates	Health at a Glance 2023: OECD Indicators (*5)*
Annual per-patient treatment cost for stroke	Santos et al. (2023) *(6)*, International Monetary Fund (*7)*
Annual per-patient treatment cost for IHD	Santos et al. (2023) *(6)*, International Monetary Fund (*7)*
Annual per-patient treatment cost for breast cancer	Santos et al. (2023) *(6)*, International Monetary Fund (*7)*
Annual per-patient treatment cost for diabetes type II	IDF Diabetes Atlas (*8)*, International Monetary Fund (*7)*
Annual per-patient treatment cost for COPD	Rehman et al. (2023) *(9)*, International Monetary Fund (*7)*
Labour force participation rate by sex	International Labour Organization (*10)*
Employment rate by sex	International Labour Organization (*10)*
Gross domestic product	International Monetary Fund (*7)*
Workplace productivity reduction due to stroke	Estimated from Kotseva et al. (2019) *(11)*

Workplace productivity reduction due to IHD	Estimated from Kotseva et al. (2019) *(11)*
Workplace productivity reduction due to COPD	Estimated from Dierick et al. (2021) *(12)*
Workplace productivity reduction due to diabetes	Estimated from Breton et al. (2013) *(13)*
Workplace productivity reduction due to breast cancer	Estimated from Łyszczarz et al. (2024) *(14)*
Minimum working age	Assumption (15 years)
Retirement age	Assumption (64 years)
Discount rate	3%

Annex 3. Assumptions used to model the impact of diabetes interventions in Portugal

A. Parameters at baseline

Parameter	Value	Reference
Number of people living with diabetes	**1 261 788**	Estimated based on aged and gender-specific prevalence data of the Portuguese Society of Diabetology (P.9)
New cases of stroke in people living with diabetes	**7120**	Corresponds to the total number of hospitalizations for strokes in people living in diabetes in 2021 according to the Portuguese Society of Diabetology (P.25). We used the IHME's distribution of stroke in the general population to spread the cases across age groups and gender.
New cases of IHD in people living with diabetes	**3571**	Corresponds to the total number of hospitalizations for AMI in people living in diabetes in 2021 according to the Portuguese Society of Diabetology (P.25). We used the IHME's distribution of stroke in the general population to spread the cases across age groups and gender.
New cases of end-stage renal disease (ESRD) in people living with diabetes and chronic kidney disease	**2310**	We first estimated the prevalence of CKD among people living with diabetes using prevalence data from the Portuguese Society of Diabetology (P.25) and evidence from Fenta et al. (2023)[2]. We then applied incidence rates from Gonzalez-Perez et al. (2021)[3] to estimate those who will reach ESDR every year.

[2] Fenta, E.T., Eshetu, H.B., Kebede, No. et al. Prevalence and predictors of chronic kidney disease among type 2 diabetic patients worldwide, systematic review and meta-analysis.*Diabetol Metab Syndr* **15**, 245 (2023). https:/doi.org/10 1186/s13 098–023–01 202-x

[3] Antonio González-Pérez, Maria Saez, David Vizcaya, Marcus Lind, Luis Garcia Rodriguez – Incidence and risk factors for mortality and end-stage renal disease in people with type 2 diabetes and diabetic kidney disease: a population-based cohort study in the United Kingdom: BMJ Open Diabetes Research and Care 2021;9:e00 2146.

New cases of diabetic retinopathy	**50 472**	We used an incidence rate of 4%, corresponding to the percentage of diabetes patients screened every year who require treatment for diabetic retinopathy, according to Portuguese Society of Diabetology (P.9). This estimate is coherent with incidence rate estimated by Medeiros et al. (2015) in the Lisbon Region[4].
New cases of lower extremity amputation (LEA)	**2445**	Corresponds to the total number of LEA in 2021 according to the Portuguese Society of Diabetology (P.22). We used the One-health Tool's distribution of stroke in the general population to spread the cases across age groups and gender.
Coverage rate of glycaemic control	55.9%	Corresponds to the percentage of people living with diabetes diagnosed and receiving medication according to the Portuguese Society of Diabetology (P.8, P.28)

B. Impact of intensive glycaemic control on complications related to diabetes

Complications	**Direct impact[5]**	**Reference**
Stroke	Reduction in incidence: -9%	Giuliano et al. (2019)[6]
IHD	Reduction in incidence: -9%	Giuliano et al. (2019)[4]

[4] Dutra Medeiros M, Mesquita E, Gardete-Correia L, Moita J, Genro V, Papoila AL, Amaral-Turkman A, Raposo JF. First Incidence and Progression Study for Diabetic Retinopathy in Portugal, the RETINODIAB Study: Evaluation of the Screening Programme for Lisbon Region. Ophthalmology. 2015 Dec;122*(12)*:2473–81. doi: 10 1016/j.ophtha.2015.08 004. Epub 2015 Sep 15. PMID: 26 383994.

[5] Indirect impacts were estimated using case-fatality rates from the literature.

[6] Giugliano D, Maiorino MI, Bellastella G, Chiodini P, Esposito K. Glycemic Control, Preexisting Cardiovascular Disease and Risk of Major Cardiovascular Events in Patients with type 2 Diabetes Mellitus: Systematic Review With Meta-Analysis of Cardiovascular Outcome Trials and Intensive Glucose Control Trials. J Am Heart Assoc. 2019 June 18;8*(12)*:e01 2356. doi: 10 1161/JAHA.119 01 2356. Epub 2019 June 5. PMID: 31 166153; PMCID: PMC66 45638.

