4PCAN

D3.1 –Direct cost analysis

2024

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Summary

Deliverable D3.1 offers an exhaustive analysis of the direct costs of cancer, emphasizing national government expenditures on cancer-related programs and patient care. The document starts with an overview of its objectives and scope, highlighting the importance of understanding the economic burden of cancer through governmental spending on interventions, including personnel, facilities, supplies, and medications. The methodology section details a multi-level analysis approach, encompassing a systematic literature review to establish a framework for current direct cost measurements and a data dictionary compiling relevant datasets. The literature review introduces the topic, outlines the search strategy, and provides a bibliometric overview of research on cancer costs, identifying major trends.

Subsequent sections delve into direct costs as healthcare expenditures and out-of-pocket expenses, presenting the Cancer Risk Factors Index (CRFI) to underscore the significance of various cancer risk factors at the national level. The document also includes case studies of direct costs in non-EU member states such as Moldova, Montenegro, North Macedonia, and Ukraine, detailing their general characteristics, direct costs, institutional monitoring, and cancer registries. These case studies were particularly challenging, contributing to a delay in the deliverable's submission. Analyzing data from non-EU countries involved extensive data collection and interpretation, necessitating additional time to ensure accuracy and comprehensiveness. The deliverable concludes with a summary of findings and recommendations, offering a thorough assessment of cancer's economic impact and guiding future policy interventions for cancer prevention and management across different regions.

1. Objective and scope

This document presents an updated analysis of the direct costs of cancer as expenditures made by the national governments with cancer (i.e., national cancer programs or other expenditures related to cancer patients) that are publicly available. The deliverable also contains a systematic literature review of past studies on direct cost analysis to establish the baseline parameters of the model. Direct costs are the governmental resources used to design and implement an intervention (i.e., personnel, facilities, supplies, and medications). The up-to-date modeling of the cost-effectiveness ratio for newer member states aims to contribute to a relatively scarce and fragmented knowledge baseline. To measure the economic efficiency of public spending with cancer programs for overall economic improvement, the research estimates the net cost of public intervention compared to the status-quo scenario where the current situation is preserved in terms of health policies. We thus developed a Cancer Risk Factors Index (CRFI) for all EU member state countries, designed to raise awareness on the relative importance of different cancer risk factors at the national level and guide targeted interventions for cancer prevention in EU countries.

2. Methodology

As part of WP3 we conducted a multi-level analysis of direct costs of cancer. Firstly, we compiled a relevant literature database, through a systematic literature review, based on specific topical and specific keywords. This allowed us to extract the conceptual framework and overlapping taxonomies for measuring direct costs of cancer nowadays. Secondly, we created a data dictionary with all relevant existing datasets that portray the direct costs of cancer. Based on existent international data sources and a systematic mapping of domestic data sources in the countries of intervention (i.e. Romania, Bulgaria, Portugal, Italy) we developed an updated original assessment of the comparative direct cost of cancer in old member states (i.e. Belgium and France) and new member states from the different peripheries (i.e. Ireland, Portugal, Italy, Romania and Bulgaria). Thirdly, we explored in-depth non-EU member states institutional approach towards national cancer programs and other expenditures related to cancer patients in non-EU member state countries covered in the project (i.e. Ukraine, Moldova, North Macedonia, Montenegro). Finally, we developed a comprehensive index for evaluating the impact of cancer risk factors at the national level in all EU countries, based on the existent data repositories.

3. Systematic Literature Review

Introduction

Cancer is a leading cause of morbidity and mortality worldwide, with significant personal, societal, and economic consequences (Bray et al., 2018). Understanding the costs associated with cancer is crucial for informing healthcare policy, resource allocation, and economic planning. To this end, a substantial body of research has examined the various costs of cancer, including direct medical costs, indirect costs, and out-of-pocket expenses.

From an economic perspective, costs related to cancer can be included in three major categories: direct costs, indirect costs and out-of-pocket expenses. *Direct medical costs* refer to the expenses incurred for cancer-related healthcare services, such as physician visits, hospitalizations, diagnostic tests, and treatment (Luengo-Fernandez et al., 2013). These costs can vary widely depending on factors like cancer type, stage at diagnosis, treatment modalities, and healthcare system characteristics. Several studies have attempted to quantify the direct costs of cancer, with estimates ranging from tens of thousands to hundreds of thousands of dollars per patient, depending on the country and healthcare context (Torkki et al., 2022; Lana et al., 2020; Mariotto et al., 2011; Yabroff et al., 2011).

Indirect costs, on the other hand, encompass the productivity losses and foregone earnings associated with cancer (Bradley et al., 2008). These include absenteeism from work, reduced work hours, and premature mortality. The indirect costs of cancer can be substantial, often exceeding the direct medical costs, and have significant implications for individuals, families, and society as a whole (Bradley et al., 2008).

Out-of-pocket expenses refer to the costs borne by patients and their families, including copayments, deductibles, and expenses not covered by insurance (Zafar & Abernethy, 2013). These expenses can create significant financial burdens, especially for low-income and uninsured individuals, and may lead to delays in seeking care or financial hardship (Zafar & Abernethy, 2013).

This systematic review aims to synthesize the available evidence on the costs of cancer, examining the direct medical costs, indirect costs, and out-of-pocket expenses across different cancer types, treatment modalities, and healthcare systems around the world. The review is structured in four main parts, as follows. The first part describes the search strategy performed in the Scopus database, one of the main tertiary sources for academic works. The second part highlights the bibliometric characteristics of the published research on cancer and is complemented by the visual analysis of this research undertaken with VoSViewer, in the third part of the review. Moreover, the use of VoSViewer allows for the delineation of the major research directions in relation to cancer costs over time. The fourth part of the review is focused on direct costs of cancer and outlines the methodologies and data sources used by scholars to determine/estimate the direct costs of cancer.

Search strategy

The review was conducted by searching the Scopus database using a specific search algorithm in February 2024. Several reasons prompted us towards Scopus, as follows:

1. Scopus is the largest abstract and citation database of peer-reviewed literature, covering over 22,000 active titles from more than 5,000 international publishers (Elsevier, 2023). This comprehensive coverage ensures that a systematic review can capture a wide range of relevant scholarly studies on the costs of cancer.
2. Scopus indexes publications across various academic disciplines, including medicine, health sciences, social sciences, and economics. This broad disciplinary scope is essential for a systematic review on the economic aspects of cancer, as the relevant literature may be spread across different fields.
3. Scopus only includes peer-reviewed journals, conference proceedings, and book series, ensuring a high level of quality and reliability in the included studies, which is paramount for conducting a rigorous systematic review and synthesizing high-quality evidence.
4. Scopus offers advanced search functionalities, such as the ability to search by keywords, author, affiliation, and publication year. These features facilitate the efficient identification and screening of relevant studies for the systematic review.

The alternative choices for a robust tertiary source were PubMed/MEDLINE, Web of Science – Clarivate Analytics and Google Scholar, but each of them is disadvantageous when compared to Scopus. While PubMed/MEDLINE is a highly respected and widely used database for biomedical literature, it primarily focuses on the clinical and biological aspects of cancer. Scopus provides a more comprehensive coverage of the economic and social aspects of cancer, which are crucial for a systematic review on cancer costs. Web of Science is another leading database for scholarly literature, with a strong presence in the natural sciences and social sciences. However, Scopus often has a broader coverage of journals, particularly in the health sciences and economics, which is advantageous for a systematic review on cancer costs. Google Scholar is a valuable resource for locating a wide range of scholarly literature, including grey literature and non-peer-reviewed sources. However, the lack of quality control and the difficulty in systematically searching and screening the results make it less suitable for a rigorous systematic review compared to Scopus.

The search on Scopus was based on several specific keywords, presented in Table 1. They were selected in such a way as to allow for a broad view of research on cancer costs, with the aim of including in the set of papers all relevant approaches to cancer economics. Therefore, the specific search strategy was the following: (TITLE-ABS-KEY ("cancer costs" OR "cost of cancer" OR "costs of cancer") OR TITLE-ABS-KEY ("direct cost of cancer" OR "direct costs of cancer") OR TITLE-ABS-KEY ("indirect cost of cancer" OR "indirect costs of cancer") OR TITLE-ABS-KEY ("economic burden of cancer") OR TITLE-ABS-KEY ("national expenditure on cancer") OR TITLE-ABS-KEY ("oncological cost*") OR TITLE-ABS-KEY ("morbidity costs of cancer") OR TITLE-ABS-KEY ("mortality costs of cancer") OR TITLE-ABS-KEY ("opportunity cost of cancer" OR "opportunity costs of cancer") OR TITLE-ABS-KEY ("informal cost of cancer" OR "informal costs of cancer") OR TITLE-ABS-KEY ("financial toxicity of cancer" OR "financial burden of cancer").

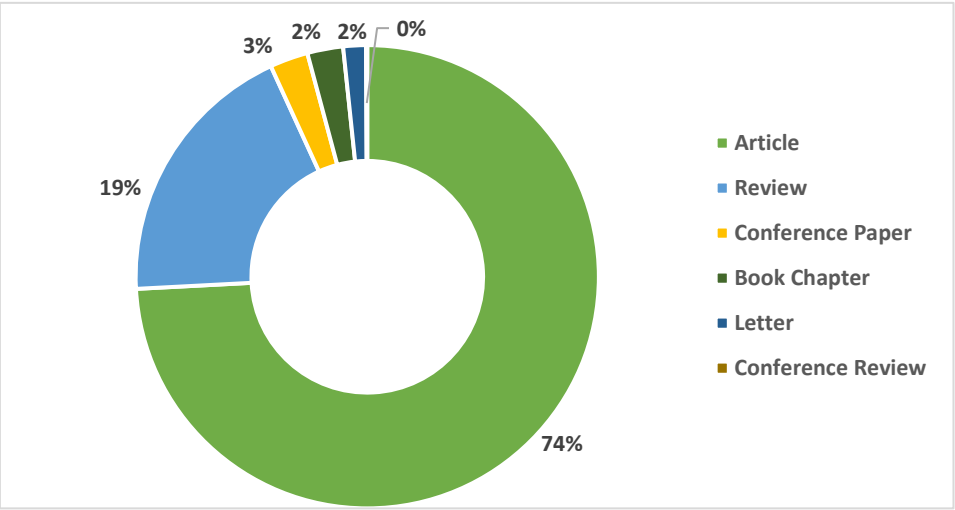
Table 1 Key words for systematic literature review on direct costs of cancer

	Topical Keyword	Specific Keyword
1.	**Direct and Indirect Costs**	**Cancer Costs**: A broad term encompassing all costs associated with cancer. **Cancer Economics/Oncology Economics**: The study of economic aspects and implications of cancer and its treatment. **Direct Costs of Cancer**: Expenses directly related to cancer treatment, such as hospital stays, medications, and medical procedures. **Indirect Costs of Cancer**: Costs not directly linked to medical treatment but resulting from cancer, like lost productivity, transportation to treatment centers, and home care expenses. **Out of the pocket money**: Costs associated with cancer, but supported entirely by the patients because of the malfunction of the Health System (to avoid delays in diagnosing, treatment, medication, etc.)
2.	**Economic Burden and National Expenditures**	**Economic Burden of Cancer**: The overall economic impact of cancer on society, including both direct and indirect costs. **National Expenditures on Cancer**: Total spending by a country on cancer-related healthcare and services. **European Expenditures on Cancer**: Relevant to European region spending by on cancer-related healthcare and services.
3.	**Global and Oncological Costs**	**Global Cost of Cancer/Oncology**: The worldwide financial impact of cancer, encompassing all associated costs on a global scale. **Oncological Costs**: Specific costs associated with oncology, the branch of medicine dealing with cancer.
4.	**Morbidity and Mortality Costs**	**Morbidity Costs of Cancer**: Costs associated with the decreased quality of life and health complications due to cancer. **Mortality Costs of Cancer**: Financial implications related to cancer fatalities, often measured in terms of lost potential earnings.
5.	**Opportunity and**	**Opportunity Costs of Cancer**: Economic opportunities lost

	Topical Keyword	Specific Keyword
	Informal Costs	due to cancer, such as missed work or career advancement. **Informal Costs of Cancer**: Unofficial or hidden costs borne by patients and families, like caregiving time and emotional stress.
6.	**Financial Toxicity and Burden**	**Financial Toxicity of Cancer**: The financial strain and hardship experienced by patients due to the high costs of cancer treatment. **Financial Burden of Cancer**: The overall financial strain on individuals and families, encompassing both direct and indirect costs.

The search strategy was not limited to a specific time interval. The number of documents found in Scoups using this strategy was 1,395, ranging from 1919 to 2024. Further, the search was restricted to documents in English, which reduced the number of documents to 1,318. Moreover, the search was restricted to specific document types, including articles, reviews, conference papers, book chapters, letters and conferences reviews, which led to 1,200 documents. Of these 1,200 documents, 1,189 were in their final publication stage and 11 were "In press". We decided to include the "In press" articles because they represent the latest research that has been accepted for publication but not yet officially published. Excluding these articles could lead to missing out on the most recent and relevant information on our topic of interest, which is essential for a thorough systematic review. Figure 1 shows the distribution of documents in our panel. Most documents are articles (890), which are accompanied by reviews (228), conference papers (32), book chapters (30), letters (19), and conference reviews (1).

Figure 1. Distribution of documents by type

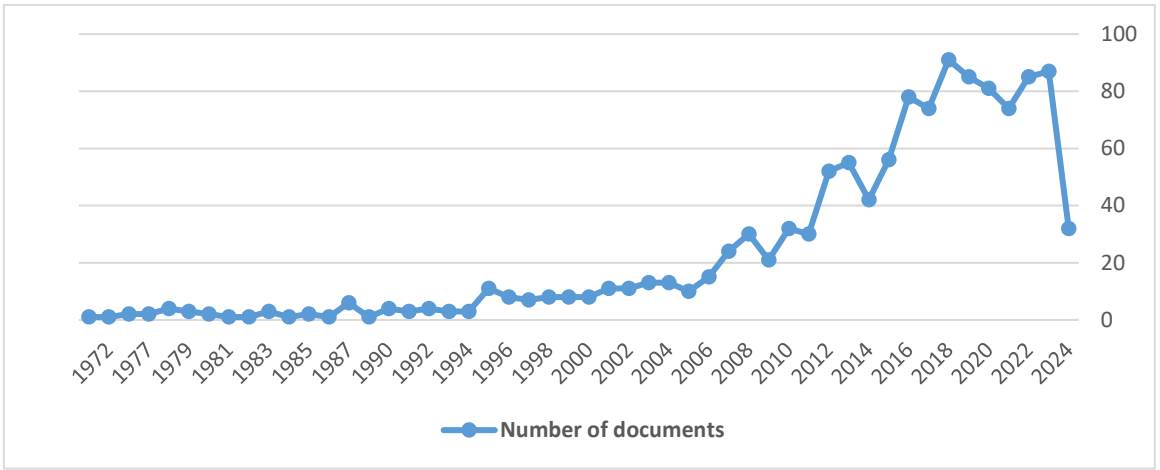


Bibliometric overview of research on cancer costs

This section of the systematic review presents a brief bibliometric analysis of the 1,200 documents extracted from the Scopus database, highlighting the evolution of publications overs years, the most important sources that hosted the research, the prominent authors, countries and institutions for the research on costs of cancer, as well as the funders of these works. Also, it overviews the most important scholarly works on the topic evidenced by the number of citations.

Figure 1 shows the number of publications per year over time, which reveals the evolution of research on the topic. The first publication on this topic was published in 1919 – Gade (1919) – and was a pioneering work on the calculation of economic losses to Norway brought about by deaths from the cancerous diseases (carcinoma and sarcoma) in that country. The calculations are based on one side upon the mortality statistics of Norway for the years 1902–1911, reporting 22,093 deaths caused by malignant tumours; and on the other, upon the valuation of Norwegian lives in 1912, as published by Mr. A. N. Kiaer in Statsovekonomisk Tidsskrift in 1913 – unfortunately, we could not find this latter source. Until the 1970s Scopus did not identify any other work on the topic, but several studies were published in the following decade (14), followed by 20 more between 1981 and 1990. The publications in this research field significantly increased in recent decades, with a sharp rise starting in the early 2000s. The most publications are observed in the last 5-6 years, indicating growing research interest and importance of this topic. The highest number of scholarly studies was published in 2018 (91), but Figure 1 also shows a drop in the number of publications on these topics from this upper limit between 2019 and 2021, followed by an increase until 2023. For 2024, the number of documents is only 32, but the year is not completed yet.

Figure 2. Number of documents per year, 1919-2024

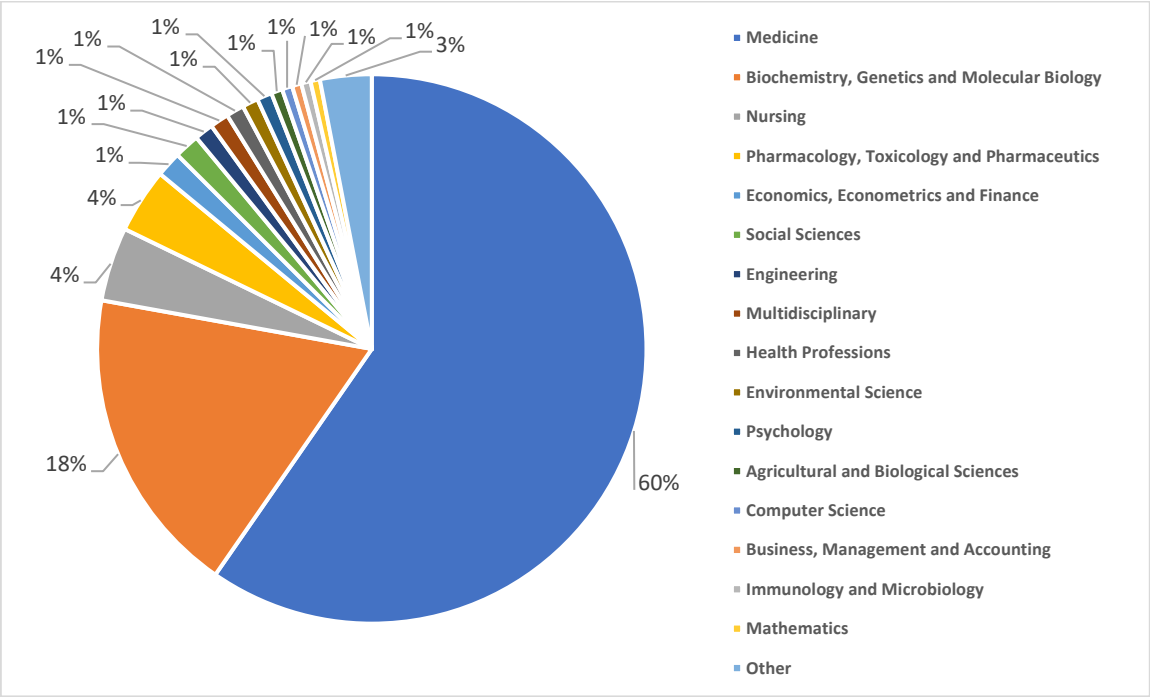


The chart presented in Figure 3 breaks down the publications by broad academic subject areas based on journal domains as defined by Scopus. The predominant subject is Medicine, with 1,082 documents (60% of the total documents), followed by

Biochemistry, Genetics and Molecular Biology with 330 documents (18%). They are followed at a distance by Nursing (79 documents) and Pharmacology, Toxicology and

Pharmaceutical (69 documents). Certainly, there is no surprise that medical subjects are at the forefront of published research on cancer costs. However, we note that subjects such as Economics, Econometrics & Finance, and Business, Management and Accounting have also accommodated studies on this topic (27 and 10, respectively), which underscores the importance of understanding the economic implications of cancer. At the same time, the presence of other domains (Engineering, Sciences, Computer Science, etc.) aligns with interdisciplinary nature of cancer cost research.