ESDR	Reduction in incidence: -65%	Perkovic et al. (2013)[7]
Diabetic retinopathy	Reduction in incidence: -65%	One-health Tool – NCD Module
Lower extremity amputation	Reduction in incidence: -35%	One-health Tool – NCD Module

C. Drugs and Supplies

Intervention	Population in Need (PIN)	PIN (%) x	Drugs and Supplies				
			Item	Unit	Unit cost (€)‡	Times per day	Day per case
Intensive glycaemic Control	People with diabetes	100%	HbA1c test	1	0.29	1	2
	Diabetic patients with HbA1C < 7.5%	7.0%	Metformin, tablet, 850 mg	1	0.03	3	365
	Diabetic patients with HbA1C < 7.5% + High Cholesterol	22.2%	Metformin, tablet, 850 mg	1	0.03	3	365
			Sitagliptin, tablet, 100mg	1	0.38	1	365
	Diabetic patients with HbA1C < 7.5% + Obesity	20.9%	Metformin, tablet, 850 mg	1	0.03	3	365
			Dulaglutide, tablet, 0.75mg	1	13.37	1	52

[7] Perkovic V, Heerspink HL, Chalmers J, Woodward M, Jun M, Li Q, MacMahon S, Cooper ME, Hamet P, Marre M, Mogensen CE, Poulter N, Mancia G, Cass A, Patel A, Zoungas S; ADVANCE Collaborative Group. Intensive glucose control improves kidney outcomes in patients with type 2 diabetes. Kidney Int. 2013 Mar;83*(3)*:517–23. doi: 10 1038/ki.2012 401. Epub 2013 Jan 9. PMID: 23 302714.

	Diabetic patients with HbA1C between 7.5% and 9%	17.5%	Metformin, tablet, 850 mg	1	0.03	3	365
			Sitagliptin, tablet, 100mg	1	0.38	1	365
	Diabetic patients with HbA1C between 7.5% and 9% + Obesity	12.5%	Metformin, tablet, 850 mg	1	0.03	3	365
			Dulaglutide, 0.75mg	1	13.37	1	365
	Diabetic patients with HbA1C > 9%	11.6%	Metformin, tablet, 850 mg	1	0.03	3	365
			Sitagliptin, tablet, 100mg	1	0.38	1	365
			Insulin	0.3	0.62	1	365
	Diabetic patients with HbA1C > 9% + Obesity	8.4%	Metformin, tablet, 850 mg	1	0.03	3	365
			Dulaglutide, tablet, 0.75mg	1	13.37	1	52
			Insulin	0.3	0.62	1	365

The treatment regimen were adapted so that they align as much as possible with the national guidelines in Portugal.

x The percentage of people living with diabetes eligible for each treatment was approximated from data published by the Portuguese National Observatory of Diabetes (*18)*.

ǂThe unit cost of the drugs was obtained from the Infomed database (*19)*.

D. Labour

Intervention		**PIN (%)**	**Labour**

	Population in Need (PIN)		Health-care provider	Annual salary (€)‡	Minutes	Visit
Glycaemic control	People with diabetes	100%	Nurse	27 000	10	4
			Specialist	81 000	10	1
			Generalist	59 400	10	2

Standard assumptions from the One-health Tool were used to estimate the time spent by health-care provider and the number of visit per patient (*20)*.

‡Annual salaries were approximated from data published in the OECD iLibrary (*21.22)*.

Annex 3. Assumptions used to model the impact of COPD interventions in Portugal

A. Drugs and Supplies

Intervention	Population in Need (PIN)	PIN (%) x	Drugs and Supplies				
			Item	Unit	Unit cost (€)‡	Times per day	Day per case
Bronchodilator	People with COPD (Gold A)	40%	Inhaled Salmeterol, 25–50mcg	1	0.19	2	365
LABA + LAMA	People with COPD (Gold B)	35%	Formoterol 12 mcg + Aclidinium 340 mcg	1	0.90	2	365
LABA + LAAMA + ICS	People with COPD (Gold E)	11%	Fluticasone 92 mcg + Umeclidinium, 55 mcg + Vilanterol 22 mcg	1	2.02	1	365
Exacerbation treatment with antibiotics	People with COPD (Gold E)	11%	Amoxicillin, 875 mg + Acido clavulanico, 125 mg	1	0.27	2	7
Exacerbation treatment with anti-inflammatory	People with COPD (Gold E)	11%	Roflumilast, 500 mcg	1	1.52	1	365
Exacerbation treatment with oxygen	People with COPD (Gold E)	11%	Oxygen, 1000 litres, primarily with oxygen cylinders	0	2.15	1440	7

The treatment regimen were adapted so that they align with the GOLD Guidelines on COPD (*23)*.

x The distribution as per GOLD criteria was determined from Silva et al. (2024) *(24)*.

‡The unit cost of the drugs was obtained from the Infomed database (*19)*.

B. Labour

Intervention	Population in Need (PIN)	PIN (%)	Labour			
			Health-care provider	Annual salary (€)‡	Minutes	Visit
Bronchodilator	People with COPD (Gold A)	40%	Generalist	59 400	20	1
			Nurse	27 000	10	2
LABA + LAMA	People with COPD (Gold B)	11%	Generalist	59 400	20	1
			Nurse	27 000	10	2
LABA + LAAMA + ICS	People with COPD (Gold E)	11%	Generalist	59 400	20	1
			Nurse	27 000	10	2
Exacerbation treatment with antibiotics	People with COPD (Gold E)	11%	Generalist	59 400	6	7
			Nurse	27 000	4	14
Exacerbation treatment with anti-inflammatory	People with COPD (Gold E)	11%	Generalist	59 400	20	1
			Nurse	27 000	10	2
Exacerbation treatment with oxygen	People with COPD (Gold E)	11%	Generalist	59 400	8	7
			Nurse	27 000	4	14

Standard assumptions from the One-health Tool were used to estimate the time spent by health-care provider and the number of visit per patient (*20)*.

‡Annual salaries were approximated from data published in the OECD iLibrary (*21.22)*.

Annex 4. Assumptions used to model the impact of CVD interventions in Romania

A. Drugs and Supplies

Intervention	Population in Need (PIN)	PIN (%) x	Drugs and Supplies				
			Item	Unit	Unit cost (€)	Times per day	Day per case
Treatment for those with absolute risk of CVD/Diabetes	People with a 20–30% chance of developing CVD or diabetes	100%	Simvastatin, 15 mg	1	0.19	1	365
		95%	Hydrochlorothiazide, tablet, 25 mg	1	0.10	1	365
		40%	Enalapril, tablet, 20 mg	1	0.14	1	365
		25%	Atenolol, tablet, 50 mg	1	0.18	1	365
		25%	Amlodipine, tablet, 10 mg	1	0.08	1	365
		7%	Colchicine, tablet, 0.5 mg	1	0.28	1	365
Treatment of new cases of AMI	People with acute strokes or acute IHD – < 4.5 h duration	59%	Intravenous thrombolysis with alteplase	1	890	1	1
	People with acute strokes or acute IHD – ≥4.5 h duration	41%	Mechanical thrombectomy	1	6715	1	1
Treatment of cases of established IHD	People with post-acute IHD	100%	Acetyl salicylic (aspirin), tablet, 75 mg	1	0.08	1	365
		100%	Ticagrelor, tablet, 90mg	1	1.49	2	365
		100%	Prasugrel, tablet, 10mg	1	0.92	1	365
		40%	Enalapril, tablet, 20 mg	1	0.14	1	365
		25%	Atenolol, tablet, 50 mg	1	0.18	1	365

		100%	Simvastatin, 15mg	1	0.19	1	365
		13%	Colchicine, tablet, 0.5 mg	1	0.28	1	365
		100%	Blood glucose level test	1	0.20	1	2
		100%	Cholesterol test	1	0.20	1	2
		100%	Urine analysis	1	0.20	1	2
Treatment for those with established cerebrovascular disease and stroke	People with post-acute strokes or both post-acute strokes and IHD	97.5%	Acetyl salicylic (aspirin), tablet, 75 mg	1	0.08	1	365
		2.5%	Clopidorgel, tablet, 75 mg	1	0.18	1	365
		40%	Enalapril, tablet, 20 mg	1	0.14	1	365
		25%	Atenolol, tablet, 50 mg	1	0.18	1	365
		13%	Colchicine, tablet, 0.5 mg	1	0.28	1	365
		100%	Blood glucose level test	1	2.00	1	2
		100%	Cholesterol test	1	2.00	1	2
		100%	Urine analysis	1	1.83	1	2

The treatment regimen were adapted so that they align as much as possible with the European Society of Cardiology guidelines on cardiovascular disease prevention (*25)*.

x The One-health Tool standard assumptions were used to determine the percentage of target population eligible for each treatment (*20)*. The distribution of people with acute strokes or acute IHD over or less 4.5 hours was derived from de Almeida Moraes (2023) *(26)*.

ǂIn absence of country-specific data for Romania, we used the Infomed database (*19)* to estimate the cost of the drugs. The cost intravenous thrombolysis with alteplase and mechanical thrombectomy were approximated from Candio et al. (2021) *(27)*.

B. Labour

Intervention	n in Need (PIN)	PIN (%)	Labour			
			Health-care provider	Annual salary (€)‡	Minutes	Visit
Treatment for those with absolute risk of CVD/Diabetes	People with a 20–30% chance of developing CVD or diabetes	100%	Generalist	40 000	10	4
Treatment of new cases of AMII	People with acute strokes or acute IHD – < 4.5 h duration	59%	- x	- x	0	0
	People with acute strokes or acute IHD – ≥4.5 h duration	41%	- x	- x	0	0
Treatment of cases of established IHD	People with post-acute IHD	100%	Generalist	40 000	5	6
		100%	Nurse	18 160	20	4
Treatment for those with established cerebrovascular disease and stroke	People with post-acute strokes or both post-acute strokes and IHD	100%	Generalist	40 000	5	6
		13%	Nurse	18 160	20	4
		20%	Nurse	18 160	20	4

Standard assumptions from the One-health Tool were used to estimate the time spent by health-care provider and the number of visit per patient (*20)*.

x We did not assign time to these interventions since cost estimates used in the previous table already included the labour cost.

‡Annual salaries were approximated from data published in the OECD iLibrary (*21.22)*.

Annex 5. Parameters and assumptions used to convert the health benefits from scaling up diabetes interventions in Portugal into economic benefits

A. General parameters

Parameters	**Source**
Population	United Nations World Population Prospects (*1)*
GDP per capita	The World Bank (*17)*
Labour force participation rate (%) – Females	International Labour Organization (*10)*
Employment rate (%) – Females	International Labour Organization (*10)*
Labour force participation rate (%) – Males	International Labour Organization (*10)*
Employment rate (%) – Males	International Labour Organization (*10)*
Life expectancy by age group and by sex	World Health Organization (*2)*
Retirement age	67 (Assumption)

B. Parameters linked to direct health care costs and productivity

Type	Complications	Value	Reference
Direct health care costs	Stroke	€1683 adjusted and converted from Santos et al. (2023). Data used in the economic burden analysis.	**Santos et al. (2023):**
	IHD	€724 adjusted and converted from Santos et al. (2023). Data used in the economic burden analysis.	**Santos et al. (2023):**
	ESRD	€8026 adjusted and converted from Jha et al. (2023). The per patient cost in Spain was used as a proxy.	**Jha et al. (2023)**