Figure 3. Distribution of documents by subjects



The number of publications per journal, shown in Figure 4, provides insights into the most important journals for research in this field. Journals that published many studies on the topic may be considered influential and/or specialized in this specific research area. By far, the journal Cancer, published by Wiley, published the highest number of studies (40), followed by Journal of Clinical Oncology and Journal of Oncology Practice, both published by ASCO Publications, with 26 and 25 studies respectively. Other prominent journals are Asian Pacific Journal Of Cancer Prevention, Supportive Care in Cancer and Journal of Cancer Policy. When the journals in the Economics and Business subjects are considered, the sources with most papers on this topic are Value in Health Regional Issues (7 documents), European Journal of Health Economics (6 documents), and American Health and Drug Benefits, Applied Health Economics and Health Policy (4 documents each).

Figure 4. Most important 15 sources for research on cancer costs

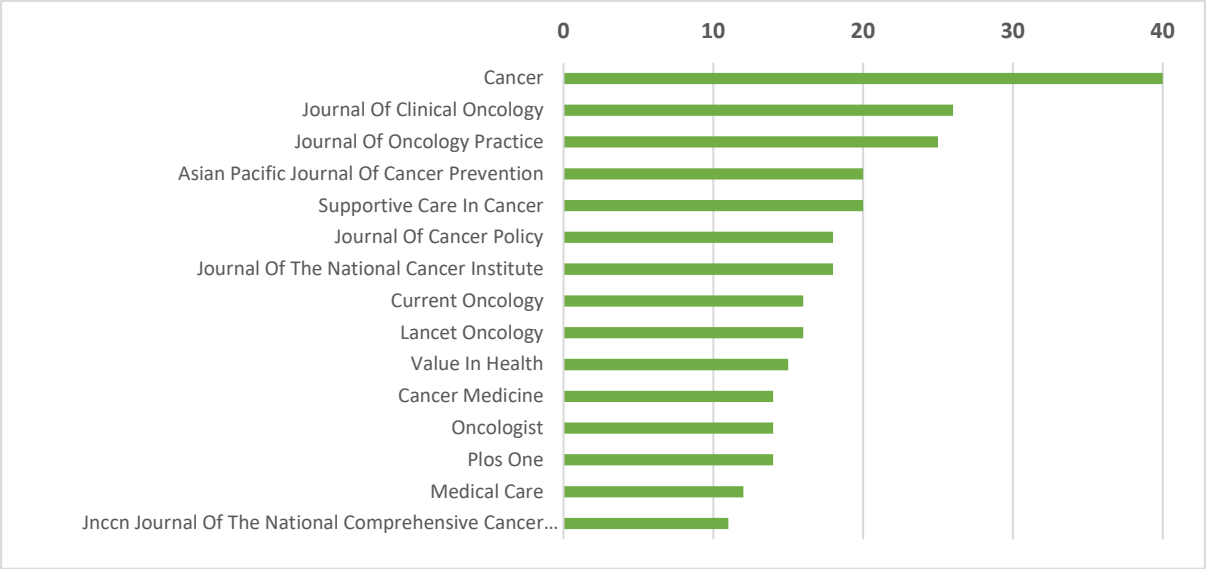
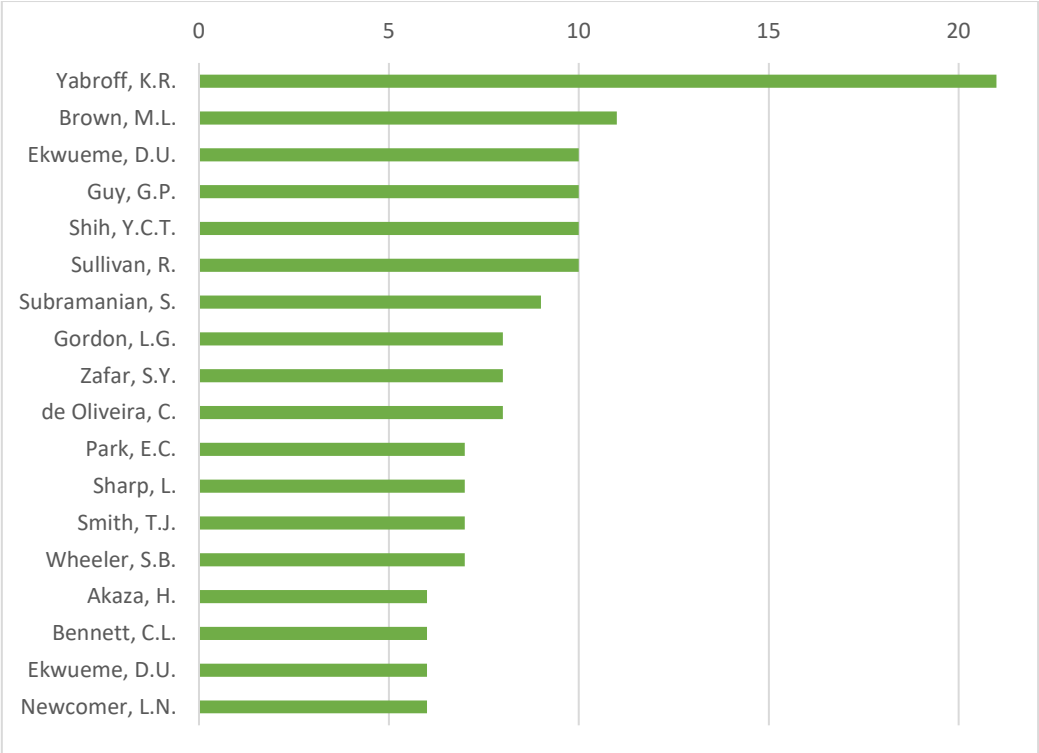


Figure 5 presents the most important scholars in this research area, based on the number of documents published over time. Robin Yabroff (PhD, MBA), which is currently the Scientific Vice President for Health Services Research at the American Cancer Society, is the most prolific author, with 21 studies published between 2005 and 2023. She is followed by Martin L. Brown, PhD, affiliated with the Surveillance Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, United States, with 11 studies published. Four authors have published 10 studies each: (1) Donatus U. Ekwueme, from Office of the Associate Director for Policy and Strategy, Centers for Disease Control and Prevention, United States; (2) Gery P. Guy Jr., PhD, MPH, from Massachusetts General Hospital Cancer Center and Harvard Medical School, United States; (3) Ya-Chen Tina Shih from the Department of Health Services Research, The University of Texas MD Anderson Cancer Center, United States; and (4) Richard Sullivan, PhD, affiliated with the Institute of Cancer Policy, King's College London, United Kingdom.

Figure 5. Most important authors on cancer cost research, based on number of documents



At country level, the United States clearly dominate the research on cancer costs, as illustrated by Figure 6. Between 1919 and 2024 authors from the United States have authored or co-authored 619 documents, or 39% of all documents in our sample. The second country as importance is the United Kingdom, with 99 documents authored (6.25% of all documents), while Canada is in the third place, with 75 documents authored (4.75% of all documents). Six European countries are present in the top 15 countries as importance considering the number of documents – United Kingdom, Italy, Netherlands, France, Germany, and Sweden – with a total of 267 documents (16.8% of the total documents), but this represents only 43% of the documents authored by scholars from the United States. Other countries in the top 15, besides the ones already mentioned, are Australia (66 documents), India (42 documents), China (40 documents), South Korea (32 documents), Japan (26 documents), Iran (25 documents) and Brazil (20 documents). While the prominence of developed countries is likely due to greater research funding and infrastructure in these regions, the presence of China, Iran, or Brazil in the top countries suggests growing interest and capacity for cancer cost research in emerging economies as well. Among European emerging economies, Poland and Turkyie are the leading countries in publications on cancer costs with 9 publications each, followed by Romania (6 documents), Serbia (4), Croatia (3), and Hungary (2).

Figure 6. Most important countries for research on cancer cost based on the number of documents

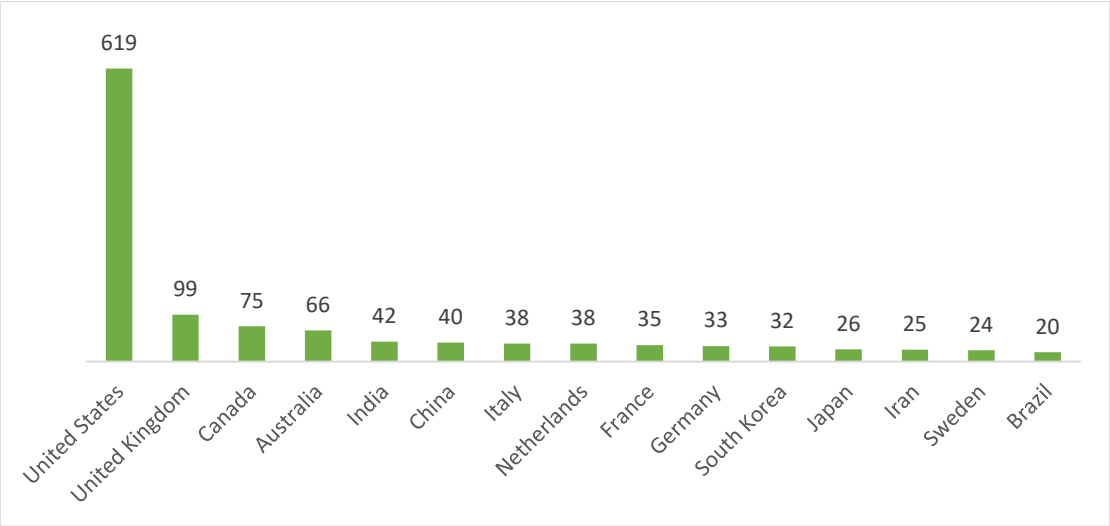
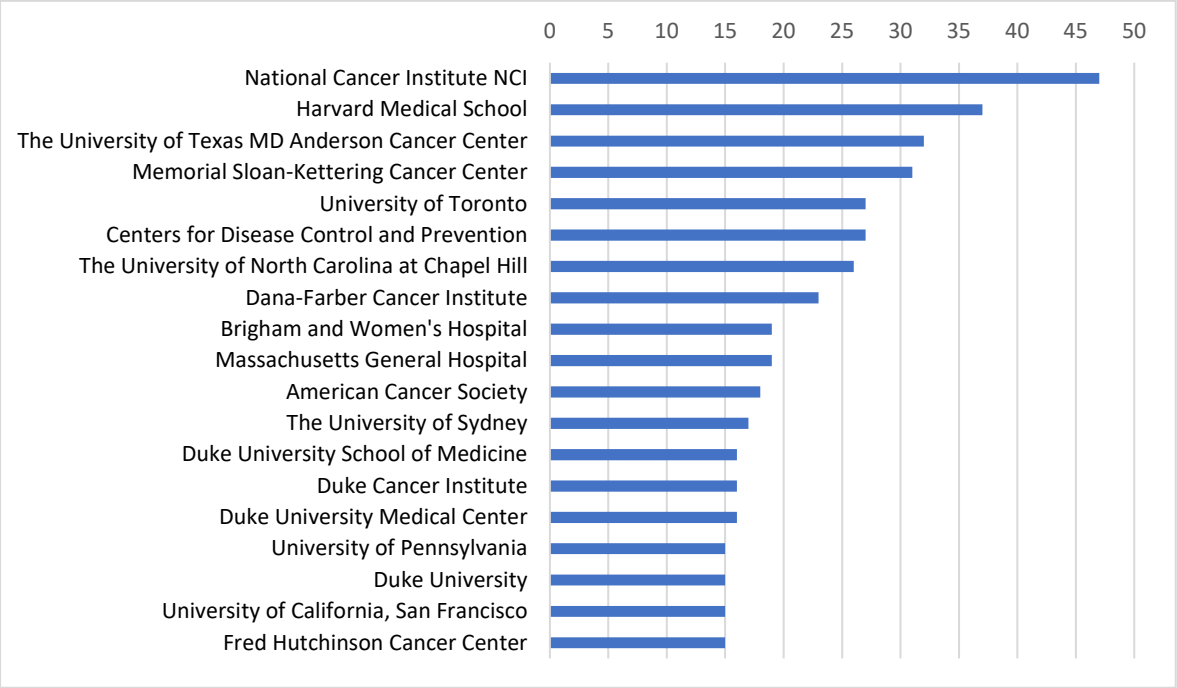


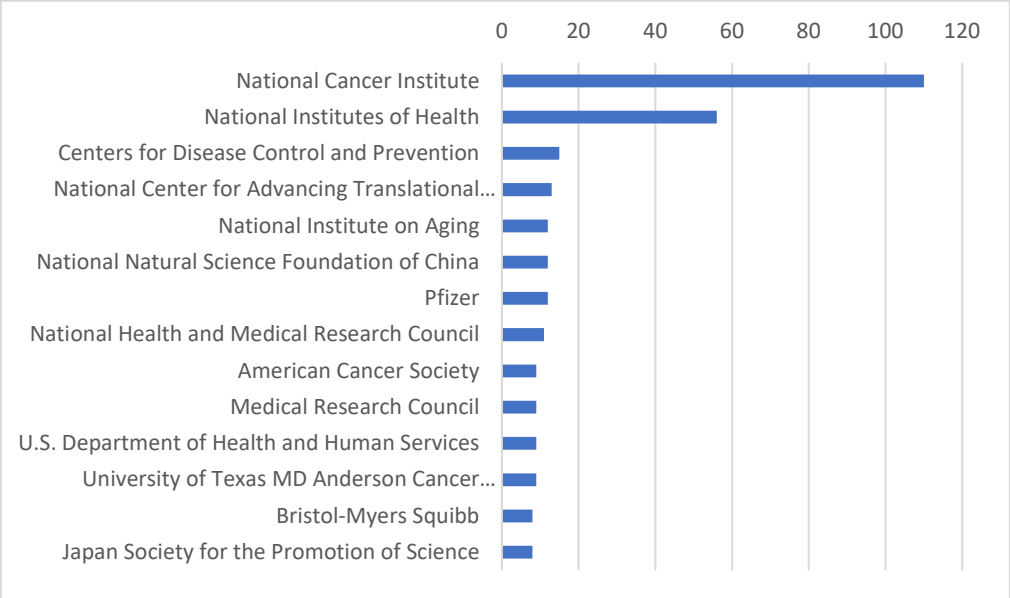
Figure 7 identifies the top institutional affiliations of researchers publishing on cancer costs. The leading institutions include prestigious universities, hospitals, and research centres, mainly from the United States, Canada, Europe and Australia. The prestigious National Cancer Institute from the United States is the institution with most documents on the topic (47), followed by Harvard Medical School (37 documents) and The University of Texas MD Anderson Cancer Center (32 documents). The University of Toronto (27) is the only Canadian institution in the top 20 institutions, while the University of Sydney is the only Australian institution in the top 20. The presence of these renowned organizations indicates that cancer cost research is being conducted at high-calibre academic and healthcare institutions. No European institution enters the top 20. King's College London and University of Oxford from the United Kingdom, and Karolinska Institute from Sweden, share positions 31 to 42 in the ranking of institutions with publications on cancer costs. This evidences a reduced interest of European public, academic and research bodies on this research area, connected with lower funding and fragmented and national level.

Figure 7. The most important affiliations for research on cancer costs based on the number of documents



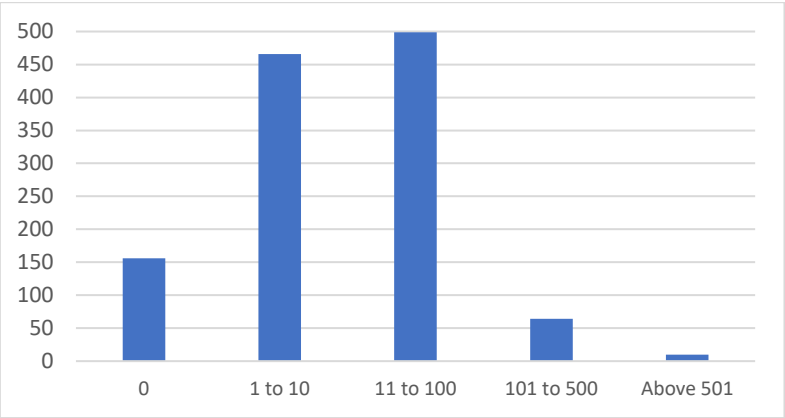
The key organizations and companies that have provided funding for cancer cost research are highlighted in Figure 8. Overall, 159 funders provided financing for studies on the topic. The top funders include healthcare organizations, and government agencies but also pharmaceutical companies, suggesting a diverse range of stakeholders interested in understanding the economic burden of cancer. The substantial number of studies (70) financed by the private sector, mostly companies such as Pfizer, Bristol-Myers Squibb, AstraZeneca, Merck, etc. demonstrates the significant investment and importance placed on this research area. There are several reasons behind pharmaceutical companies' involvement in cancer costs research: (1) Pharmaceutical companies that develop cancer drugs and treatments have a keen interest in understanding the full economic impact of cancer, which can inform pricing, market access, and reimbursement strategies for their products; (2) By funding research on cancer costs, pharmaceutical companies can showcase the value that their drugs and therapies provide in terms of reducing the economic burden of cancer, which in turn can support pricing and reimbursement negotiations with healthcare payers; (3) Insights from cancer cost research can help pharmaceutical companies identify unmet needs and prioritize their research and development efforts towards areas with the greatest economic impact; (4) In some healthcare systems, pharmaceutical companies may be required to provide economic data, including cost-effectiveness analyses, as part of the drug approval and reimbursement process; hence, funding research on cancer costs can help generate the necessary evidence. However, there is a potential conflict of interest in pharmaceutical companies funding this type of research. The findings could be perceived as biased or skewed to favour the commercial interests of the companies, rather than presenting an objective assessment of the cancer cost landscape.

Figure 8. The most important funders of research on cancer costs – number of studies funded



The 1200 documents in our sample generated over the entire time period of our analysis 38,499 citations, for a mean of 32.22 citations per document and a median of 9 citations per document. Figure 9 presents the distribution of citations per document for the entire sample. Most documents have been cited between 11 to 100 times (499) and then by 1 to 10 times (466). There are 156 documents that were never cited. At the other end, 64 documents received between 101 to 500 citations and 10 documents were cited at least by 501 times. The highest number of citations, 2014, belongs to the paper by Mariotto et al. (2011), which estimated and projected the cost of cancer for the United States between 2010 and 2020. Other highly cited works belong to Zafar et al. (2013) on financial toxicity of cancer treatment (781 citations), Luengo-Fernandez et al. (2013) on the economic burden of cancer in Europe (687 citations), and Potosky et al. (1993) which used a tumour registry database to calibrate cancer related health services (648 citations).

Figure 9. Distribution of citations per document



This brief bibliometric review has provided an overview of the scholarly research on the costs of cancer, synthesizing evidence from 1,200 studies published between 1919 and 2024. The analysis reveals several key insights. First, the research landscape on cancer costs has evolved significantly over time, with a sharp increase in publications observed since the early 2000s, indicating the growing importance of this topic. Second, The United States dominates this research field, contributing nearly 40% of the total publications, followed by the United Kingdom and Canada. This geographic distribution likely reflects the availability of research funding and infrastructure in these developed countries. Third, the research is highly interdisciplinary, spanning medical, health economics, and social science disciplines. While oncology and health services research are the primary contributors, the involvement of economists and business scholars underscores the relevance of understanding the economic implications of cancer. Fourth, a notable finding is the significant role of pharmaceutical companies in funding research on cancer costs, accounting for nearly half of the studies in the sample. While this reflects the industry's increased interest in the economic burden of cancer, it also raises concerns about potential conflicts of interest and the need for transparent and rigorous methodologies to ensure the objectivity of the findings.

Major directions and trends in cancer costs research

The objective of the third part of the systematic review relies in identifying the most relevant research directions and trends in the research on costs of cancer. For this purpose, we have used the freely available VoSViewer software developed by Nees Jan van Eck and Ludo Waltman from the Centre for Science and Technology Studies (CWTS) at Leiden University, Netherlands. The software is designed to create, visualize, and explore bibliometric networks and is particularly useful for analyzing and visualizing co-occurrence relationships between various bibliometric elements, such as keywords, authors, journals, and institutions – see, in this respect, the following technical papers on VoSViewer: Waltman et al. (2010), Van Eck et al. (2010), Van Eck and Waltman (2011), or Perianes-Rodriguez (2016). Up to now VoSViewer has been widely used in various scholarly disciplines to conduct systematic reviews and bibliometric analyses, which demonstrate its versatility and effectiveness in supporting systematic reviews and bibliometric analyses across various research domains. For example, Zupic and Čater (2015) performed a citation and co-citation analysis to map the intellectual structure of the Organizational Research Methods journal, Zhang et al. (2012) used it to analyse the co-occurrence of keywords and identify the research themes in the patient adherence literature, Fahiminia et al. (2015) provided visualizations of co-occurrence of keywords and the evolution of research themes in green supply chain management, and Popescu et al. (2023) applied it to systematically review the research on Sustainability, ESG Ratings and Corporate Performance in the Manufacturing Sector.