	Diabetic retinopathy	€545 for yearly treatment and follow-up of any DR. The cost was adjusted to inflation.	**Shaikh et al. (2019):**
	Lower extremity amputation	€8926 cost calculated based on distribution of minor and major LEA. The cost was adjusted to inflation and converted to euros. The post-amputation costs are estimated to €4556 (*£2968 for annual prosthesis provision and care)*.	**Kerr et al. (2019)**
Productivity reduction due to absenteeism	Stroke	102.4 absent days per year. Absenteeism rate = **45%** based on 226 annual workdays	**Persson et al. (2019)**
	IHD	13.8 absent days per year. Absenteeism rate = **6%** based on 226 annual workdays	
	ESRD	69.6 absent days per year. Absenteeism rate = **31%** based on 226 annual workdays	
	Diabetic retinopathy	14.6 absent days per year. Absenteeism rate = **7%** based on 226 annual workdays	
	Lower extremity amputation	29.1 absent days per year. Absenteeism rate = **13%** based on 226 annual workdays	
Productivity reduction due to presenteeism	Stroke	**4.1%.** Equivalent to nine days per year.	**Kotseva et al. (2019)**
	IHD	**2.7%.** Equivalent to six days per year.	**Kotseva et al. (2019)**
	ESRD	33 and 85 hours of work lost for transplant recipients and dialysis patients, respectively. The average value gives a presenteeism rate of **3.7%** based on 226 workdays and seven working hours per day.	**De Vries et al. (2021)**
	Diabetic retinopathy	N/A	-
	Lower extremity amputation	N/A	-

Employment rate	Stroke	**29.1%**	**Noorjte et al. (2014)**
	IHD	**44.1%**	**Jiang et al. (2018)**
	ESRD	**68.5%** are unemployed. The average between dialysis patients (74%) and transplant patients (63%) was taken.	**Kirkeskov et al. (2021)**
	Diabetic retinopathy	N/A	-
	Lower extremity amputation	In a study conducted in the Kingdom of the Netherlands**, 34%** of patients with jobs at the time of amputation had stopped working.	**Schoppen et al. (2001)**

Annex 6. Parameters and assumptions used to convert the health benefits from scaling up COPD interventions in Portugal into economic benefits

Parameters	Source
Population	United Nations World Population Prospects (*1)*
GDP per capita	The World Bank (*17)*
Life expectancy by age group and by sex	World Health Organization (*2)*
Retirement age	64 (Assumption)

Annex 7. Parameters and assumptions used to convert the health benefits from scaling up cardiovascular interventions in Romania into economic benefits

Parameters	Source
Population	United Nations World Population Prospects (*1)*
GDP per capita	The World Bank (*17)*
Labour force participation rate (%) – Females	International Labour Organization (*10)*
Employment rate (%) – Females	International Labour Organization (*10)*
Labour force participation rate (%) – Males	International Labour Organization (*10)*
Employment rate (%) – Males	International Labour Organization (*10)*
Absenteeism-related productivity reduction rate due to stroke	Estimated from Kotseva et al. (2019) *(11)*
Presenteeism-related productivity reduction rate due to stroke	Estimated from Kotseva et al. (2019) *(11)*
Absenteeism-related productivity reduction rate due to IHD	Estimated from Kotseva et al. (2019) *(11)*
Presenteeism-related productivity reduction rate due to IHD	Estimated from Kotseva et al. (2019) *(11)*
Life expectancy by age group and by sex	World Health Organization (*2)*
Retirement age	64 (Assumption)

Annex 8. Parameters used to estimate the costs and benefits of comprehensive breast cancer treatment in Sweden

Parameters	Value	Reference
Health benefits		
Cohort size	48 092	Socialstyrelsen (*33)*
All-cause mortality rates (per 100 000)	Adjusted by five-year age group	Socialstyrelsen (*33)*
Breast cancer incidence rate (per 100 000)	Adjusted by five-year age group	Global Cancer Observatory (*4)*
Distribution of breast cancer cases at diagnosis	Stage I: 46.9%	Abdoli et al.(2017) *(34)*
	Stage II: 43.9%	
	Stage III: 5.3%	
	Stage IV: 3.9%	
Transition rates	Stage I to II: 0.19	Ralaidovy et al.(2018) *(35)*
	Stage II to III: 0.33	
	Stage III to IV: 0.43	
Case fatality rates (not treated patients)	Stage I: 0.02	Ralaidovy et al.(2018) *(35)*, Groot et al.(2006) *(36)*, Zelle et al.(2012) *(37)*
	Stage II: 0.06	
	Stage III: 0.15	
	Stage IV: 0.30	
Case fatality rates (treated patients)	Stage I: 0.01	Ralaidovy et al.(2018) *(35)*, Groot et al.(2006) *(36)*, Zelle et al.(2012) *(37)*
	Stage II: 0.04	
	Stage III: 0.09	
	Stage IV: 0.23	
Disability weights (not treated patients)	Stage I: 0.068	Zelle et al.(2012) *(37)*
	Stage II: 0.071	
	Stage III: 0.073	
	Stage IV: 0.090	
Disability weights (not treated patients)	Stage I: 0.068	Zelle et al.(2012) *(37)*
	Stage II: 0.070	

	Stage III: 0.072	
	Stage IV: 0.073	
Economic valuation of the health benefits		
GDP per worker	95 329	The World Bank (*17)*, International Labour Organization (*10)*, United Nations World Population Prospects (*1)*
Labour force participation rate (%) – Females	81.3%	International Labour Organization (*10)*
Employment rate (%) – Females	92.1%	International Labour Organization (*10)*
Retirement age	64	Assumption
Discount rate	3%	Analysts' choice

Annex 9. Treatment assumptions (A) and cost of the ingredients (B) of comprehensive breast cancer treatment

(A)