We have selected the *co-occurrence analysis* to perform the review, one of the modules in VosViewer that is the best adapted to our research objective. Co-occurrence analysis is a technique used to identify the relationships between different elements (such as keywords, authors, or institutions) within a set of academic publications. In the context of a systematic review, co-occurrence analysis of keywords is particularly useful for understanding the major research themes and directions in a specific field. The underlying principle of co-occurrence analysis is that keywords that appear together frequently in the same articles are likely to be related to each other and represent

important concepts or topics within the research area. By analysing the co-occurrence patterns of keywords, researchers can uncover the thematic structure and evolution of the research field over time.

When applied to a systematic review dataset, VoSViewer can generate several types of visualizations that support the identification of major research directions. We will use two of them, as follows:

1. Co-occurrence Network Visualization: VoSViewer creates a network visualization where each keyword is represented as a node, and the links between nodes indicate the co-occurrence of those keywords in the articles. The size of the nodes reflects the frequency of the keyword, and the thickness of the links represents the strength of the co-occurrence relationship. This visualization allows to identify the most prominent keywords and the clusters of closely related concepts within the research field.

2. Overlay Visualization: VoSViewer can overlay additional information, such as the temporal trend of keyword co-occurrences, on the network visualization. This feature enables the tracking of research themes evolution over time and identify emerging or declining areas of focus.

Using these visualizations one can identify the main research themes and topics within the research area covered by the systematic review, understand the relationships and interconnections between different concepts and research areas, observe the temporal shifts and the emergence of new research directions over time, and recognize potential research gaps or underexplored areas that could guide future research priorities.

To conduct the analysis, we have used Author keywords to conduct the analysis and the Full counting option, which means that the software does not divide co-occurrences by the number of authors (i.e., if a document has 2 authors, the occurrence and the links are not divided by 2, each author enters the network as single). We set the minimum number of occurrences of a keyword to 5, which initially identified 111 keywords that met the threshold (to note that there is no rule for setting this threshold, but setting it too low leads to many keywords and an agglomerated network that is difficult to analyse). After manually reviewing the generated keywords and grouping similar keywords under one keyword (for example, cancer and neoplasm have been grouped under “cancer”), 67 keywords were identified by VoSViewer.

Figure 10 shows the map created by VoSViewer based on co-occurrences, allowing us to observe the keywords with the highest occurrences (given by the size of the circles), the links between the keywords and the presence of four clusters in cancer costs research.

Figure 10. Map of co-occurrences

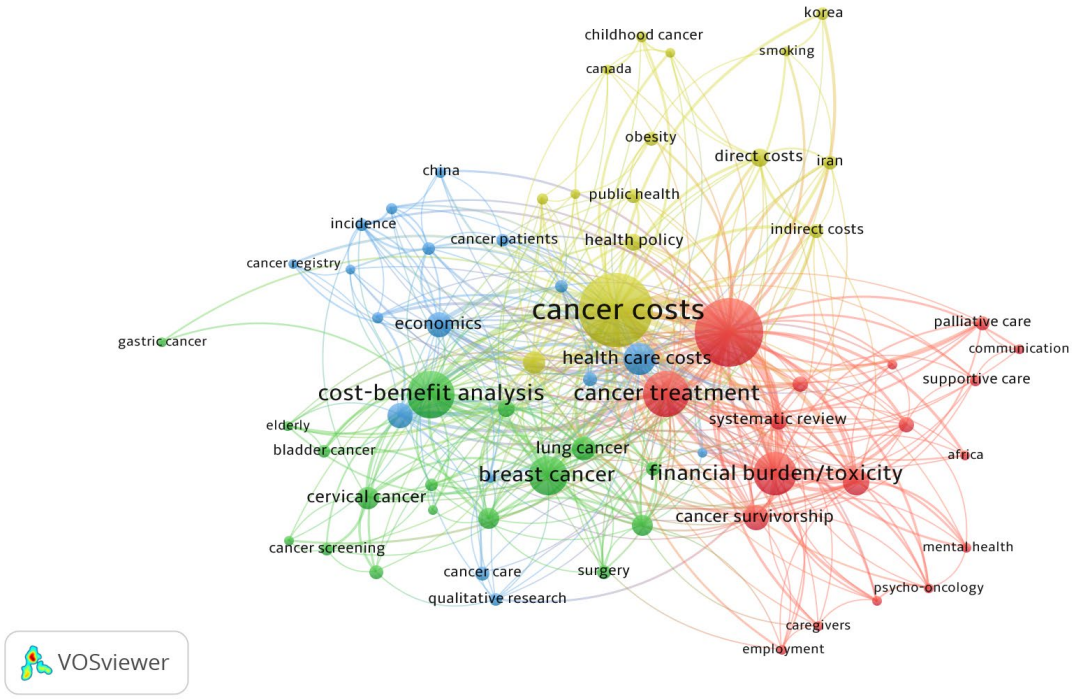


Table 2 shows the 14 keywords with the highest co-occurrences, but not lower than 20. As expected, "cancer costs" is the keyword with most co-occurrences (235), which is normal considering the research topic investigated. It is followed by "cancer" (206 occurrences) and "cost-benefit analysis" (100 occurrences, however much lower than the ones for "cancer costs"). When contemplating the economic implications of cancer, besides "cost-benefit analysis" other keywords emerge as important in terms of co-occurrences: "financial burden/toxicity" (84) and "health care costs" (27). The same keywords from Table 2 have the highest importance when links and total link strength are considered. The total link strength of a keyword is a measure that reflects the strength of the co-occurrence relationships between it and all the other keywords in the network and, in the context of the co-occurrence relationships, it represents the total number of co-occurrences of that keyword with all the other keywords in the dataset. A higher total link strength for a keyword indicates that it has stronger co-occurrence relationships with other keywords, suggesting that it is a more central and influential concept within the research field. Conversely, a lower total link strength suggests that the keyword is less strongly connected to other keywords in the network, and it may be peripheral or less prevalent in the research literature. Therefore, the most important concepts encountered in the research literature on cancer costs are, besides "cancer costs" and "cancer", "cost-benefit analysis", "cancer treatment", and "financial burden/toxicity". These keywords are likely to appear frequently in research articles on cancer costs and are integral to understanding the topic. The strong co-occurrence relationships with these keywords suggest that they play a crucial role in shaping the discourse surrounding cancer costs. On the other hand, keywords with lower link strength may still be relevant but may not be as central to the overall discussion on this topic.

Table 2. Keywords with the highest co-occurrences

Keyword	Cluster	Occurrences	Links	Total link strength
cancer costs	4	235	62	379
cancer	1	206	57	331
cost-benefit analysis	2	100	38	128
cancer treatment	1	93	42	159
financial burden/toxicity	1	84	33	151
breast cancer	2	69	28	90
health care costs	3	44	30	81
quality of life	1	30	24	70
economics	3	27	22	54
health insurance	3	27	20	53
cancer survivorship	1	27	22	48
lung cancer	2	25	20	47
health economics	4	23	27	54
cervical cancer	2	22	14	32

To identify the clusters, we imposed a minimum number of 10 keywords per cluster to avoid unnecessary fragmentation. There are 4 clusters identified by the co-occurrence analysis, reflected with a different colour in Figure 10: cluster 1 in red, cluster 2 in green, cluster 3 in blue and cluster 4 in yellow. All are consistent in terms of keyword content.

Cluster 1, which may be named "Psychosocial and Economic Impacts of Cancer", includes 18 keywords that cover several interconnected themes related to the broader psychosocial and economic consequences of cancer, including: the financial burden and toxicity of cancer treatment, the quality of life and cancer survivorship, the supportive and palliative care needs, the psychosocial impacts on patients, caregivers, and young adults, the employment and mental health challenges, and the communication and clinical trial participation. Together, these research themes suggest an emphasis on the complex impacts of cancer beyond just the direct medical costs and treatment. Therefore, this cluster reflects the growing recognition of the importance of addressing the financial, psychological, social, and practical challenges faced by cancer patients and their families throughout the cancer care continuum.

Cluster 2, with a possible name of "Cancer Screening, Treatment, and Epidemiology", comprises 17 keywords that address various aspects of cancer epidemiology, screening, and treatment modalities, such as specific cancer types (breast,

lung, cervical, colorectal, prostate, bladder, gastric), cancer screening and early detection, cancer treatment approaches (radiotherapy, surgery), biomarkers and risk factors, such as human papillomavirus, and considerations for specific populations, such as the elderly and in the Indian context. These themes suggest a cluster that is centred around the epidemiological and clinical aspects of cancer, including the identification, diagnosis, and treatment of different cancer types. At the same time, the inclusion in this cluster of the keyword “cost-benefit analysis" indicates an interest on the evaluation and optimization of cancer screening and management strategies from an economic perspective.

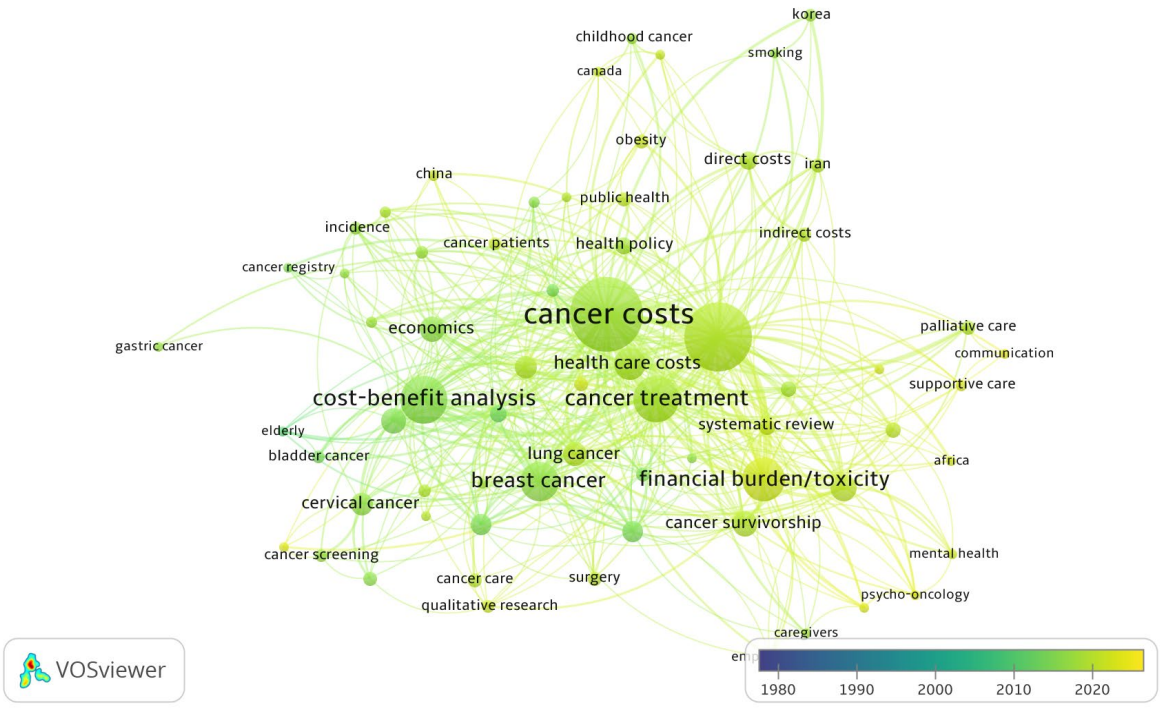
The *third cluster*, which may be entitled "Cancer Economics, Health Policy, and Epidemiology", also includes 17 keywords that portend to the economic, policy, and epidemiological aspects of cancer. The most important are related to health care costs and economics of cancer care, health insurance and access to cancer drugs, pharmaco-economics and cost-effectiveness analyses, qualitative research on patient perspectives, cancer incidence, mortality, prevalence, and epidemiology, phases of cancer care (e.g., diagnosis, treatment, survivorship), health services research and guidelines, and cancer registries and data sources. As its content suggests, this is a cluster that investigates the broader healthcare system and policy implications of cancer, including the economic burden, access to care, and epidemiological trends. Moreover, the inclusion of keywords like "qualitative research" and "patients" indicates a consideration of the patient experiences and perspectives by the research whose keywords are included in this cluster. From these perspectives, this cluster represents the important intersection between cancer care, healthcare systems, and public health, with a focus on informing health policies, resource allocation, and improving cancer outcomes at a broader, societal level.

The *last cluster, 4,* is the smallest with 15 keywords included, and may be named "Global Perspectives on the Economics and Public Health Impacts of Cancer". This name is based on the research topics covered in this cluster: cancer costs, including direct and indirect costs; health economics and economic evaluations of cancer care; health policy and public health implications of cancer, including administrative data sources; specific cancer types, such as ovarian, endometrial, and childhood cancer; contextual factors, such as obesity and smoking, and geographical diversity, as this research strand includes Iran, Korea, and Canada. Therefore, this cluster examines the economic burden and public health impacts of cancer from a global perspective, considering different healthcare systems, policies, and population-level factors that influence cancer outcomes. The research highlighted by the keywords in this cluster is essential for cancer investigations that can support evidence-based decision-making and resource allocation to improve cancer prevention, care, and outcomes globally.

Figures 11 and 12 show the temporal perspective on cancer costs research, which permits the detection of research trends over time. In Figure 11 we have plotted the keywords used in research published between 1990 and 2024. The lighter the colour, the more recent the research is. Research on our topic of interest was mostly developed after 2010, which may be explained by advancements in technology and increased funding for cancer research in recent years. Additionally, the shift towards personalized medicine and targeted therapies may have also contributed to the rise in research on cancer costs. An important result refers to the keyword “financial burden/toxicity”, which is the most important keyword plotted in Figure 11 as used in the research surrounding the pandemic year 2020. It is followed by “quality of life” and “psycho-oncology”, which underscore the

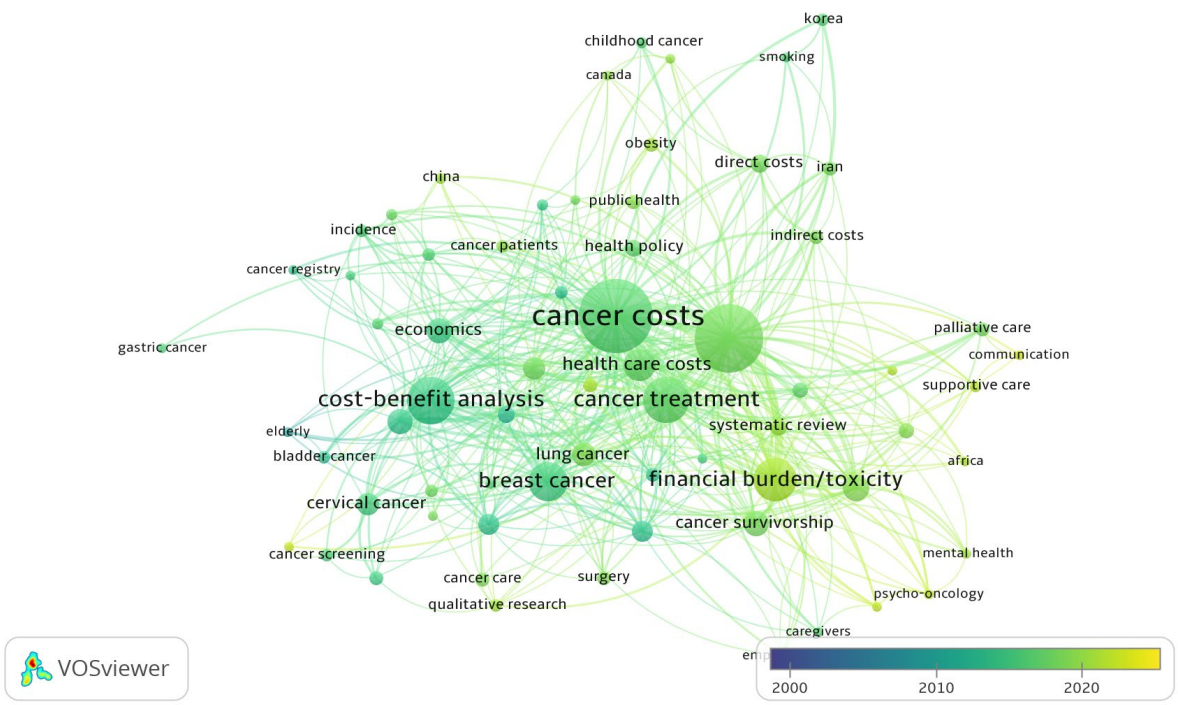
increased recent interest given by the research to the patient and his/her burden when cancer is diagnosed.

Figure 11. Map of co-occurrences – temporal perspective 1980-2024



A more recent perspective on the cancer costs research is presented in Figure 12, which shows the temporal evolution of the literature after 2000. As in the case of Figure 11, lighter colours indicate higher recency. Several keywords are identified as being prominent in studies after 2020: “communication”, “India”, “psycho-oncology”, “young adult”, “supportive care”, “Africa”, “clinical trial” and “cancer drugs”. This highlights the shift towards a more holistic approach to cancer research, focusing not only on treatment options but also on communication, psychosocial aspects, and support systems for cancer patients. The inclusion of keywords such as "India", "Africa", and "young adult" suggests a growing awareness of the global impact of cancer and the need for tailored approaches to address the diverse needs of different populations. The emphasis on "clinical trials" and "cancer drugs" reflects the ongoing efforts to develop new and more effective treatments for cancer patients.

Figure 12. Map of co-occurrences – temporal perspective 2020-2024



Methodologies and data sources to calculate/estimate the direct costs of cancer

This section of the literature review is concentrated on the specific methodologies and data sources used in scholarly studies to calculate, whenever possible, or estimate, the direct costs of cancer. Two tables, 3 and 4, support this section. Both tables provide a synopsis of the methodologies and data sources used to calculate or estimate the direct costs of cancer in 10 scholarly papers that were considered relevant to our research.

There are several methods employed to determine/estimate the direct costs of cancer:

1. *Prevalence-based approach*: This method calculates the total economic burden of cancer by estimating the direct medical costs, indirect costs (e.g., lost productivity), and intangible costs (e.g., reduced quality of life) associated with all individuals living with cancer during a specific time period, usually a year.
2. *Incidence-based approach*: This method calculates the lifetime costs associated with new cancer cases diagnosed during a specific time period. It tracks the costs from diagnosis until death or the end of the study period.
3. *Cost-of-illness approach*: This approach quantifies the economic impact of cancer by estimating the direct medical costs (e.g., hospitalization, outpatient care, medications), indirect costs (e.g., lost productivity, caregiver time), and intangible costs (e.g., pain, suffering, reduced quality of life).
4. *Budget impact analysis*: These studies estimate the financial consequences of adopting a new cancer intervention or technology by projecting the changes in healthcare resource utilization and associated costs.

5. *Regression-based methods*: Regression models are used to estimate the incremental costs associated with cancer by comparing healthcare costs between individuals with and without cancer, while controlling for other factors.
6. *Claims data analysis:* This approach utilizes administrative claims data from healthcare providers or insurers to quantify the direct medical costs associated with cancer diagnosis and treatment.

The choice of method depends on the research question, available data sources, and the specific objectives of the cost analysis. Many studies employ a combination of these approaches to provide a comprehensive assessment of the economic burden of cancer.

The most frequently used data sources for the assessment of direct costs of cancer in the scholarly literature include:

1. Administrative claims data, such as health insurance claims databases (e.g., Medicare, Medicaid, private insurance), hospital discharge databases, Pharmacy claims databases
2. Cancer registries: National cancer registries, state or regional cancer registries, hospital-based cancer registries
3. Medical records: Electronic medical records (EMRs), hospital financial and billing records
4. Patient-reported data: patient surveys, patient-reported outcomes (PROs)
5. National health expenditure data: national health accounts, government health expenditure reports

The choice of data source depends on the research question, the availability of data, and the level of detail required for the cost analysis. Administrative claims data and cancer registries are commonly used for population-level cost assessments, while medical records and patient-reported data provide more detailed information at the individual level. National health expenditure data can be useful for estimating the overall economic burden of cancer from a societal perspective. To note that researchers often combine multiple data sources to obtain a more comprehensive understanding of the direct costs of cancer, accounting for various components of healthcare resource utilization and associated expenditures.

Table 3. Methods and data sources for the analysis of direct costs of cancer

Paper	Summary	Countries studied and period	Methods Used	Data sources
Voda and Bostan (2018)	- Analyzed healthcare expenditures and cancer care costs across 28 European Union member states - Highlighted disparities in healthcare spending and low cancer care funding - Emphasized the need for increased funding for cancer care development	- 28 European Union member states (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Gemany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, The Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom) - Period of analysis: 2010-2014	- Analysis conducted using SPSS Statistics V20.0 and Stat World Explorer software - Quantitative methods: regression analysis (multinormal and linear) and analysis of variance - Linear models and logistic regression - Sensitivity and cost-effectiveness analysis	- Country-specific data for drug sales from hospitals and retailers - Estimates based on geographical proximity and GDP per capita similarity - Reports, databases, and other sources for healthcare expenditure data - Reports and studies from the Knoema database and World Bank estimates
Torkki et al. (2022)	- Analyzed cancer care costs in Nordic countries from 2012-2017 - Costs increased in all countries, with varying trends in cost components - Medicine costs surged; inpatient care costs varied across countries - Cancer mortality decreased over time	- Nordic countries: Finland, Denmark, Iceland, Norway, Sweden - Period of analysis: 2012-2017	- Bottom-up method was used to evaluate the direct cost of cancer care - Data collected from national registers and published literature	- Published literature - National registers - National medicine sales statistics - Existing studies on cancer and medicine costs - NORDCAN project data
Schlueter et al. (2020)	- Study compares cancer costs to other chronic diseases in Europe - Cancer has high disease burden but low healthcare expenditure - Direct medical costs of cancer decreased over a 10-year period	- Countries: France, Germany, Italy, Spain, United Kingdom - Period of analysis: 2006-2015	- Calculated the prevalence of cancer in the included countries - Determined per patient expenditure on each disease by dividing disease-specific expenditure by disease-specific prevalence for each country - Calculated compound annual growth rates (CAGR) to analyse trends in per patient	- Global Burden of Diseases results tool for prevalence and incidence rates - Global Burden of Diseases, Innjuries, and Risk Factor Study - System of Health Accounts (SHA) by WHO and OECD - Global Health Data Exchange (GHDx)

			cancer drug expenditure and overall direct costs per patient over the study period	- United Nations report 'World Population Prospects' for population age structure (from 2017)
Nguyen et al. (2020)	- Economic burden of infection-related cancers in Korea in 2014 - Direct costs: USD 676.9 million, indirect costs: USD 2.57 billion - Infection-related cancers accounted for 10.7% of all Korean cancer cases - Economic burden was 0.23% of national GDP and 1.36% of healthcare expenditure	- Country: Korea - Period of analysis: 2014	- The study analysed health insurance claims data from NHIS, focusing on selected patients with a special code V193 for severe diseases like cancer - Calculated future income loss, productivity loss, and job loss due to cancer	- NHIS (National Health Insurance Service) data from 2014 used to obtain data on medical care coverage, transportation costs, caregivers costs, and utilization rates - Korea Health Panel Survey from 2014 used to collect information on: caregivers' daily wage and utilization rates - Ministry of Employment and Labour statistics from 2014 used to collect information on: employment rates and average annual wages
Nguyen et al. (2019)	- Economic burden of smoking-related cancers in Korea, 2014 - Direct costs were $595 million, indirect costs were $2.2 billion - Lung, liver, and stomach cancers had the highest economic impact - Job loss accounted for over one-fifth of smoking-associated cancer costs	- Country: Korea - Period of analysis: 2014	- Human capital approach to calculate productivity loss due to premature death, considering potential earnings until the end of average life expectancy - Used NHIS claims data to determine outpatient visits and inpatient admission days, combined with employment rates and wage data to estimate productivity loss - Job loss was assessed by identifying pre-existing and newly diagnosed smoking-attributed cancer cases along with overall job loss	- NHIS (National Health Insurance Service) used to get information on: treatment amounts - KHPS (Korea Health Panel Survey) used to get information on: indirect cost estimation -Statistics Korea used to get information on: cause of death and life tables - Ministry of Employment and Labour used to get information on employment rates and wage data
Lana et al. (2020)	- Analysed federal government expenditures on cancer care in Brazil - Costs per patient ranged from $5782.10 for breast cancer to	- Country: Brazil - Period of analysis: 2001-2015	- Descriptive analysis to report patient characteristics and estimated central tendency and variability measures for costs based on demographic and clinical variables - Historical analysis was conducted to determine	- National Oncological Database, which is a national population-based cohort encompassing all records of patients undergoing oncological treatment within the Brazilian Unified Health System (SUS)

	$16,656 for cervical cancer - Predicted higher costs for male patients, younger age, colorectal cancer - Limitations include lack of data on disease progression and treatment specifics		mean annual costs per patient adjusted by follow-up time, stratified by the year of treatment initiation and cancer type - Multivariate regression analysis using ordinary least squares was performed to analyse the data, considering demographic and clinical variables as predictors of costs - To address the asymmetric distribution of cost data, a power transformation using the Box-Cox model with maximum likelihood approach was applied	- The National Database of Health provided the foundation for the dataset, utilizing record linkage techniques to integrate information from major SUS Information Systems, including the Outpatient Information System (SIA), Hospital Information System (SIH), and Mortality Information System (SIM)
Jonsson (2019)	- The study compares cancer costs to other chronic diseases in Europe - Cancer has high disease burden but low healthcare expenditure - Direct medical costs of cancer decreased over a 10-year period	- Countries: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, United Kingdom - Period of analysis: 2005-2014	- Cost-of-illness framework to estimate the economic burden of cancer, focusing on direct and indirect costs - The study utilizes economic models, statistical analyses, and cost estimation techniques to derive comprehensive and accurate results on the costs of cancer care	- Healthcare expenditure data from national health accounts of various countries
Hofmarcher et al. (2020)	- The total cost of cancer in Europe in 2018 was estimated at 199 billion euros, impacting society significantly - This cost includes direct costs, informal care costs, and productivity loss	- 31 European countries - Period of analysis: 1995-2018	- Eurostat data was used to check on employment rates and earnings - Earnings were utilized to calculate direct costs, informal care costs, and productivity loss - National estimates for 20 countries were obtained directly, while data for the remaining 11 countries were	- OECD (Organization from Economic Co-operation and Development - WHO (World Health Organization) - MIDAS database maintained by IQVIA

			imputed based on geographical proximity and similarity in gross domestic product (GDP) per capita	
Chen et al. (2023)	- Global economic cost of cancers estimated across 204 countries - Study highlights substantial costs and disparities in cancer burden	- -204 countries and territories - Period of analysis: 2020-2025 (with projections)	- The study utilized a health-augmented macroeconomic model to estimate the economic cost of cancer - Data used were publicly accessible and not specifically collected for the analysis, following the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) reporting guideline - Sensitivity analyses were conducted by varying mortality and morbidity rates based on Global Burden of Disease data to assess the robustness of the results	- Global Burden of Disease 2019 - World Bank World Development Indicators database - World Economic Outlook database - Barro and Lee Dataset - Penn World Table
Brenner et al. (2023)	- Cancer impact in Alberta to grow due to population growth - Projections show a significant increase in cancer cases and deaths - Direct cost of cancer management in Alberta to rise by 53%	- Canada, specifically focusing on Alberta (province in Canada) - Period of analysis: 1998-2018	- Utilized age-period-cohort models implemented using Canproj and R software - Studied cancer trends by analysing incidence, prevalence, mortality and survival rates in Alberta	- Alberta Cancer Registry - International Cancer Survival Benchmarking (ICBP) SURVMARK-2 online tool

Table 4. Analysis of direct costs of cancer and limitations

Study	Types of cancers analysed	Analysis of direct costs of cancer	Limitations
Voda and Bostan (2018)	- Prostate cancer, breast cancer in women, lung cancer in men, and colorectal cancer in both men and women	- Direct costs of cancer care vary significantly across European Union countries - High costs associated with anti-cancer drugs	- Lack of targets for value affects new cancer drug development - Disparities in healthcare systems due to economic, cultural, and social factors

		impact healthcare expenditure - Total health expenditures on cancer healthcare services, healthcare expenditures on cancer per capita, and healthcare expenditure on anti-cancer drugs	
Torkki et al. (2022)	- ICD-10 codes C00-C97 - Specific cancer diagnoses were not mentioned in the provided context	- Direct costs of cancer include primary care, secondary care, and medicines - Treatment costs were evaluated using a bottom-up method	- Limited data sharing across countries hinders comprehensive analysis - Time-consuming process to obtain cost data per diagnosis - Difficulty in allocating medicine costs for each cancer diagnosis
Schlueter et al. (2020)	- All cancers, no specific types mentioned	- Cancer costs decreased per patient over 10 years -Cancer had the second-lowest healthcare expenditure among major chronic diseases - Cancer was associated with the highest disease burden - Cancer costs accounted for a low proportion of total healthcare expenditure	- Lack of comprehensive data on overall expenditure for major disease areas - Data quality variations across European countries impact findings
Nguyen et al. (2020)	- Kaposi's sarcoma, Hodgkin's sarcoma, non-Hodgkin's lymphoma, non-cardia gastric cancer, hepatocellular carcinoma, cholangiocarcinoma, Burkitt's lymphoma, and mucosa-associated lymphoid tissue gastric lymphoma	- -Direct costs include medical and non-medical expenses during treatment - Non-covered medical costs were estimated at 19.9% of total direct costs	- Study may have underestimated cancer costs attributed to infection - Outpatient pharmaceutical costs and alternative medicine costs were excluded
Nguyen et al. (2019)	- Cancers of the oral cavity, pharynx, oesophagus, stomach, colorectum, liver, pancreas, larynx, lung, cervix uteri, ovary, kidney, and bladder	- -Direct costs of cancer include both medical and non-medical expenses	- Low incidence cancers like ureter and myeloid leukaemia not included - Outpatient pharmaceutical costs and certain item cost estimations are not verifiable in NHIS data
Lana et al. (2020)	- Breast cancer, prostate cancer, colorectal cancer, cervix cancer, lung cancer, and stomach cancer	- Expenses related to chemotherapy, radiotherapy, surgeries and so on	- Exclusion of patients treated in the private sector from the study - Costs assessed represent federal government only, not total cancer treatment costs - Lack of data on disease progression and palliative care procedures

			- Inability to evaluate post-treatment costs and adverse treatment effects
Jonsson (2019)	- Breast cancer, lung cancer, colorectal cancer, and other prevalent forms	- Direct costs are broken down into categories such as screening, ambulatory care, inpatient care, and drugs for a detailed analysis	- Lack of systematic recording and reporting on accounting costs for cancer - Variability in estimates of healthcare expenditures related to cancer - Uncertainty in indirect costs due to morbidity for cancer
Hofmarcher et al. (2020)	- All neoplasms (ICD-10 C00-D48)	- Highlighted differences in direct costs across regions in Europe - The study estimated the direct costs of cancer in Europe in 2018 at 103 billion euros, which accounted for 6.2% of the total health expenditure	- Lack of disease-specific health expenditure data from public authorities in some countries, leading to reliance on cost-of-illness studies which may underestimate healthcare expenditure - The estimates of cancer drug expenditure were considered overestimated due to sales data not reflecting actual final sales prices because of confidential rebates - The costs of certain therapeutic radiopharmaceuticals and supportive medications used in cancer treatment were not included in the analysis, potentially impacting the overall cost estimation
Chen et al. (2023)	- 29 different types of cancers were analysed (for example: tracheal, bronchus, lung cancer, colon and rectum cancer, breast cancer, liver cancer, leukaemia)	- The study estimated the direct medical costs for each cancer type based on treatment expenses obtained from previous research	- Relied on imputations or projections for calculating various data points, potentially introducing uncertainties - Did not consider changes in labour force participation of family members providing informal care for cancer patients, which could underestimate economic costs - The model did not include unemployment or explicitly address price movements and endogenous savings, indicating areas for further refinement
Brenner et al. (2023)	- Breast, lung, prostate, colorectal, bladder, melanoma, lymphoma, kidney, thyroid, and uterus cancer	- Studied costs across four phases: diagnosis, initial treatment, continuing care, and terminal phase - Continuing care is expected to have the largest cost increase, followed by initial treatment, with	- Relies on historical data that may not fully capture future trends accurately - Projections based on assumptions that may not hold in the real world - Data limitations include lack of information on sexual orientation and gender

		haematological cancer having the highest direct costs	

4. Direct Costs as Healthcare Expenditure and Out-of-pocket expenses

Health statistics provide crucial insights into the well-being of populations, guiding policy decisions and resource allocation. By examining data from diverse sources such as the Global Health Observatory (GHO), ECHI Data Tool, Healthcare Expenditure Statistics from EU member states, and the Peterson Centre on Healthcare in corroboration with Cancer Registries such as European Network of Cancer Registries one can explore how investments in healthcare correlate with health outcomes, the efficiency of spending in various healthcare systems, and how economic factors influence healthcare budgets.

Universal access to quality healthcare at an affordable cost is one of the core values of EU health system and is regarded as a basic need. However both public and private expenditure on healthcare varies significantly across EU Member States. Starting from an bird-eye view, like health expenditure as percentage of GDP, or health expenditure per capita, policymakers can see a more clearer picture and can optimize data-driven policy decisions on healthcare delivery together with fiscal sustainability.

Table 5 provides a similar analysis of healthcare expenditure by financing scheme, but with more detail concerning other financing schemes.

The third largest source of healthcare funding was generally household out-of-pocket payments. In 2020, the share of out-of-pocket payments accounted for more than one-third of total healthcare expenditure in Bulgaria (35.5 %), Malta (34.1 %, 2019 data) and Greece (33.4 %). The Netherlands, France and Luxembourg were the only EU Member States where household out-of-pocket payments accounted for less than one-tenth of healthcare expenditure, with shares of 9.3 %, 8.9 % and 8.4 %, respectively.

Table 5. Current healthcare expenditures, analysed by source of financing (2020, % if current healthcare expenditure)

	Government schemes	Compulsory contributory health insurance schemes & compulsory medical saving accounts	Voluntary health insurance schemes	Financing schemes of non-profit institutions serving households	Enterprise financing schemes	Household out-of-pocket payments	Rest of the world (non-resident)
EU (')	:	:	:	:	:	14.4	:
Belgium	24.5	54.7	4.8	0.0	:	16.0	0.0
Bulgaria	17.5	45.6	0.6	0.5	0.3	35.5	0.0
Czechia	17.5	70.2	0.1	0.4	0.3	11.5	:
Denmark	84.9	0.0	2.2	0.1	:	12.8	0.0
Germany	9.0	76.1	1.3	0.8	0.4	12.4	0.0
Estonia	9.1	68.1	0.2	0.2	1.1	21.4	0.0
Ireland	78.3	0.5	9.0	:	1.7	10.5	:
Greece	28.2	33.7	4.3	0.1	0.1	33.4	0.2
Spain	69.5	3.7	6.7	0.4	:	19.6	:
France	6.2	78.5	5.8	0.0	0.6	8.9	:
Croatia	8.7	75.5	5.3	0.0	0.0	10.5	0.0
Italy	75.9	0.2	2.0	0.2	0.4	21.3	:
Cyprus	34.9	43.2	6.3	1.6	0.0	14.0	:
Latvia	63.6	:	4.3	0.2	0.0	31.9	:
Lithuania	10.4	59.7	1.1	0.0	0.1	28.7	0.0
Luxembourg	7.1	79.3	2.9	1.0	0.0	8.4	1.2
Hungary	11.8	59.6	1.6	1.1	0.4	25.5	0.0
Malta (')	62.5	0.0	3.4	:	:	34.1	0.0
Netherlands	10.5	74.4	4.3	0.0	1.5	9.3	0.0
Austria	33.4	43.1	4.9	1.6	0.2	16.8	0.0
Poland (²)	9.8	62.4	5.9	1.5	0.8	19.5	0.0
Portugal	62.1	2.4	6.8	0.1	0.8	27.8	:
Romania	17.5	62.7	0.5	0.2	0.1	19.0	:
Slovenia	9.1	64.1	13.4	0.1	0.9	12.5	:
Slovakia	4.5	75.7	:	0.8	0.2	18.8	:
Finland	65.5	13.6	1.9	0.4	2.2	16.4	:
Sweden	85.9	0.0	0.6	0.1	0.4	13.0	:
Iceland	83.3	0.0	0.0	1.7	0.0	15.0	:
Liechtenstein	18.7	48.8	12.4	0.2	0.5	19.4	0.0
Norway (')	85.8	0.0	0.0	0.0	0.3	13.9	0.0
Switzerland	25.6	44.1	6.5	0.9	0.9	22.0	0.0
Bosnia and Herzegovina	4.5	66.2	0.3	0.0	0.0	28.9	0.1

(') Estimate.
(²) Provisional.
Source: Eurostat (online data code: hlth_sha11_hf)

eurostat

Direct costs for cancer include all medical expenditures related to the diagnosis, treatment, and care of cancer. These costs cover:

- Hospital and clinic visits
- Costs of chemotherapy, radiation therapy, and other medications
- Diagnostic tests like MRIs and CT scans
- Surgical procedures
- Outpatient care

These expenses are the actual payments made to healthcare providers and for medications required for cancer treatment.

There is a very large variation in how each country represents in official records and statistical databases the direct costs of cancer. Some countries do not even have an overall representation, making the analysis of cost-effectiveness even harder to grasp. Not even in the EU, despite statistical homogenization efforts, there is not a unitary representation of the direct costs of cancer across member states (IHE Report 2019). According to the IHE Report 2019, there are multiple data sources for each country with differing methodologies of estimation of overall direct costs of cancer. Some studies include such expenditure categories as: hospitalization, ambulatory care, chemotherapy, radiotherapy, medical

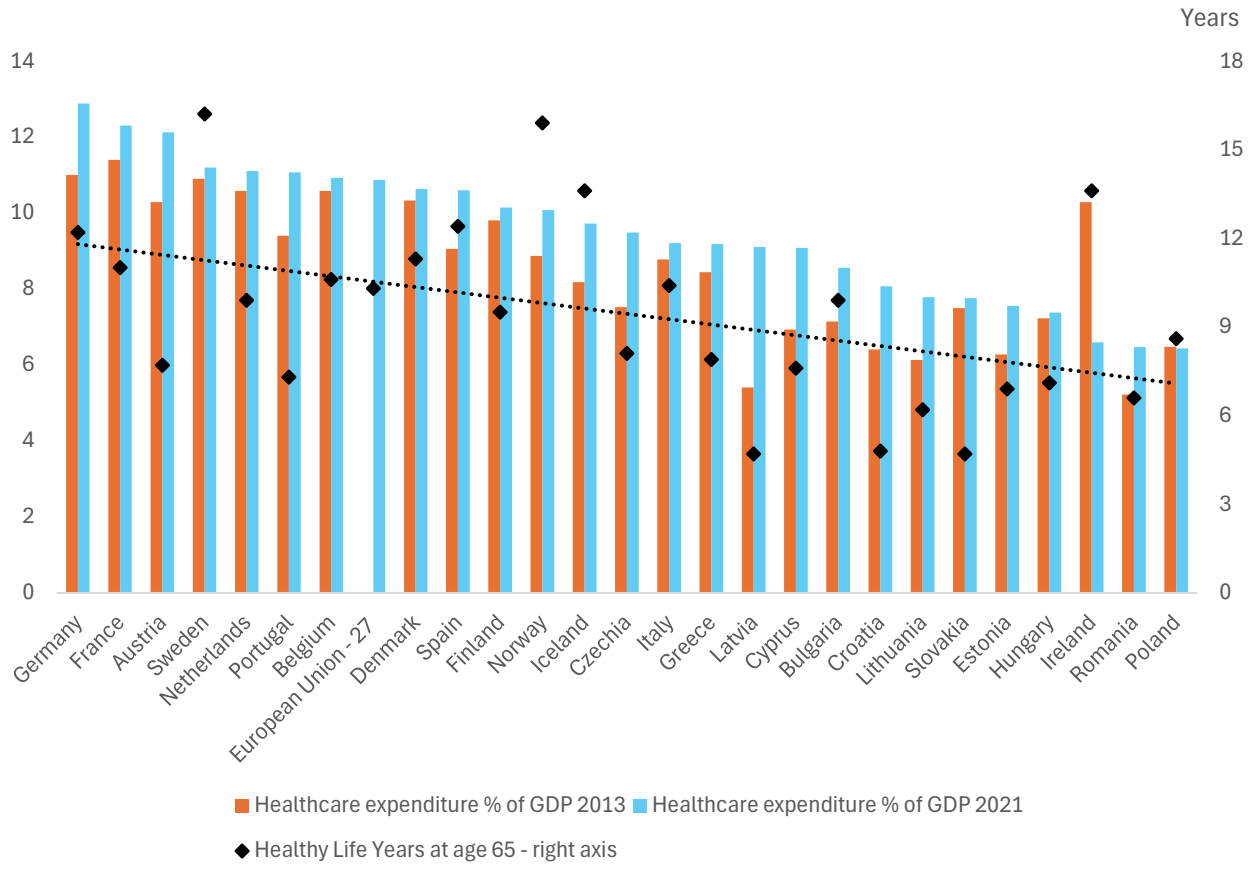
consultations, and medicine, while screening and primary prevention are not included (e.g. Portugal). Others include expenditure on: inpatient care, specialized outpatient care, cancer medicines, as well as screening, primary care, palliative care, and other services (e.g. Sweden).