Ingredient x	Stage I	Stage II	Stage III	Stage IIV
Initial diagnosis and evaluation during treatment				
No. of health centre visits†	1	1	1	1
No. of hospitalization days†	3	3	3	3
Bilateral mammography	1	1	2	0
Complete blood count	7	7	7	7
Fine needle aspiration (FNA) or core needle biopsy	1	1	1	1
Liver function tests	8	8	8	8
Ultrasonography	1	1	1	1
Renal function tests	8	8	8	8
Chest X-ray	1	1	1	1
ECG	1	1	1	1
Treatment				
No. of health centre visits†	8	10	24	10
No. of hospitalization days†	2	2	2	2
% receiving lumpsectomy	40%	30%	10%	0%
% receiving mastectomy	60%	70%	90%	100%
% receiving radiotherapy	40%	30%	100%	10%
% receiving endocrine therapy	100%	100%	100%	40%
% receiving chemotherapy	0%	20%	60%	60%
% receiving trastuzumab‡	20%	20%	20%	20%

x Ingredient and treatment assumptions were derived from Zelle et al.*(37)*

†Number of outpatient visits and hospitalization days were updated using latest assumptions from the One-health Tool (*20)*

‡For HER2-positive breast people with cancer (*38)*

(B)

Ingredient	Unit cost (€)	Reference
Visits		
Health centre visit	109	WHO-CHOICE (*39)*, International Monetary Fund (*7)*
Hospitalization day	1370	WHO-CHOICE (*39)*, International Monetary Fund (*7)*
Drugs and supplies		
Bilateral mammography	2	One-health Tool (*20)*
Complete blood count	3	One-health Tool (*20)*
Fine needle aspiration (FNA) or core needle biopsy	43	One-health Tool (*20)*
Liver function tests	4	One-health Tool (*20)*
Ultrasonography	7	One-health Tool (*20)*
Renal function tests	9	One-health Tool (*20)*
Chest X-ray	1	One-health Tool (*20)*
ECG	1	One-health Tool (*20)*
Lumpectomy	60	One-health Tool (*20)*
Mastectomy	60	One-health Tool (*20)*
Endocrine therapy x	96	Estimated from MSH (*40)*, International Monetary Fund (*7)*
Chemotherapy†	1153	Estimated from MSH (*40)*, International Monetary Fund (*7)*
Trastuzumab‡	27 702	One-health Tool (*20)*
Radiotherapy		
Radiotherapy§	6016	Estimated from Defourny et al.*(41)*, International Monetary Fund (*7)*

x Tamoxifen, 20 mg tablet, for 365 days

† Doxorubicin, 50 mg vial; Cyclophosphamide, 1 g; Paclitaxel

‡ Cost for 18 cycles.

§ Average cost for conventionally fractionated breast EBRT course.

References

Abdoli G, Bottai M, Sandelin K, Moradi T. Breast cancer diagnosis and mortality by tumor stage and migration background in a nationwide cohort study in Sweden. Breast. 2017;31:57–65.

Active Patients Access Care. European Federation of Allergy and Airways Diseases Patients' Associations; 2019.

Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, et al. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease 2024 Report. 2024.

A healthy return: investment case for a sustainably financed WHO. Geneva: World Health Organization; 2022.

Avenir Health. The One-health Tool.

Baumann A, Wyss K. The shift from inpatient care to outpatient care in Switzerland since 2017: Policy processes and the role of evidence. Health Policy [Internet]. 2021 [cited 2024 Aug 24];125:512–519. doi: 10 1016/j.healthpol.2021.01 012.

Berbecar V, Ismail G, Mircescu G. Prevalence Of Hypertension And Cardiovascular diseasesIn The Rural Population: Results From The Romanian Mobile Health Caravans. J Comm Med And Pub Health Rep. 2021;2*(7)*.

Breton MC, Guénette L, Amiche MA, Kayibanda JF, Grégoire JP, Moisan J. Burden of diabetes on the ability to work: a systematic review. Diabetes Care. 2013;36*(3)*:740–9.

Canadian Institute for Health Information. National Health Expenditure Trends, 1975 to 2019. Ottawa, ON: CIHI; 2019.

Christopoulos K, Eleftheriou K. The fiscal impact of health care expenditure: Evidence from the OECD countries. Economic Analysis and Policy. 2020;67:195–202.

Cylus J, Williams G, Carrino L, Roubal T, Barber S. Population ageing and health financing: A method for forecasting two sides of the same coin. Health Policy. 2022 Dec;126*(12)*:1226–1232.

Defourny N, Perrier L, Borras JM, Coffey M, Corral J, Hoozée S, et al. National costs and resource requirements of external beam radiotherapy: A time-driven activity-based costing model from the ESTRO-HERO project. Radiother Oncol. 2019;138:187–94.

De Meijer C, Wouterse B, Polder J, Koopmanschap M. The effect of population ageing on health expenditure growth: a critical review. Eur J Ageing. 2013 May 15;10*(4)*:353–361.

D'Errico M, Pavlova M, Spandonaro F. The economic burden of obesity in Italy: a cost-of-illness study. Eur J Health Econ [Internet]. 2022 [cited 2024 Aug 24];23:177–192. doi: 10 1007/s10 198–021–01 358–1.

Diabetes. Factos e Numeros. Relatorio Anual de Observatorio Nacional da Diabetes. Ediçao de 2023. O Observatorio Nacional da Diabetes; 2023.

Di Cesare M, Perel P, Taylor S, Kabudula C, Bixby H, Gaziano TA et al. The Heart of the World. Global Heart [Internet]. 2024 [cited 2024 Aug 24];19:11. doi: 10 5334/gh.1288.