Indirect costs involve losses not directly billed by healthcare but nevertheless impact the economy and the patient's financial situation. These costs include:

- Lost productivity due to absence from work or reduced ability to work
- Loss of income due to disability or death
- Travel and accommodation expenses for treatment at distant facilities
- Informal care costs, which may include expenses related to family or friends providing care without compensation

The distinction between direct and indirect costs is significant in understanding the total economic burden of cancer on individuals and society. These costs reflect not only the significant healthcare expenses associated with cancer treatment but also the broader economic impacts such as lost productivity and personal financial stress, which can be substantial.

Figure 13. Healthcare expenditure % of GDP and healthy life years at 65



Source: Eurostat and European Core Health Indicators data tool

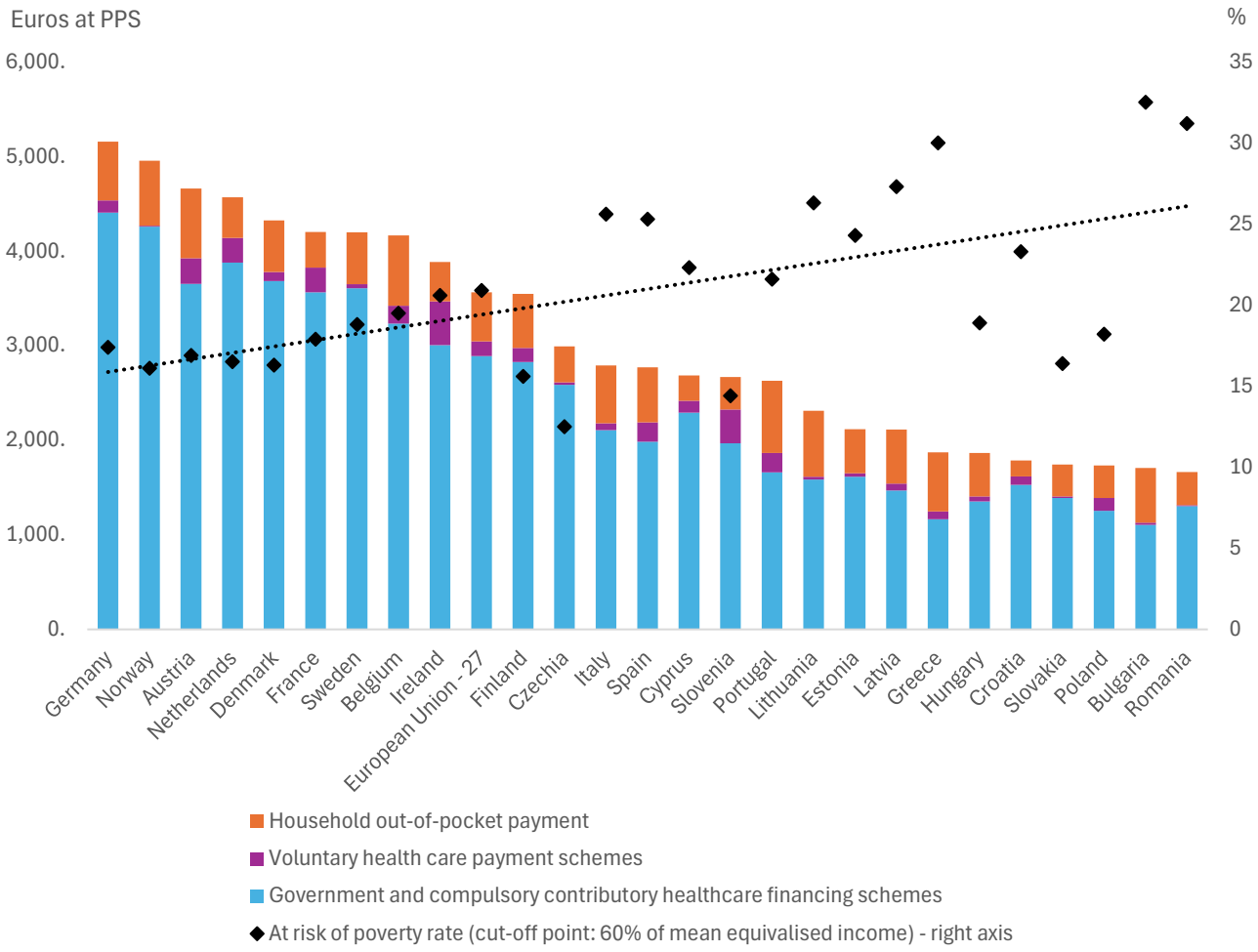
*Last data available for Healthy Life Years at age of 65 is from 2019.

The most noticeable aspect of the figure above is that healthcare expenditure as a percentage of GDP has increased in all EU Member states. There is only one exception, that is Ireland, but the relative decrease as a per of GDP is the fact that GDP has increased at a very high pace given the fact that Ireland is home to many tech giants.

The main reason behind this increase is the aging population that requires more health services and medications, in combination with the fact that the population is becoming more aware of the benefits brought by investments in health, thus putting pressure on policy makers.

And another important and relevant aspect is the number of healthy years that a person is expecting to live after retirement, that is generally at 65 in EU Member states. Even if a state's health expenditures are not the only factor that influences the hope of a healthy life in retirement, the level of pollution, the general level of stress of the population, as well as the eating habits and the attitude towards sports are also very important, the state's expenditure on health probably plays one of the most important roles in determining healthy life expectancy. It can be seen from the previous figure that there is a correlation between the size of these expenses and the number of healthy years that a person who has reached the age of 65 can hope for.

Figure 14. Structure of Healthcare financing schemes and population at risk of poverty



Source: Eurostat and European Core Health Indicators data tool

It is quite clear that the majority of healthcare is provided by public funds, either government schemes or compulsory contributory healthcare financing schemes, as it can also be observed that wealthier states allocate more funds for medical care. Although there are many types of voluntary medical insurance, they are very little used in most states and have a low share in the total healthcare financing schemes, although in some states such as Romania or Bulgaria this type of instrument is almost non-existent or insignificantly used.

Moreover, in addition to the fact that voluntary medical insurance is not used in these two previously mentioned states, out of pocket expenses have a significant role in the total medical expenses per capita, approximately 21% in Romania and 34% in Bulgaria. If we correlate this aspect with the rates of at risk of poverty (which is also an indicator that shows us the inequalities in a society), which are the highest in Romania and Bulgaria, we can draw the conclusion that it is very difficult for a person from these two states to manage to cover the necessary medical expenses from out-of-pocket money.

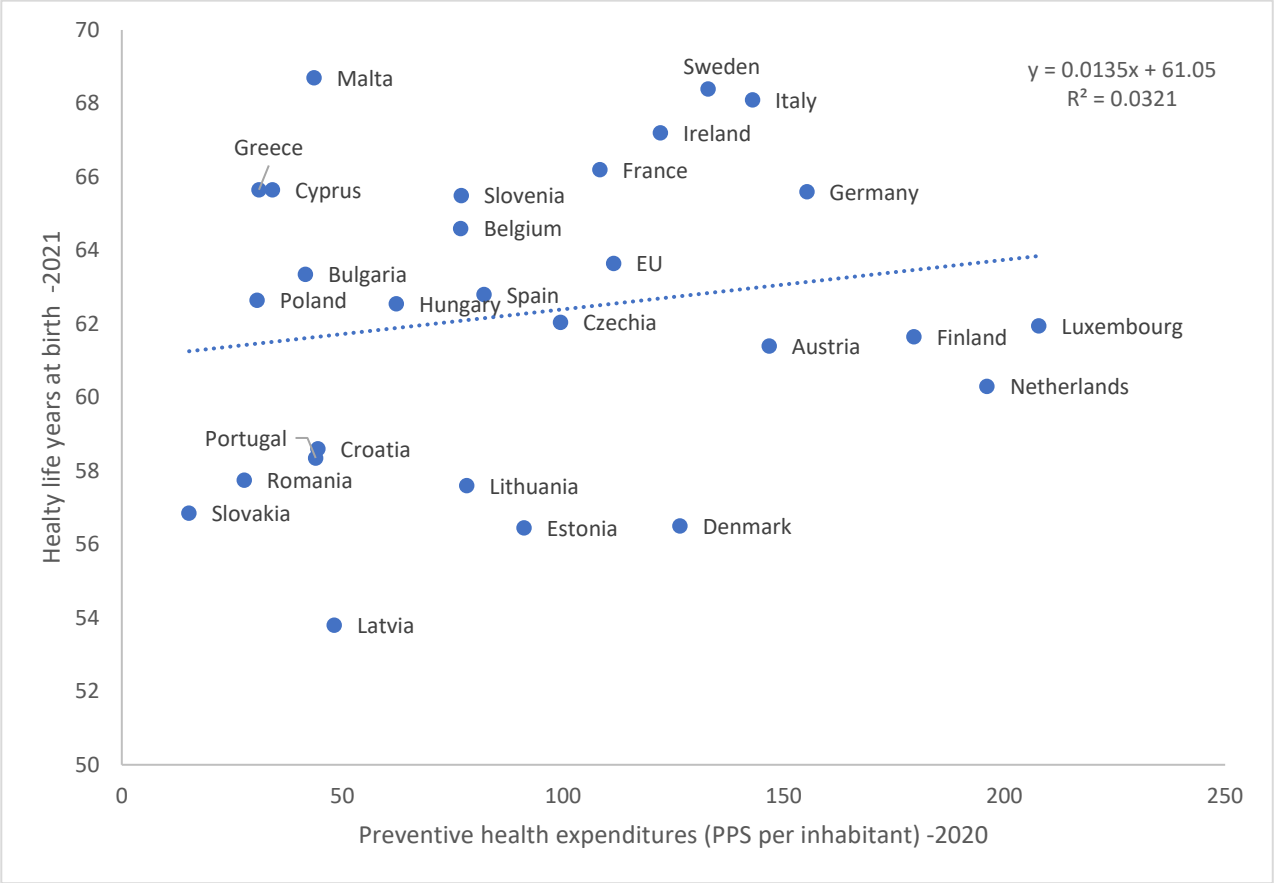
Further, in this section, we present some empirical evidence from EU Member states regarding the health sector – inputs, risk factors and outputs related to cancer patients.

The Figures below show the correlation between preventive healthcare expenditures and healthy life years both at birth and after 65 years across EU countries. Preventive Healthcare Expenditures are considered at PPS Per Inhabitant (2021 data). The adjustment for purchasing power standards (PPS) makes it possible to compare different countries' expenditures directly by eliminating differences in price levels.

Data shows that there is a large variation between countries in terms of expenditures, from 208 PPS in Luxembourg to 15 PPS in Slovakia, but also in terms of healthy life years at birth and after 65 years. For example, Austria spends 146.7 PPS on preventive healthcare per inhabitant and has an expectancy of 63.60 healthy life years at birth. In contrast, Romania spends 27.8 PPS per inhabitant on preventive healthcare and has a lower expectancy of healthy life years at 57.75.

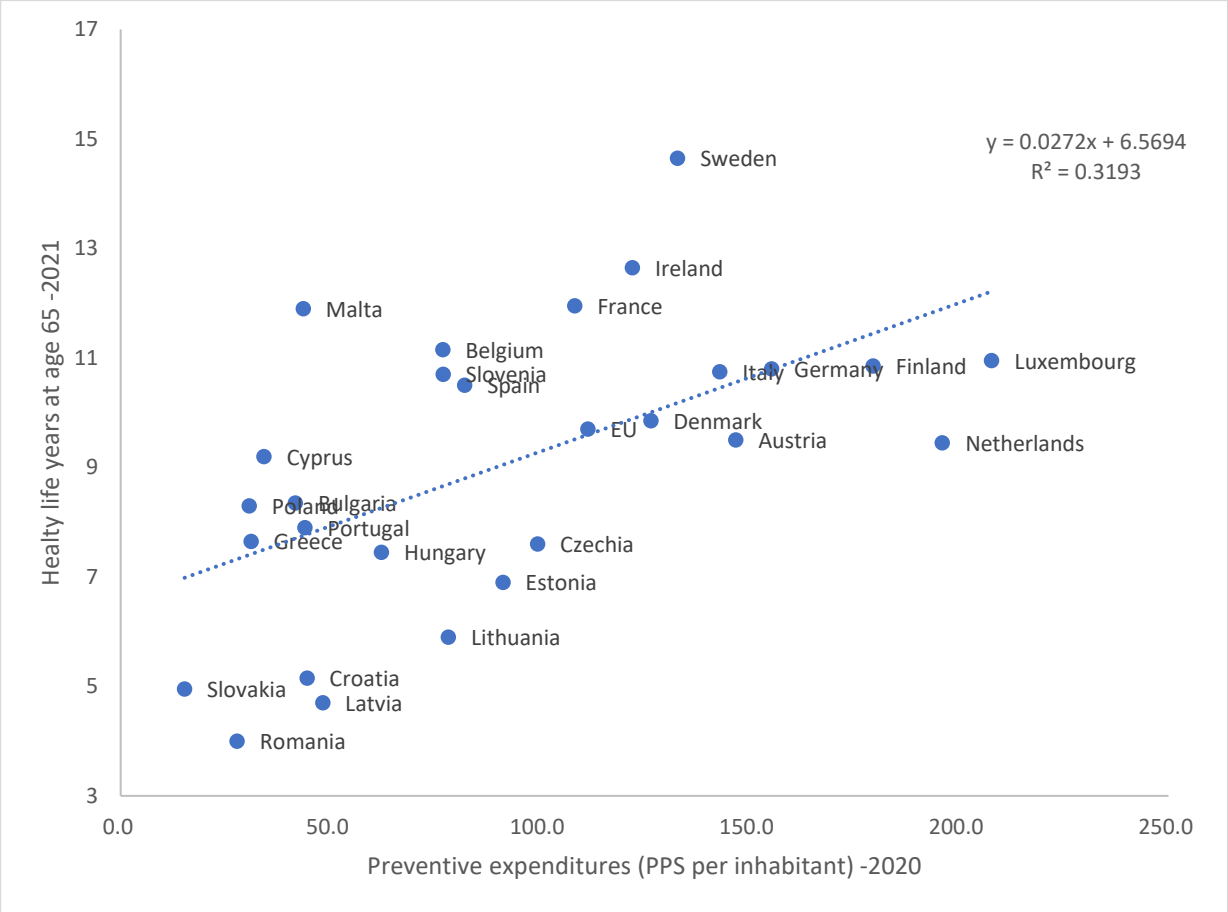
However, even that this variation isn't so clear when is linked with the Healthy life years at birth, there is a stronger relationship between the healthcare expenditure with prevention and Healthy life years after 65 years (R-squared coefficient close to 31%), which enforce the hypothesis that usually, the effects of healthcare prevention have a long- and very long-term impact, especially after a threshold.

Figure 15. Correlation between healthy life years at birth and the preventive healthcare expenditures in EU Member States



Source: authors' compilation on Eurostat data

Figure 16. Correlation between healthy life years after 65 years and the preventive healthcare expenditures in EU Member States



Source: authors' compilation on Eurostat data

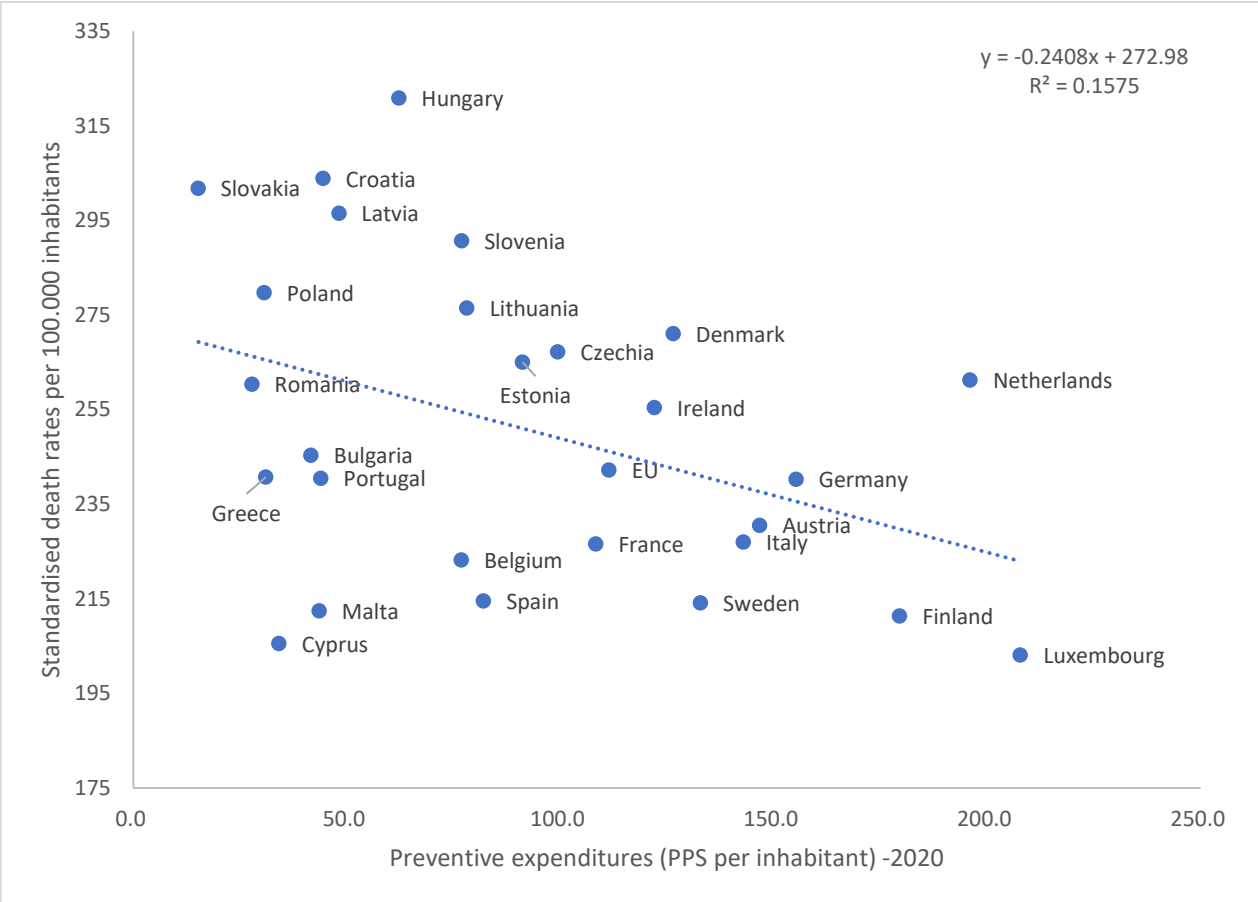
In terms of differences, there are several studies that explore differences in preventive healthcare expenditures and healthy life years (HLY) among EU countries, focusing on various explanatory factors, from healthcare expenditures and infrastructure across EU countries, to individual economic status and educational level (primary school, secondary or tertiary), and general regional economic development disparities or labor market performances. See for example, Jagger et al., (2008) which show that HLYs range significantly more than life expectancies. Factors such as GDP and expenditure on elderly care were positively associated with higher HLYs, while long-term unemployment was negatively associated, particularly in men. The study suggests that improving population health is crucial for increasing older people's participation in the labor force across all EU countries (Jagger et al., 2008). Also, based on a difference-in-difference (DiD) analysis and data envelopment analysis (DEA), Jakovljevic et al. (2016) found that countries that joined the EU in 2004 showed significant health expenditure growth and longevity increase, suggesting a strong performance in balancing these aspects compared to other sub-regions

Additionally, a comparative study across eight European countries highlighted the impact of education on disability-free life expectancy. There were significant educational differences in disability-free life expectancy in all countries, with highly educated individuals expected to live longer and healthier lives.

This variance was more pronounced in certain countries, illustrating how education levels can influence health outcomes (Mäki et al., 2013). Another study, Albulescu (2022) analysed the health expenditures in the European Union countries. The paper assessed the convergence process in health care expenditure across selected EU countries over 50 years. It analyzed public and private health expenditures, revealing mixed findings on convergence and highlighting the heterogeneity of health care systems across the EU. The study emphasizes the need for common solutions to enhance the convergence processes in EU health care systems.

For cancer, the graph below plots the relationship between preventive health expenditures per inhabitant (in purchasing power standards, PPS) and standardized death rates per 100,000 inhabitants caused by malignant neoplasms (cancer) in 2020 across EU member states. The trend line indicates a negative correlation between these variables, respectively a higher preventive health expenditures per inhabitant are associated with lower standardized death rates from malignant neoplasms (negative correlation coefficient of -0.24).

Figure 17. Relationship between preventive health expenditures per inhabitant and standardized death rates across EU member states



Source: authors' compilation on Eurostat data

Moreover, R-squared value is 0.16. That's mean that 16% of the variation in death rates from malignant neoplasms across EU states can be explained by differences in preventive health spending. This is a relatively low value, suggesting that other factors not captured in this graph also play significant roles in influencing cancer mortality rates

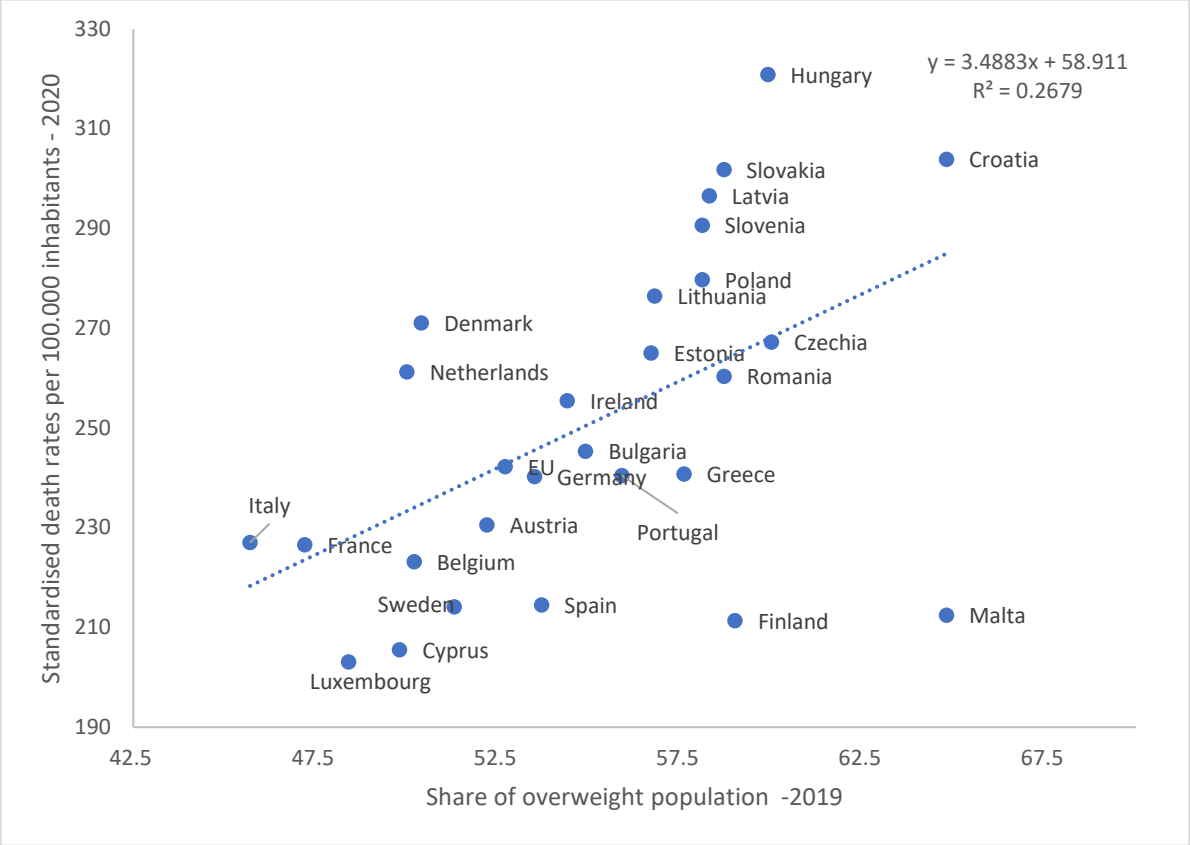
(aspects of healthcare quality, access to treatment, environmental factors, and lifestyle differences among populations).

A large body of studies collectively underline that while preventive healthcare spending is crucial, a comprehensive understanding of cancer mortality rates must also consider broader social, environmental, and lifestyle factors. These elements play a critical role in shaping the health outcomes of populations, suggesting that interventions need to address these diverse determinants.

For example, a study by Belpomme et al. (2007) highlights the significant role of environmental carcinogens, including air pollution, chemicals, and electromagnetic fields, which may contribute to the rising incidence of cancer alongside traditional lifestyle factors. Also, analysing socio-environmental patterns and cancer mortality, Pou et al. (2018) emphasized the interplay of quality of life, urban-related resources, and environmental exposures with cancer outcomes, while Weiderpass (2010) discussed how major behavioral and environmental risk factors, such as diet, physical inactivity, and exposure to pollutants, contribute significantly to global cancer mortality, with a notable impact of modifiable lifestyle choices (see also Coughlin and Smith, 2015 on the role of diet, obesity, and chemical exposures).

In the next paragraphs we analysed some of these factors that are available from the Eurostat database related to tobacco consumption, tobacco exposure and obesity. The scatter plot below shows the relationship between the share of the overweight population in 2019 and the standardized death rates from malignant neoplasms (cancer) per 100,000 inhabitants in 2020 across EU member states. The plotted trend line suggests a positive correlation between the share of the overweight population and the cancer death rates, while the R-squared coefficient indicates that approximately 26.79% of the variation in the cancer death rates across the EU member states can be explained by the variation in the percentage of the overweight population.

Figure 18. Share of the overweight population in 2019 and the standardized death rates

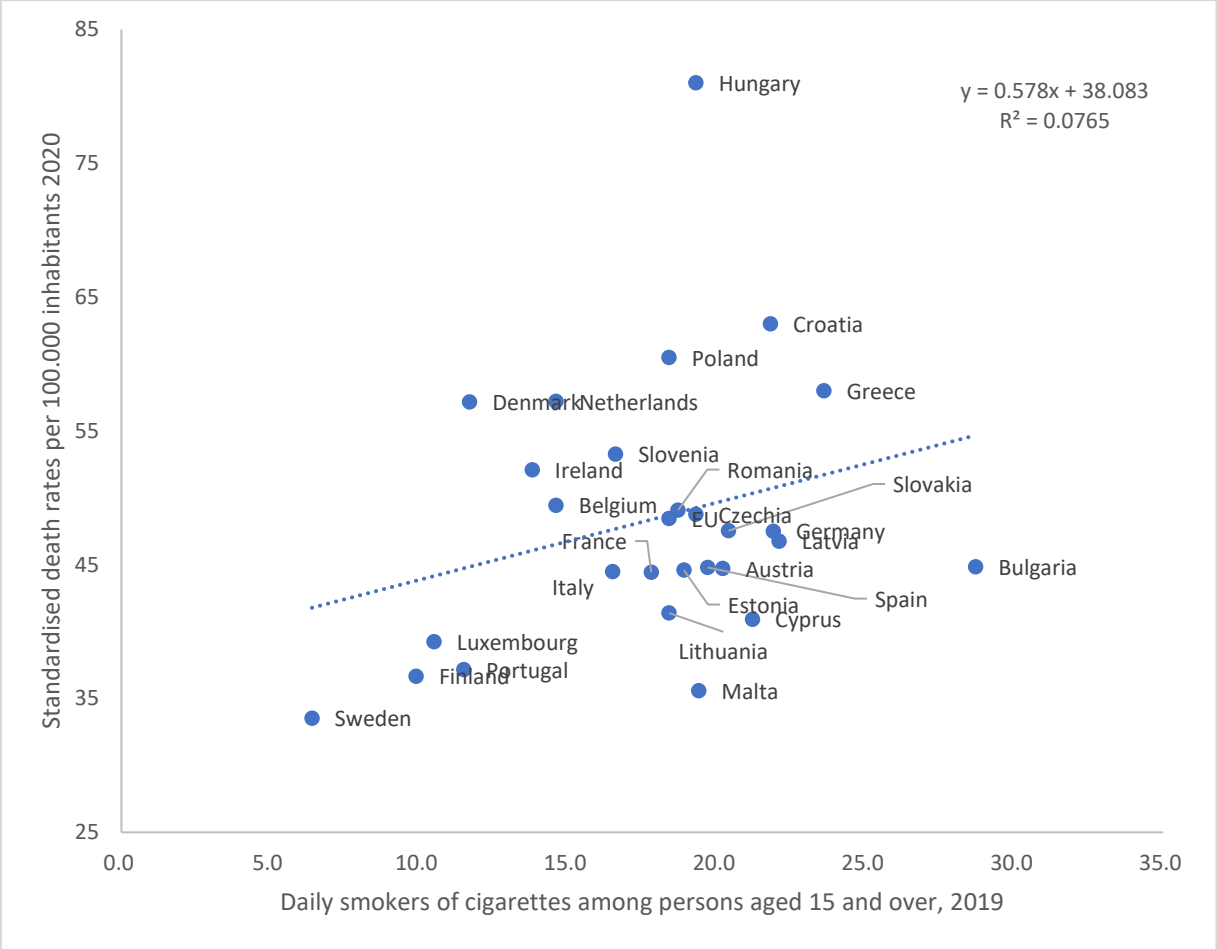


Source: authors' compilation on Eurostat data

Figure below highlight the relationship between the daily smoking rates among persons aged 15 and over in 2019 and the standardized death rates from malignant neoplasms of the trachea, bronchus, and lung per 100,000 inhabitants in 2020 across various EU member states.

The graph highlights a positive but relatively weak association between smoking rates and lung cancer mortality among EU member states. Also, there is a weak link between the daily exposure to tobacco smoke indoors (at least one hour per day) and the death rates. The low R^2 value implies that other factors play a more significant role in influencing lung cancer mortality rates than smoking alone, as also was the case for obesity.

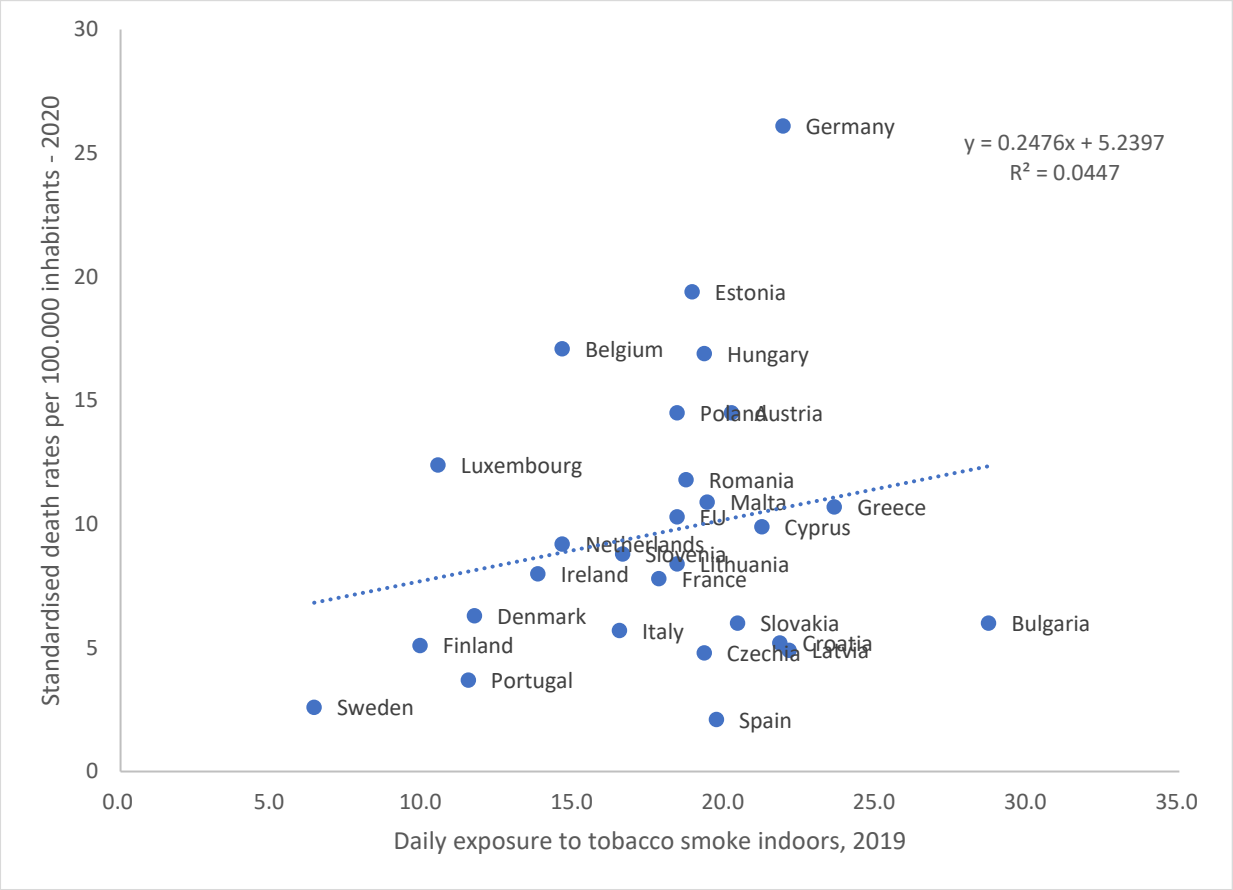
Figure 19. Smoking rates and the standardized death rates from malignant neoplasms of the trachea, bronchus, and lung



Source: authors' compilation on Eurostat data

Note: Data for Belgium and Netherlands are for 2014

Figure 20. Tobacco smoke exposure indoors and the standardized death rates from malignant neoplasms of the trachea, bronchus, and lung



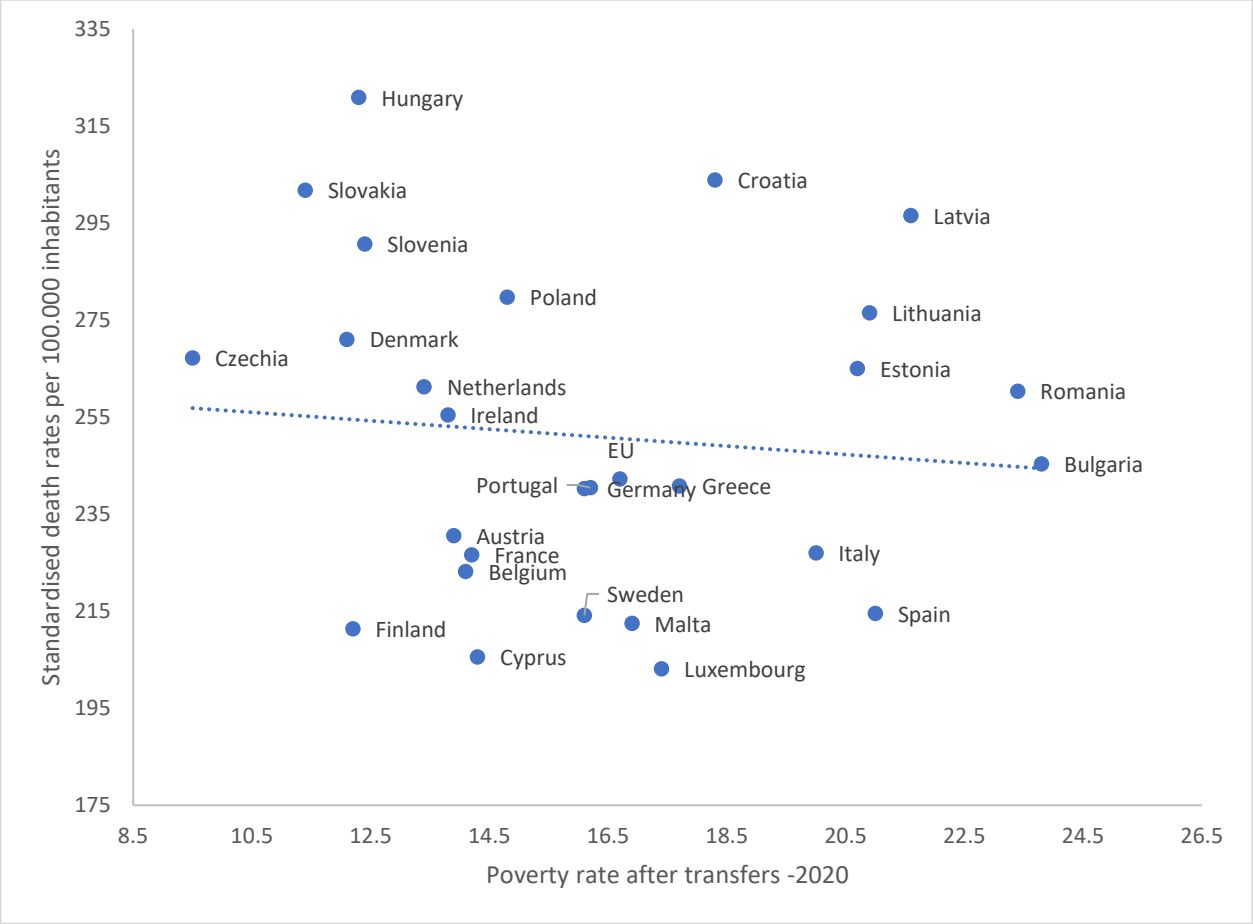
Source: authors' compilation on Eurostat data

Note: Data for Belgium and Netherlands are for 2014

The last perspective of the cancer mortality is by socio-economic factors, respectively poverty rates among EU Member States. Several studies provide insights into how income and living conditions, particularly poverty rates, can significantly influence cancer mortality rates. The social, structural, and behavioral challenges associated with persistent poverty contribute to higher vulnerability to cancer (Moss et al., 2020), while individuals in high-poverty areas are more likely to be diagnosed with cancer at a distant stage, which leads to higher mortality rates.

This is partly due to disparities in access to cancer screening and early detection services (Boscoe et al., 2016). Ward et al. (2004) shows that factors contributing to these disparities include lower access to healthcare, higher prevalence of risk factors such as tobacco use, and inadequate screening. Moreover, as poverty is generally associated with social exclusion, this independently increases the risk of cancer mortality as there is a lack of community and social support in mitigating cancer risks (Marcus et al., 2017).

Figure 21. Death rates and poverty correlation in Europe



Source: authors' compilation on Eurostat data

Note: Data for Belgium and Netherlands are for 2014

Cancer Risk Factors Index

In this section we develop a comprehensive index for evaluating the impact of cancer risk factors at the national level in EU countries. Thus, we created a "Cancer Risk Factors Index" (CRFI) to understand the relative importance of different cancer risk factors at the national level and guide targeted interventions for cancer prevention in EU countries.