Dierick BJH, Flokstra-de Blok BMJ, van der Molen T, Toledo-Pons N, Román-Rodríguez M, Cosío BG, et al. Work absence in patients with asthma and/or COPD: a population-based study. NPJ Prim Care Respir Med. 2021;31*(1)*:9.

Direção-Geral da Saúde. (2022). Plano Nacional de Saúde 2030: Saúde Sustentável: de tod@s para tod@s. Lisbon, Portugal. https:/pns.dgs.pt/files/2023/09/PNS-2030-publicado-em-RCM.pdf

Duarte R, Melo M, Silva-Nunes J, Melo P, Raposo J, Carvalho D. Recomendações Nacionais da SPD para o Tratamento da Hiperglicemia na Diabetes Tipo two -Atualização 2018/19 com Base na Posição Conjunta ADA/EASD x SPD National Recommendations for the Treatment of Hyperglycemia in type 2 Diabetes -Update Based in the ADA/EASD Joint Position Statement. 2018;13:154–80.

EFPIA. EFPIA patient wait indicator 2024 [Internet]. Brussels: European Federation of Pharmaceutical Industries and Associations; 2024 [cited 2024 Feb 12]. Available from: https://efpia.eu/media/vtapbere/efpia-patient-wait-indicator-2024.pdf

Ekdahl S, Näslund E, Smedsrud S. Optimizing a Launch – Important factors affecting a new pharmaceutical launch in Sweden [Master's thesis]. May 2019. Uppsala Universitet. https:/www.diva-portal.org/smash/get/diva2:13 21230/FULLTEXT01.pdf

Elek P, Molnár T, Váradi B. The closer the better: does better access to outpatient care prevent hospitalization? Eur J Health Econ [Internet]. 2019 [cited 2024 Aug 24];20:801–817. doi: 10 1007/s10 198–019–01 043–4.

EU Commission. Healthier together EU noncommunicable diseases initiative. 2022. https:/health.ec.europa.eu/system/files/2022–06/eu-ncd-initiative_publication_en_0.pdf

Gardete-Correia L, Boavida JM, Raposo JF, Mesquita AC, Fona C, Carvalho R, et al. First diabetes prevalence study in Portugal: PREVADIAB study. Diabet Med. 2010;27*(8)*:879–81.

Giorda CB, Manicardi V, Diago Cabezudo J. The impact of diabetes mellitus on health care costs in Italy. Expert Review of Pharmacoeconomics and Outcomes Research. 2011;11*(6)*:709–719. DOI: 10 1586/erp.11.78.

Global Burden of Disease Study 2019 (GBD 2019): Institute for Health Metrics and Evaluation, University of Washington, ; 2024 [Available from: https:/ghdx.healthdata.org/gbd-2019.

Global Cancer Observatory: World Health Organization – International Agency for Research on Cancer; 2024 [Available from: https:/gco.iarc.fr/today/en.

Goryakin Y, Thiébaut SP, Cortaredona S, Lerouge MA, Cecchini M, Feigl AB, Ventelou B. Assessing the future medical cost burden for the European health systems under alternative exposure-to-risks scenarios. PLoS One. 2020 Sep 11;15*(9)*:e02 38565.

Groot MT, Baltussen R, Uyl-de Groot CA, Anderson BO, Hortobágyi GNo. Costs and Health Effects of Breast Cancer Interventions in Epidemiologically Different Regions of Africa, North America and Asia. The Breast Journal. 2006;12(s1):S81-S90.

Health at a Glance 2023: OECD Indicators. Paris: OECD; 2023.

IDF Diabetes Atlas 2021 (tenth Edition). IDF Diabetes Atlas; 2021.

ILOSTAT: International Labour Organization; 2024 [Available from: https:/ilostat.ilo.org/data/#.

Infarmed. INFARMED – National Authority of Medicines and Health Products, I.P. Available online: https:/www.infarmed.pt/web/infarmed-en/about-infarmed#:~:text=Infarmed%20is%20a%20Government%20agency,the%20protection%20of%20Public%20Health.

Inflation rate, average consumer prices: International Monetary Fund; 2024 [Available from: https:/www.imf.org/external/datamapper/PCPIPCH@WEO/OEMDC/ADVEC/WEOWORLD.

Institute of M, National Research Council Committee on New Approaches to Early D, Diagnosis of Breast C. The National Academies Collection: Reports funded by National Institutes of Health. In: Joy JE, Penhoet EE, Petitti DB, editors. Saving Women's Lives: Strategies for Improving Breast Cancer Detection and Diagnosis. Washington (DC): National Academies Press (US) Copyright © 2005, National Academy of Sciences.; 2005.

Ivankova V, Gavurova B, Khouri S. Understanding the relationships between health spending, treatable mortality and economic productivity in OECD countries. Front Public Health. 2022 Dec 21;10:10 36058.

Janlöv N, Blume S, Glenngård AH, Hanspers K, Anell A, Merkur S. Sweden: Health system review. Health Systems in Transition, 2023; 25*(4)*: i–198. https:/eurohealthobservatory.who.int/publications/i/sweden-health-system-review-2023

Jullien S, Mateescu I, Brînzac MG, Dobocan C, Pop I, Weber MW, Butu C, Carai S. Unnecessary hospitalizations and polypharmacy practices in Romania: A health system evaluation for strengthening primary health care. J Glob Health. 2023 May 5;13:04 039. doi: 10 7189/jogh.13 04 039. PMID: 37 143374; PMCID: PMC10 160704.

KFF. "Snapshots: How Changes in Medical Technology Affect Health Care Costs." Published Mar 02, 2007. https:/www.kff.org/health-costs/issue-brief/snapshots-how-changes-in-medical-technology-affect/

Kotseva K, Gerlier L, Sidelnikov E, Kutikova L, Lamotte M, Amarenco P, et al. Patient and caregiver productivity loss and indirect costs associated with cardiovascular events in Europe. Eur J Prev Cardiol. 2019;26*(11)*:1150–7.

Pereira AMP, da Silva Laureano RM, de Lima Neto FB. Five regions, five retinopathy screening programmes: a systematic review of how Portugal addresses the challenge. BMC Health Services Research. 2021;21*(1)*:756.

Laudicella M, Li Donni P, Olsen KR, Gyrd-Hansen D. Age, morbidity or something else? A residual approach using microdata to measure the impact of technological progress on health care expenditure. Health Econ. 2022 Jun;31*(6)*:1184–1201.

Łyszczarz B. Productivity losses from short-term work absence due to neoplasms in Poland. Scientific Reports. 2024;14*(1)*:3289.

Mahmood S, Sequeira R, Siddiqui MMU, Herkenhoff MBA, Ferreira PP, Fernandes AC, Sousa P. Decentralization of the health system – experiences from Pakistan, Portugal and Brazil. Health Res Policy Sys [Internet]. 2024 [cited 2024 Aug 25];22:61. doi: 10 1186/s12 961–024–01 145–3.

Marino A, Lorenzoni L. The impact of technological advancements on health spending – A literature review. OECD Health Working Paper No. 113. Directorate for Employment, Labour and Social Affairs, Health Committee. Health Working Papers. 19 August 2019.

Miravitlles M, Vogelmeier C, Roche N, Halpin D, Cardoso J, Chuchalin AG, et al. A review of national guidelines for management of COPD in Europe. Eur Respir J. 2016;47*(2)*:625–37.

National Cause of death Register: Socialstyrelsen; 2024 [Available from: https:/www.socialstyrelsen.se/en/statistics-and-data/registers/national-cause-of-death--register/.

Nuffield Trust. Shifting the balance of care, Great expectations. London: Nuffield Trust; 2017.

Nunes AM, Ferreira DC. A Critical Analysis of Decentralizing the Portuguese Public Healthcare Provision Services. Int J Environ Res Public Health. 2022 Oct 17;19*(20)*:13 390. doi: 10 3390/ijerph19 2013390.

OECD/European Observatory on Health Systems and Policies (2023), Portugal: Country Health Profile 2023, State of Health in the EU, OECD Publishing, Paris.

OECD/European Observatory on Health Systems and Policies (2021), Romania: Country Health Profile 2021, State of Health in the EU, OECD Publishing, Paris/European Observatory on Health Systems and Policies, Brussels.

OECD/European Observatory on Health Systems and Policies (2023), Romania: Country Health Profile 2023, State of Health in the EU, OECD Publishing, Paris/European Observatory on Health Systems and Policies, Brussels.

OECD/European Observatory on Health Systems and Policies (2023), Sweden: Country Health Profile 2023, State of Health in the EU, OECD Publishing, Paris, https:/doi.org/10 1787/ec938a6d-en.

Oliveira MD, Tavares AI, Vieira A, Pacheco M. Sustainability and Resilience in the Portuguese Health System. Partnership for Health System Sustainability and Resilience. 2022. https:/www3.weforum.org/docs/WEF_PHSSR_Portugal_2022.pdf.

Olofsson S, Norrlid H, Karlsson E, Wilking U, Ragnarson Tennvall G. Societal cost of subcutaneous and intravenous trastuzumab for HER2-positive breast cancer – An observational study prospectively recording resource utilization in a Swedish health-care setting. Breast. 2016;29:140–6.

Petre I, Barna F, Gurgus D, Tomescu LC, Apostol A, Petre I, Furau C, Năchescu ML, Bordianu A. Analysis of the Health-care system in Romania: A Brief Review. Healthcare (Basel). 2023 Jul 19;11*(14)*:2069. doi: 10 3390/health care11 142069. PMID: 37 510510; PMCID: PMC10 379121.

Piscopo J, Groot W, Pavlova M. Determinants of public health expenditure in the EU. PLoS One. 2024 Mar;19*(3)*:e02 99359.

Ralaidovy AH, Gopalappa C, Ilbawi A, Pretorius C, Lauer JA. Cost-effective interventions for breast cancer, cervical cancer and colorectal cancer: new results from WHO-CHOICE. Cost Eff Resour Alloc. 2018;16:38.

Radu CP, Pana BC, Pele DT, Costea RV. Evolution of Public Health Expenditure Financed by the Romanian Social Health Insurance Scheme From 1999 to 2019. Front Public Health. 2021 Dec 1;9:79 5869. Correction in: Front Public Health. 2022;10:85 7426.

Raleigh V. Trends in Life Expectancy in EU and Other OECD Countries: Why are Improvements Slowing? OECD Health Working Paper No. 108, Health Committee, Directorate for Employment, Labour and Social Affairs. 2019. Available from: https:/one.oecd.org/document/DELSA/HEA/WD/HWP (2019)1/En/pdf

Rehman AU, Hassali MAA, Muhammad SA, Harun SN, Shah S, Abbas S. The economic burden of chronic obstructive pulmonary disease (COPD) in Europe: results from a systematic review of the literature. Eur J Health Econ. 2020;21*(2)*:181–94.

Richard A. Rettig, "Medical Innovation Duels Cost-containment," Health Affairs (Summer 1994): 15.

Santos AC, Willumsen J, Meheus F, Ilbawi A, Bull FC. The cost of inaction on physical inactivity to public health-care systems: a population-attributable fraction analysis. The Lancet Global Health. 2023;11*(1)*:e32-e9.

Self-reported screening of cardiovascular diseases and diabetes risks by sex, age and educational attainment level: Eurostat; 2020 [Available from: https:/ec.europa.eu/eurostat/databrowser/view/hlth_ehis_pa2e/default/table?lang=en.