Based on the literature review and cancer reports this index will consider several categories of factors: obesity, alcohol and tobacco use, physical activity, pollution, socio-economic conditions, and diet. These categories of factors and considered indicators are detailed in Table 6 below.

Table 6. Cancer Risk Factors Index (CRFI)– Data Sources

Category	Sub-Factor	Description (Eurostat code)	Impact on Cancer (References)
1. Obesity tendency (OB)	OB2: Prevalence of Overweight	Percentage of adults (18+) with a BMI between 25 and 29.9 [hlth_ehis_bm1e__custom_11172597]	Overweight status increases cancer risk, but to a lesser degree than obesity (Bhaskaran et al., 2014)
2. Alcohol and Tobacco Use (AT)	AT1: Alcohol Consumption	Frequency of heavy episodic drinking (weekly) [hlth_ehis_al3e$defaultview]	Alcohol consumption is strongly linked to liver, colorectal, and breast cancers (LoConte et al., 2018)
	AT2: Tobacco Smoking Prevalence	Percentage of adults (15+) who are daily smokers [hlth_ehis_sk3e__custom_11140379]	Smoking is a leading cause of lung cancer and is linked to other cancers (IARC, 2012)
	AT3: Daily exposure to smoking	Daily exposure to tobacco smoke indoors – At least 1 hour per day [hlth_ehis_sk4e__custom_11140189]	Declining smoking rates are correlated with lower lung cancer mortality (Jemal et al., 2018)
3. Sports Activity (SA)	SA1: Physical Activity	Percentage of adults performing health-enhancing physical activity [hlth_ehis_pe9e__custom_11172934]	Regular physical activity reduces the risk of colon, breast, and endometrial

			cancers (Moore et al., 2016) Sedentary behavior is linked to higher risks of colorectal, endometrial, and lung cancers (Schmid & Leitzmann, 2014) Increasing physical activity rates are associated with reduced cancer risk (de Rezende et al., 2018)
4. Socio-Economic Conditions (SEC)	SEC1: At risk of poverty rate	Percentage of the population living below the poverty line (cut-off point: 60% of median equivalized income after social transfers) [tessi010__custom_11140589]	Poverty is associated with higher cancer mortality due to limited access to healthcare and late diagnosis (Moss et al., 2020)
	SEC2: Education Level	Percentage of adults with higher education Tertiary educational attainment [sdg_04_20__custom_11182781]	Higher education levels are linked to better health behaviors and lower cancer risk (Ward et al., 2004)
	SEC3: Preventive healthcare expenditures	Preventive healthcare expenditure in PPS per inhabitant [hlth_sha11_hc]	Access to healthcare ensures early detection and treatment, reducing mortality (Singh & Jemal, 2017)
5. Pollution (POL)	POL1: Greenhouse emissions	Net greenhouse gas emissions - Tonnes per capita [sdg_13_10__custom_11182667]	Air pollution is linked to lung cancer and other respiratory tract cancers (Loomis et al., 2013)

Source: authors based on the literature review

Based on Eurostat data for the most recent period (2019, 2020, 2021 or 2022) we calculated the CRFI. To normalize the sub-factors effectively we use the Min-Max normalization method. It scales each value to a range between 0 and 100. This method is straightforward and maintains the distribution's relationships, making it suitable for comparison across different sub-factors.

We chose the Min-Max normalization method because it makes different sub-factors directly comparable on the same scale, ensures all sub-factors contribute evenly to the index and makes it easier to interpret normalized scores ranging from 0 to 100.

Thus, to normalize using Min-Max Method we calculated for each sub-factor the minimum (min) and maximum (max) values across all countries, then we applied the following formula to each country's sub-factor value:

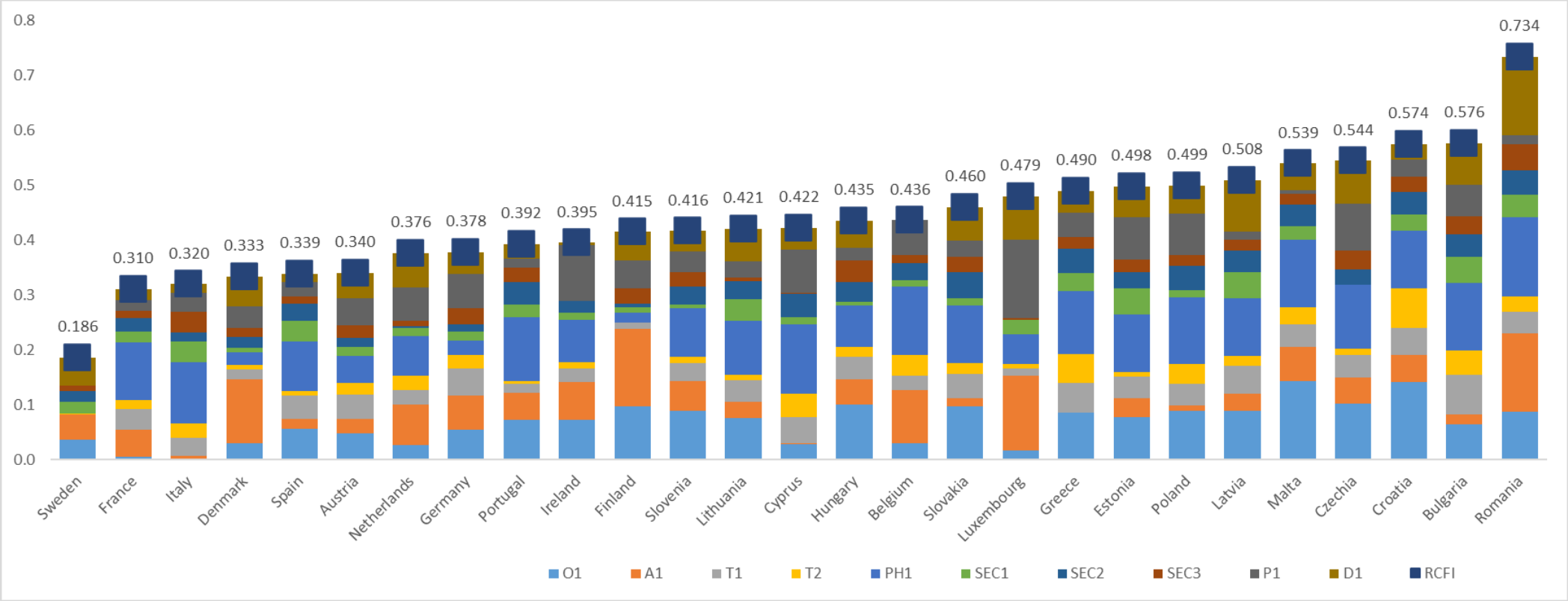
$$Normalized\ value\ = \frac{Actual\ value\ -\ Min\ value}{Max\ value\ -\ Min\ value}\ *\ 100$$

This formula scales the values to a range of 0 to 100, where 0 corresponds to the minimum observed value and 100 to the maximum. A normalized score closer to 100 indicates a higher impact of that sub-factor on cancer risk (depending on whether the sub-factor is positively or negatively correlated with risk). If a sub-factor is inversely related to cancer risk (e.g., education level), we reversed the scale by subtracting the normalized value from 100 to interpret the risk correctly.

For the aggregated score we multiplied the normalized sub-factor scores by their weights and summed the results. However, in this case we considered every category the same weight, so it was equivalent to an arithmetic average of values for each category. After determining the aggregate scores for each country, we rank countries based on RCFI, where a higher score indicates a greater overall impact of cancer risk factors.

The aggregated index for EU Member States reflects some important aspects based on the values of the subfactors (see Figure 22 below)[1].

Figure 22. Cancer Risk Factor Index (CRFI) results



Source: own calculations

[1] The codes for every subfactor are Share of overweight persons (O1), Excessive drink habits (A1), Tobacco smoking prevalence (T1), Exposure to smoking (T2), Sedentary behavior (PH1), Poverty rate (SEC1), Preventive expenditures (SEC2), Education level (SEC3), Emissions per capita (P1), Fruits and vegetables consumption (D1).

Further, to demonstrate the validity of the index we correlated the RCF values for EU Member States with two important aspects of the disease and general healthcare issue: Cancer mortality (ASR [2]per 100.000 persons – data from WCFR.org) and healthcare expenditures from all the sources excluding out-of-pocket money from the patient households. The first indicator is correlated with the effect of cancer disease, while the second indicator is correlated with the general (private and public) effort to reduce the risk factors.

The scatter plot below displays the relationship between the values of composite Risk Cancer Factor (RCF) Index and cancer mortality rates in European Union (EU) Member States. The x-axis represents the RCF Index, which measures the combined impact of various risk factors associated with cancer. The y-axis represents cancer mortality rates. There is a positive relationship between the two variables. Romania, Hungary, and Slovakia are examples of countries with both high RCF Index values and cancer mortality rates, while Sweden, Luxembourg and Finland exhibit low RCF Index values and cancer mortality rates.

However, there we can identify Malta as an outlier with a significantly low cancer mortality rate compared to its RCF Index value. Efficient screening programs, advanced treatments, and accessibility to healthcare could mitigate the impact of risk factors on mortality rates. At the same time, many countries are clustered in the middle range for both RCF Index and cancer mortality rates, including France, Ireland, Germany, and Austria.

Also, countries with effective public health campaigns promoting healthy lifestyles and cancer prevention strategies may have lower mortality rates. These measures could include anti-smoking campaigns, vaccination programs, or healthy diet promotions.

Lifestyle differences such as diet, exercise, smoking rates, and alcohol consumption could vary significantly between countries. Socioeconomic status, which affects access to healthcare and healthy lifestyle options, also plays a significant role.

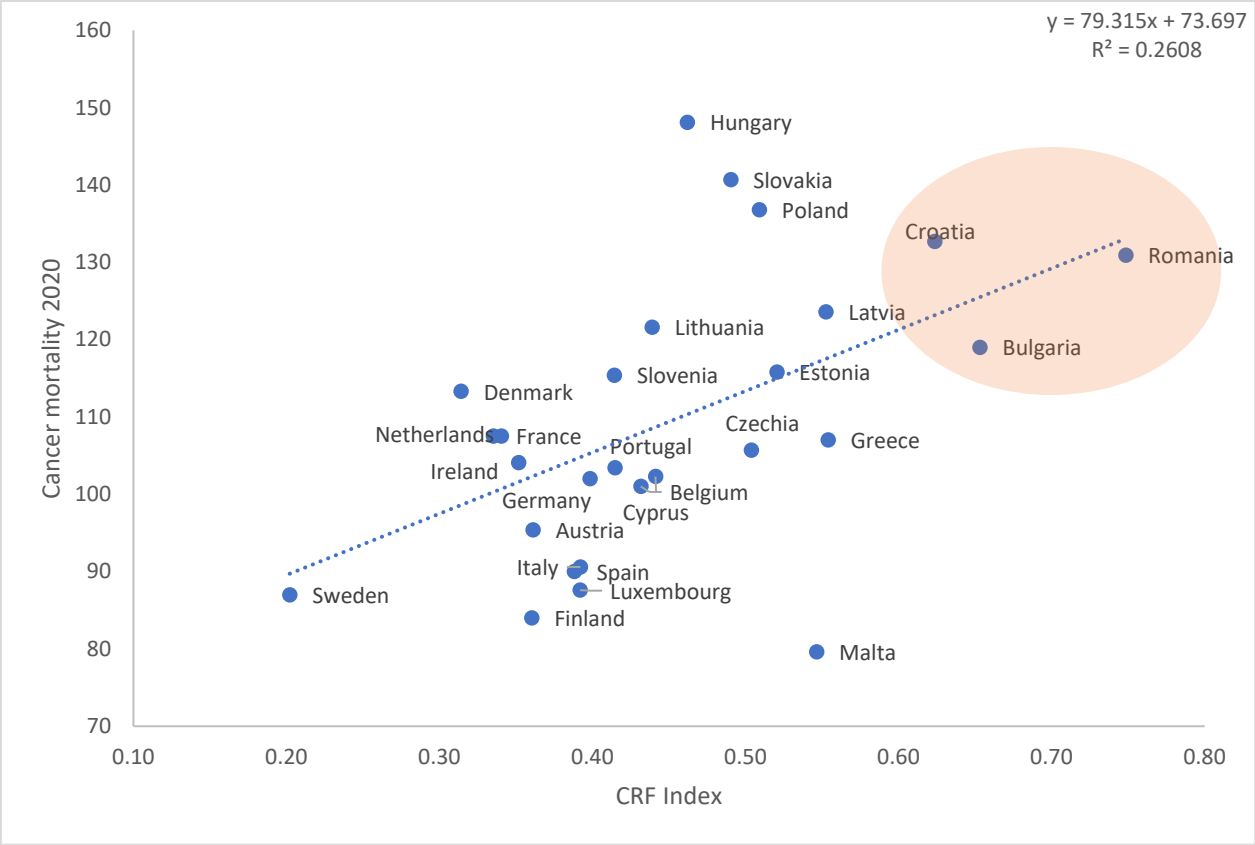
Lastly, environmental influences such as pollution, exposure to carcinogens, and urbanization can vary widely and impact cancer rates differently across countries.

However, all these factors imply massive expenditures per capita and investment from both public and private sources. This fact is shown in Figure 3 where is a solid and strong negative relationship between the value of index and the health expenditures per capita at PPP.

Countries like Germany, Sweden, and the Netherlands, which typically have robust healthcare systems, are seen towards the higher end of healthcare spending and lower end of the RCF Index. On the opposite end, countries such as Romania, Bulgaria, and Latvia have higher RCF Index values and lower healthcare spending, indicating possible gaps in healthcare funding or access, which could impact overall health outcomes negatively.

[2] ASR = age-standardised rates. ASR represent a summary measure of the rate of disease that a population would have if it had a standard age structure. Standardisation is necessary when comparing populations that differ with respect to age because age has a powerful influence on the risk of dying from cancer (Source: https://www.wcrf.org/cancer-trends/global-cancer-data-by-country/)

Figure 23. Relationship between Cancer Risk Factor Index (CRFI) and Cancer Mortality Rate

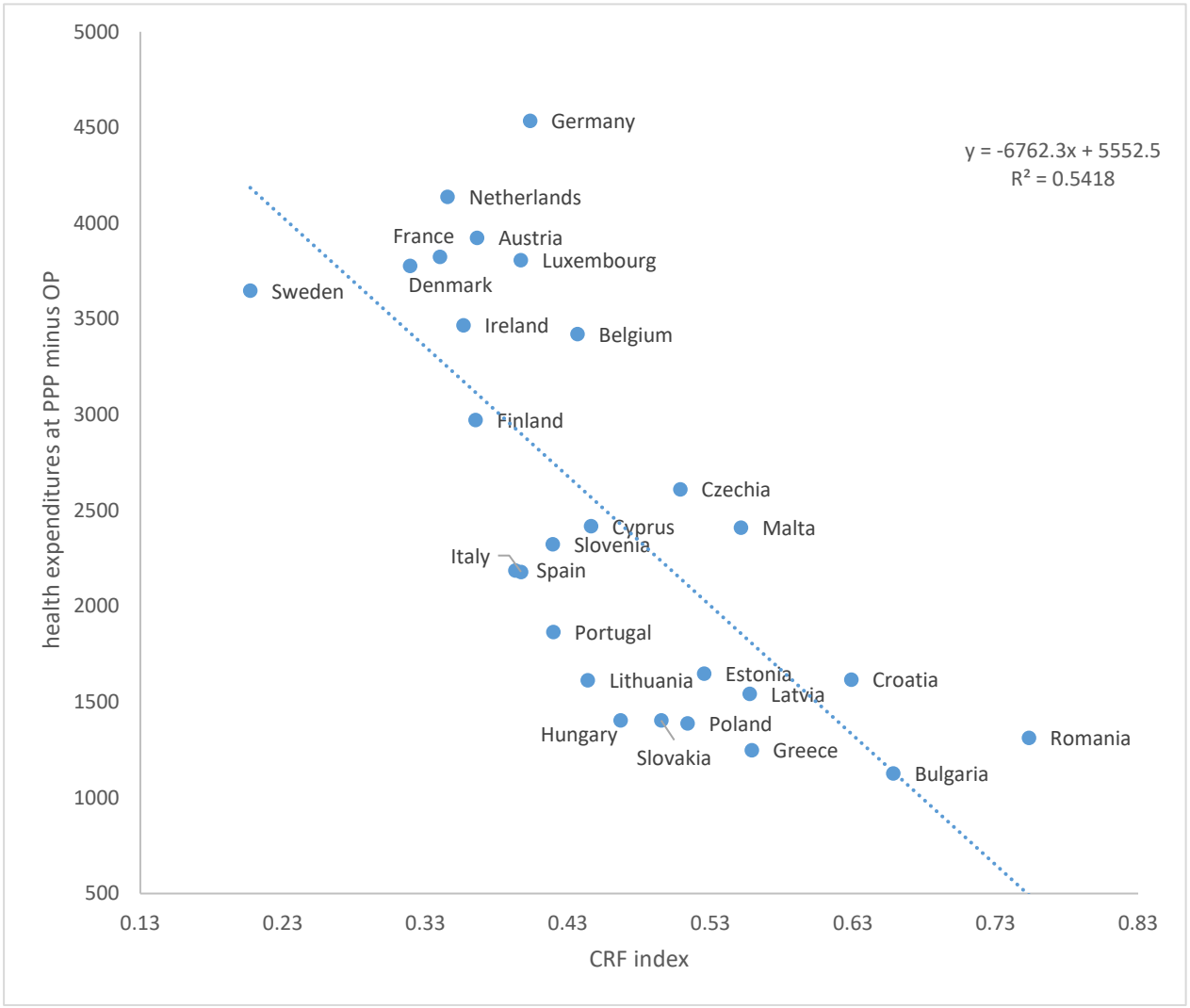


Source: own calculations and wcfr.org

The graph suggests that countries with lower RCF Index values tend to invest more in healthcare, potentially contributing to better health outcomes through prevention and early intervention strategies. Conversely, higher-risk countries might be under-investing relative to their needs, possibly due to economic constraints, lower fiscal revenues, or different governmental policy priorities. Some countries, like Malta and Cyprus, despite having low healthcare expenditures, manage to maintain lower RCF Index values, possibly due to other mitigating factors like lifestyle, environmental conditions, or more efficient health system management.

Overall, this plot highlights the complex relationship between healthcare investment and cancer risk factors, suggesting that higher investments in healthcare might be associated with lower aggregate risk factors for cancer across the EU.

Figure 24. Cancer Risk Factor Index (CRFI) and Cancer Mortality Rate



Source: own calculations based on Eurostat data

5. Case Studies of Direct Costs in Non-EU Member States

5.1. Moldova

5.1.1. General characteristics

On 27 August 1991, as the dissolution of the Soviet Union was underway, the Moldavian SSR declared independence and took the name Moldova. Moldova is the second poorest country in Europe by GDP per capita in current prices (5726 USD in 2022) (Statista, 2024), after Ukraine, and much of its GDP is dominated by the service sector. It has one of the lowest Human Development Indexes in Europe, ranking 76th in the world, in 2022 (Wikipedia, 2024). In 2019 public spending on health as a share of GDP was 3.8%, which was below the average of the EU (6%) and South-Eastern Europe (SEE) (5%) (WHO Moldova, 2022, p.9). According to national data for 2020, public health expenditure as a percentage of GDP rose to 4.8%. This notable increase is likely attributed to two main factors: the additional healthcare spending required to address the challenges posed by COVID-19, and the decline in GDP resulting from restrictions on economic activities. The Republic of Moldova experienced an annual GDP decrease of -7% from 2019 to 2020 (World Bank, 2022). The portion of the government budget designated for health has varied over the years, reaching its apex at 13.6% in 2010 and declining to 12.1% by 2019 (WHO Moldova, 2022, p.9).

In July 2022, the Ministry of Health approved an anticorruption action plan in the health sector, for the period 2022-2023, but health sector corruption remains widespread.