Soares AR, Coelho M, Tracey M, Carvalho D, Silva-Nunes J. Epidemiological, Social and Economic Burden of Severe Hypoglycaemia in Patients with Diabetes Mellitus in Portugal: A Structured Literature Review. Diabetes Ther. 2023 Feb;14*(2)*:265–291. doi: 10 1007/s13 300–022–01 358–1. Epub 2023 Jan 21.

Stenberg K, Axelson H, Sheehan P, Anderson I, Gülmezoglu AM, Temmerman M, et al. Advancing social and economic development by investing in women's and children's health: a new Global Investment Framework. Lancet. 2014;383(9925):1333–54.

Stucki M. Factors related to the change in Swiss inpatient costs by disease: a 6-factor decomposition. Eur J Health Econ. 2021 Mar;22*(2)*:195–221.

Tatu-Chiţoiu G, Arafat R, Deleanu D, Vinereanu D, Udroiu C, Petris A. Impact of the Romanian national programme for interventional therapy in ST-elevation myocardial infarction. EuroIntervention. 2012;8(P):P126-P32.

Technical briefing for Annex 3 of the Global Action Plan for noncommunicable Diseases, Cancer Interventions Technical Briefing. World Health Organization; 2022.

The Global Health Observatory: World Health Organization; 2024 [Available from: https:/www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-life expectancy-and-healthy-life expectancy.

Thomson S, García-Ramírez JA, Akkazieva B, Habicht T, Cylus J, Evetovits T. How resilient is health financing policy in Europe to economic shocks? Evidence from the first year of the COVID-19 pandemic and the 2008 global financial crisis. Health Policy. 2022 Jan;126*(1)*:7–15.

Trastuzumab for early stage, HER2-positive breast cancer: a meta-analysis of 13 864 women in seven randomized trials. Lancet Oncol. 2021;22*(8)*:1139–50.

United Nations World Population Prospects 2022: United Nations, Department of Economic and Social Affairs, Population Division; 2022 [Available from: https:/population.un.org/wpp/.

Viscusi WK, Masterman CJ. Income Elasticities and Global Values of a Statistical Life. Journal of Benefit-Cost Analysis. 2017;8*(2)*:226–50.

Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC Guidelines on cardiovascular diseasesprevention in clinical practice: Developed by the Task Force for cardiovascular diseasesprevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies With the special contribution of the European Association of Preventive Cardiology (EAPC). European Heart Journal. 2021;42*(34)*:3227–337.

Vončina L, Strizrep T, Bagat M, Pezelj-Duliba D, Pavić N, Polašek O. Croatian 2008–2010 health insurance reform: hard choices towards financial sustainability and efficiency. Croatian Medical Journal. 2012 Feb 15;53*(1)*:66–76.

WHO Guide to Cost–effectiveness Analysis. World Health Organization; 2003.

Willemé P, Dumont M. Machines that go 'ping': Medical technology and health expenditures in OECD countries. Health Econ. 2015 Aug;24*(8)*:1027–41.

Woodward RS, Wang L. The oh-so straight and narrow path: can the health care expenditure curve be bent? Health Econ. 2012 Aug;21*(8)*:1023–9.

Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet. 2021;398(10 304):957–80.

Zelle SG, Nyarko KM, Bosu WK, Aikins M, Niëns LM, Lauer JA, et al. Costs, effects and cost–effectiveness of breast cancer control in Ghana. Tropical Medicine and International Health. 2012;17*(8)*:1031–43.

Jha V, Al-Ghamdi SMG, Li G, Wu M-S, Stafylas P, Retat L, et al. Global Economic Burden Associated with Chronic Kidney Disease: A Pragmatic Review of Medical Costs for the Inside CKD Research Programme. Advances in Therapy. 2023;40(10):4405–20.

Shaikh J, Manchanda P, Chiva-Razavi S. Economic burden associated with diabetic retinopathy: Evidence from a literature review. 22nd ISPOR Europe. 2019.

Kerr M, Barron E, Chadwick P, Evans T, Kong WM, Rayman G, et al. The cost of diabetic foot ulcers and amputations to the National Health Service in England (United Kingdom). Diabetic Medicine. 2019;36(8):995–1002.

Persson S, Johansen P, Andersson E, Lindgren P, Thielke D, Thorsted BL, et al. Days absent from work as a result of complications associated with type 2 diabetes: Evidence from 20 years of linked national registry data in Sweden. Diabetes, Obesity and Metabolism. 2020;22(9):1586–97.

de Vries EF, Los J, de Wit GA, Hakkaart-van Roijen L. Patient, family and productivity costs of end-stage renal disease in the Kingdom of the Netherlands; exposing non-health care related costs. BMC Nephrol. 2021;22(1):341.

Maaijwee NAMM, Rutten-Jacobs LCA, Arntz RM, Schaapsmeerders P, Schoonderwaldt HC, van Dijk EJ, et al. Long-term increased risk of unemployment after young stroke. Neurology. 2014;83(13):1132–8.

Jiang Z, Dreyer RP, Spertus JA, Masoudi FA, Li J, Zheng X, et al. Factors Associated With Return to Work After Acute Myocardial Infarction in China. JAMA Netw Open. 2018;1(7):e18 4831.

Kirkeskov L, Carlsen RK, Lund T, Buus NH. Employment of patients with kidney failure treated with dialysis or kidney transplantation—a systematic review and meta-analysis. BMC Nephrology. 2021;22(1):348.

Schoppen T, Boonstra A, Groothoff JW, de Vries J, Göeken LN, Eisma WH. Employment status, job characteristics and work-related health experience of people with a lower limb amputation in The Kingdom of the Netherlands. Arch Phys Med Rehabil. 2001;82(2):239–45.