Entitlement to publicly financed health services is based on a health insurance system. In 2021 the share of the population covered by the National Health Insurance Company (CNAM) was 87.7%. Out-of-pocket payments accounted for 36% of health spending in 2019, despite the efforts made to address informal payments. These still hinder access to health services, particularly hospital care, and lead to financial hardship (WHO Moldova, 2022, p.7).

The count of publicly funded primary care facilities has surged from 67 in 2008 to 277 in 2015, further increasing to 293 by 2021. Over the past 25 years, the significance of primary care has grown notably, particularly with the establishment of the family medicine specialty in 1998. International donors have played a crucial role by aiding in the development of standardized clinical protocols for primary care and establishing criteria for referrals to specialists, laboratory tests, and additional investigations. Financial reforms have further reinforced primary care by promoting gatekeeping for specialist services and covering the expenses of primary care consultations for the uninsured population (WHO Moldova, 2022, p.11). Alcohol consumption and tobacco use are among the key health risks for most Moldovans. Both alcohol and tobacco products are easily accessible, even for children and adolescents, leading to high consumption (Tirdea, Ciobanu & Obreja, 2019 cited in WHO Moldova, 2022, p.17).

5.1.2. Direct Costs of Cancer in Moldova

The Republic of Moldova faces prolonged financial crisis, lack of program coordination, of a lack of experience, that affected, obviously, the battle against cancer. For cervical cancer risk, for example (but not only for this type of cancer), Moldova is classified by WHO in the field of sexually transmitted diseases at the level of countries of the third world (Jarynowski, 2019).

Characteristics of Moldova are late tumor detection in approximative half of the cases and the concentration of specialized treatment services in Chisinau, a fact that negatively influences the person's chances of survival. Cancer mortality produces a considerable increase in the treatment costs of this disease and other social costs, associated with the disease: exclusion of the person from socioeconomic activity, care, time and resources from other family members, transportation, etc. The high burden of cancer in the Republic of Moldova is determined by the high presence of risk factors (smoking, alcohol consumption, unhealthy diet, limited physical activity etc.), which causes a large part of cancer cases, late detection of the disease, limited access to complex treatment services, including palliative services. Access to effective therapies and application of the clinical approach principle of multidisciplinary in the management of cancer patients is not ensured. Infrastructure undeveloped, insufficient financial resources, lack of modern medical devices and the lack of well-trained human resources prevents the improvement of treatment results of cancer. Despite the high incidence and mortality, in the regions/districts of the republic there is only one institution, the Oncological Institute, which offers specialized treatment to people with cancer. Thus, annually, about 9 thousand newly diagnosed people are treated in this institution, additional to those diagnosed in previous years. The presence and provision of specialized services predominantly by a single institution produces enormous additional social costs borne by patients and their families (transport) and does not ensure the realization of the principle of bringing services closer to the people who need them (Guvernul Republicii Moldova, 2016).

According to the Government Decision, the total costs of Action plan for the years 2016-2020 regarding the implementation of the National Control Program of Cancer for the years 2016 – 2025 was estimated, in 2016, to 1.645.835.000 Lei (1 euro was 26.741 MDL). The budget of the National Cancer Control Program for the years 2016-2020 was around 3.200.000 thousand MDL, with a planned deficit of over 900.000 thousand MDL (Guvernul Republicii Moldova, 2016, Annex no.2).

In 2012-2019, the number of cancer patients in the country increased from 163.2 to 173 cases per 100 thousand inhabitants. More than 6.1 thousand people die from various types of cancer annually, while mortality among men is 1.5 times higher than among women (InfoMarket, 2021). During 2022, mortality from malignant tumors in the Republic of Moldova was 225.8 cases per 100 thousand inhabitants, increasing compared to 2021. The most frequently diagnosed malignant tumors are breast, colorectal, prostate, skin and trachea cancer which amounts to 52.6% of the total number of such conditions, notes the National Agency for Public Health (Radio Moldova, Feb. 2024).

The government, through the National Health Insurance Agency of Moldova (CNAM) is struggling to increase the number of services offered to cancer patients within the framework of the Unified Compulsory Health Insurance Program. According to official declarations, in 2020, about 41 million MDL was allocated for cancer services, from the

compulsory health insurance funds, which is 10 million more than the amount planned in 2019. Within the framework of inpatient treatment, CNAM pays the costs of treating patients, including expensive consumables, radiation therapy sessions, chemotherapy and anticancer drugs: last year, 245 million MDL were allocated for these purposes (due to the pandemic, expenses were 46 million MDL less than in 2019). The compulsory health insurance funds also cover the cost of high-tech services for the diagnosis and treatment of cancer at the Oncological Institute. In 2020, the list of such medical services was replenished with cytomorphological studies necessary for screening, earlier diagnosis and treatment of oncological diseases. About 10 million MDL was allocated for the provision of such services to patients with oncological diseases. In addition, from 2020, from the compulsory medical insurance funds, patients receiving outpatient radiation and chemotherapy services will cover the costs of suburban and intercity public transport. Cancer patients also receive anesthetic drugs with compensation during episodic treatment in a day hospital, treatment rooms, at home: such drugs are provided for children-patients free of charge, for adults - with 70 percent compensation. In addition, funds are allocated for the implementation of performance indicators within the framework of primary medical care for the prevention, early detection and surveillance of oncological diseases, for example, in the first quarter of 2020, about 10 millionMDL were allocated for these purposes, and 0.26 million lei from the prevention fund was allocated for breast cancer screening with mobile radiological equipment, etc. (infoMarket, 2021).

Studies on cancer in Moldova focused mostly on specific types of cancer (Jarynowski, 2019; Mustetea 2023), and authors underline the difficulties to access detailed information about cancer patients. Some data are not reliable, existing the suspicions of reporting "virtual patients" (Jarynowski, 2019, p. 4). Most of the studies looks to medical aspects, as incidence, subtypes of disease, impact on different age or gender groups, using other methods than financial (as DALY[3]) to evaluate the impact or the effectiveness of different cancer programs, preventions, types of treatments and so on (Jarynowski, 2019; Mustetea 2023). A recent literature started to develop on the new challenge for cancer patients generated by the military aggression of Russia against Ukraine, due to high number of Ukrainian refugees (Pandey et al., 2023; Price et al., 2023; Vulpe et al.2023; Vulpe et al.2024).

6.1.3. Institutional monitoring of cancer in Moldova

As in other former communist countries, in Moldova, the health system is centralized and has a single purchaser of publicly financed health services.

The health system has a large range of public and private medical facilities, as well as government agencies and authorities involved in the provision, financing, regulation and administration of health services.

The Ministry of Health (MoH) is primarily responsible for health policy and the development of legislation regulating the organization and provision of health services (WHO Moldova 2022, p.8). It has under his supervision the National Agency for Public

[3] One DALY represents the loss of the equivalent of one year of full health. DALYs for a disease or health condition are the sum of the years of life lost to due to premature mortality (YLLs) and the years lived with a disability (YLDs) due to prevalent cases of the disease or health condition in a population (WHO, Global Health Observatory, 2024.https://www.who.int/data/gho/indicator-metadata-registry/imr-details/158).

Health that manages public health services. MoH has the capacity of founder of public on 77 institutions (MS, 2024). Other 10 public health centers, 17 directions, 3 services and 1 section for the management of documents operate under the leadership of National Agency for Public Health (ANSP, 2024). Other important stakeholders are the Agency for Medicines and Medical Devices that regulates and supervises medicines and medical devices, and the Centre for Centralized Public Procurement in Health that plans and conducts public procurement of medical and protective equipment at the request of public providers (WHO Moldova 2022, p.8).

In Moldova, Institute of Oncology (IO) is the sole provider of radiotherapy services, delivering only rudimentary 3D plans with virtually no access to targeted drugs, immunotherapy or bone marrow transplantation. In recent months, there has been significant investment by the Ministry of Health (MoH) and IO in upgrading cancer services and a new national cancer control plan aims to narrow the gap in all areas of oncology practice (Vulpe, 2023, p. 3).

In 2015, the Government disposed to institute National Program of Cancer Control in the Republic of Moldova for the years 2016-2025. According to the 1291/02.12.2016 Decision, the authority responsible for the implementation of this Program is the Ministry of Health. Other Central Public Authorities partnering in the implementation of the Program are: Ministry of Agriculture and Food Industry, Ministry of Environment, Ministry of Economy, Ministry of Finance, Ministry of Labor, Social Protection and Family, Ministry of Education, National Medical Insurance Company, State University of Medicine and Pharmacy "Nicolae Testemițanu", as well as local public administration authorities and civil society organizations: associations of professionals, service providers, patient associations, mass media, etc. (Guvernul Republicii Moldova, 2016)

In December 2023, NNSA, the Oncology Institute of Moldova, and the International Atomic Energy Agency (IAEA) broke ground this month on a new facility for advanced cancer treatment in Chişinău. The Oncology Institute is the sole treatment center in Moldova, which has a population of 2.5 million and since 2022 has been home to more than 100,000 Ukrainian refugees. “Over 800 cancer patients have been detected among the Ukrainian refugees who could benefit from radiotherapy services,” (Dr. Ruslan Baltaga, Director of the Institute of Oncology).

5.1.4. Cancer Registries

There is no functional Cancer National Registry in Republic of Moldova. According to the authorities, the lack of a functional Cancer Registry does not allow the real monitoring and evaluation of the situation regarding cancer in Moldova, as well as the taking of decisions informed by the records. The register will ensure the digitization of the processes of collection, validation, analysis, interpretation and dissemination of health data regarding oncological diseases in adults and children.

However, official interest in monitoring Cancer and in implementing sustainable measures in reducing the burden of cancer existed. Traditionally, the Cancer Registry, within the Public Health and Medical Institution, the Oncological Institute from Moldova, was created in 1983, the basis of which was the completion of the data on about 41 thousand patients diagnosed and/or treated with an oncological disease. At that time, the Cancer Registry served as a tool for controlling the oncological situation in the territory, identifying patients in real time, for completing or specifying some data. Supplying that register with information served internal sources (the departments of the Oncological

Institute, consulting offices), as well as external ones (Public Health and Medical Institutions from the territory/districts or other republican medical institutions – Republican Clinical Hospital, etc.). Until the mid of '90s, this registration functioned and some data were available for interested institutions and for reporting. In 2015, however, due to many crises Republic of Moldova went through, it was not possible to report the standardized indicators regarding the problem of malignant tumors in the current structure of the Cancer Registry (Ghervas, 2015, p.125). Lack of one Functional Cancer Registry, according to the recommendations of the International Agency for Research in the field of cancer (IARC) does not allow real monitoring and evaluation of the situation through cancer in the Republic of Moldova, as well as making decisions informed by evidence (Government of the Republic of Moldova, 2016).

5.2. Montenegro

5.2.1. General characteristics

Montenegro became an independent state in 2006, after the organization of a referendum on the independence. On 28 June 2006, Montenegro joined the United Nations as its 192nd member state.

According to the International Monetary Fund, the nominal GDP of Montenegro was $5.424 billion in 2019. The GDP PPP for 2019 was $12.516 billion, or $20,083 per capita. According to Eurostat data, the Montenegrin GDP per capita stood at 48% of the EU average in 2018 (Wikipedia, 2024).

In 2022, Montenegro switched to a fully tax-funded health insurance system. Revisions to the health insurance law in 2017 made residency an additional basis for entitlement to health benefits, extending population coverage to close to 100%. Out-of-pocket spending as a share of current spending on health fluctuated between 2011 and 2019 (the years for which internationally comparable data are available). In 2019, 39% of current health spending was paid out of pocket, the same level as in 2011 (WHO 2022 Montenegro, p.10). Almost 10% of all households experienced catastrophic health spending in 2017 (WHO 2022 Montenegro, p.7). Cancer, stroke and ischemic heart disease were the leading causes of death in 2009, the latest year for which the country reported data to WHO (WHO 2022 Montenegro, p.16).

5.2.2. Direct Costs of Cancer in Montenegro

Since 1 January 2022, financing of health services has changed from a combination of payment of insurance contributions and government transfers to fully tax-based funding. However, the practical implementation of this new funding model still lacks clarity at the operational level and there are concerns on the long-term financial sustainability of the current health financing system that appears to lack a sound fiscal space analysis (WHO 2022 Montenegro, p.9).

In 2019, public spending on health amounted to 5% of Montenegro's gross domestic product (GDP) and 11% of its government budget. This was below the European Union (EU) average (6% of GDP), but in line with the average of SouthEastern Europe (SEE) (5% of the GDP) (WHO 2022 Montenegro, p.9).

In 2019, curative care comprised 42.6% of current health expenditures, while medical goods accounted for 8.9% (WHO, 2022b). Surprisingly, preventive care received only a minimal share, amounting to 1.2% during the same period. Moreover, a significant

portion of spending (40.9%) fell under unclassified categories, indicating potential for enhancing health financing data accuracy (WHO 2022 Montenegro, p.11).

There are things that can be improved in addressing cancer in Montenegro. In a study developed by Kovačević et al. (2024), on colorectal cancer screening, some aspects have been revealed. There is a lack of facilities and lack of trained staff to perform specific procedures (in the study cited, many hospitals either do not have gastroenterologists or the staff is not trained to perform the colonoscopy procedures). Also, some healthcare providers use a different platform that is not compatible with the information system of the screening program, therefore, the individual level monitoring of follow-up, diagnosis and treatment is not feasible after screening (Kovačević et al., 2024, p.3).

5.2.3. Institutional monitoring of cancer in Montenegro

The health system is largely centralized, without substantial involvement by local self-government in health service provision and planning (WHO 2022, Montenegro, p.8). The health system of Montenegro is based on a social health insurance system, with more than 95% of the population being covered by social health insurance. Additional funds come from the state budget, as well as substantial out-of-pocket payments, with the latter amounting to 40% of current health expenditure in 2018. The Ministry of Health, the Health Insurance Fund and public and private health care institutions are responsible for health care service delivery. The Health Insurance Fund is responsible for the implementation of health policy related to health insurance. For the implementation of pharmaceutical policy, the state has set up the Agency for Medicines and Medical Devices (CALIMS). Health care providers in the public sector include 18 health centres, seven general hospitals, three specialized hospitals, the Clinical Centre of Montenegro, the Institute for Public Health, the network of emergency services, the Blood Transfusion Institute, and the Pharmacies of Montenegro "Montefarm". Primary care is provided by the "chosen doctor" in the health centre. Secondary and tertiary health care is provided through specialized clinics and hospital wards (WHO, 2024).

The Ministry of Health is the primary administrative, regulatory and governing authority in the health sector. The Health Insurance Fund (HIF) is the single purchaser of health services. The Institute for Medicines and Medical Devices is responsible for pharmaceutical policy. Health services are provided through the network of publicly owned health facilities and contracted private facilities. The network of certified providers aims to ensure equal geographical access to health care (WHO 2022 Montenegro, p.8).

One of the challenges for the health system is that data collection is fragmented, statistics are often not publicly available, and data are not sufficiently used for decision-making purposes. Major health threats include unhealthy diets, tobacco and alcohol consumption, and relatively poor air quality, with poverty and unemployment aggravating ill health and unmet needs (WHO 2022 Montenegro).

There is a National Program for Cancer Control, launched by the Government in 2008, and in 2009 a pilot screening program on colorectal cancer was putted in place. Until 2014 the pilot screening program worked (https://www.integratedcare4people.org/media/files/Montenegro.pdf), but, according to sources (https://en.vijesti.me/news/society/576358/an-entire-municipality-suffering-from-cancer, 2021) it has not been evaluated or updated. However, Montenegro is preparing the National Cancer Control Plan for the next five-year period, in which priorities

will be defined, which concern: 1) increasing the availability of innovative oncology therapy, diagnostic procedures, as well as quality medical services for oncology patients in Montenegro; 2) development and full implementation of primary and secondary prevention programs and 3) decentralization of the oncology service when it comes to the application of therapy and the provision of palliative care, which would significantly facilitate the treatment of these patients (https://4p-can.eu/closing-the-care-gap-in-montenegro-expectations-and-possibilities/).

5.2.4. Cancer Registries

In the European Network of Cancer Registries, Montenegro counts on a Registry of Malignant Neoplasms of Montenegro (https://www.encr.eu/node/266). Since 2013, Montenegro has established the chronic non-communicable diseases registers: malignant neoplasm, diabetes, acute coronary syndrome and cerebral-vascular diseases (Government of Montenegro, 2017).

Covid 19 disrupted cancer-screening programmes. For example, cervical cancer screening was reported not to have resumed at all in Montenegro, due to the decision to reallocate the polymerase chain reaction devices [normally used for the human papilloma virus (HPV) screening] to the detection of SARS-CoV-2 (Neamtiu et al.2022).

However, public data about the Registry of Malignant Neoplasms of Montenegro are very hard to identify, at least in English. There are some documents that mention that this registry offer information on the incidence of cancer in the country (WHO, 2024).

5.3. North Macedonia

5.3.1. General characteristics

The Republic of North Macedonia (NM) became an independent country from the former Republic of Yugoslavia, on 8 September 1991, after a Referendum. North Macedonia became UN member on 1993 under the provisional description "the former Yugoslav Republic of Macedonia". In 2018, the country renamed itself "Republic of North Macedonia", that came into effect in early 2019 (Wikipedia, 2024).

In North Macedonia, there's a comprehensive public healthcare system. Virtually all citizens are insured under a mandatory, insurance-based health scheme, ensuring nearly universal coverage, although some gaps persist (for the Roma community, for example). Oversight of health matters is handled by the Government, the Ministry of Health, and the Health Insurance Fund (WHO 2022 North Macedonia, The Euro Health Observatory). There are general hospitals in all major towns and three specialized hospitals in the major cities, but all tertiary health care services are provided solely in the capital city of Skopje. Most hospitals are in public ownership, but the share of private hospitals has increased, accounting for 4.3% of all hospital beds in 2019 (Eurostat, 2022).

North Macedonia stands out in Europe for its low allocation of funds towards public healthcare, leaving citizens heavily reliant on private spending despite their contributions to health insurance. The country's constitution enshrines the right to health, advocating for a universal, solidarity-driven, and equitable approach to healthcare organization and financing. It also emphasizes the pursuit of optimal health levels irrespective of factors such as ethnicity, gender, age, social standing, or financial capacity. All parameters for financing the healthcare system in Macedonia are below the average of public health

expenditures in the EU (World Development Indicators, 2022). Several weaknesses characterize the Health System in North Macedonia:

- Excessive allocation of resources for expensive health services in larger cities environments compared to primary care and preventive services.
- Inefficient and low-quality services due to excess capacity, poor organization, weak regulation, weak law enforcement mechanisms, lack of management skills, lack of incentives.
- High costs for patients, such as informal payments to doctors, nurses, and payments for non-covered services, drugs and medical devices. There is a strong reliance on out-of-pocket payments which represent 40.4% of total health spending, one of the highest shares in South-Eastern Europe (WHO North Macedonia, 2022, p. 7).
- The fragmented primary care network and the limited scope of practice leads to many referrals to secondary and tertiary care and high avoidable hospital admission rates.
- Significant weaknesses in financial management and internal control.

The healthcare system of North Macedonia is based on a social health insurance system with a single Health Insurance Fund (HIF) as purchaser of care in the private sector (Milevska Kostova et al., 2017). The system's funding relies on compulsory contributions deducted from personal income, typically paid by insured individuals. However, the Ministry of Health covers this contribution for the most financially vulnerable insured persons. Surprisingly, only 63% of all insured individuals make these payments directly or through their institution, while the remaining 37% access full health insurance benefits without contributing to the Fund. This situation is determined by several causes:

- a decline in the count of employed individuals,
- a rise in the number of retirees and those whose contributions are covered by the Ministry of Health,
- varying rates of health contributions among the insured population. For instance, the average rate for 2020 stands at 5.3%, indicating that despite an official health contribution rate of 7.5% (the lowest in Europe), the effective rate is even lower.

The information system Moj Termin (My Appointment) has greatly improved scheduling and has reduced waiting times for clinical appointments and diagnostic tests, but legal and operational barriers continue to undermine its use in primary care settings

All parameters for financing the healthcare system in Macedonia are below the average of public health expenditures in the EU (World Development Indicators, 2022). Health expenditure is relatively low in comparison to European Union (EU) and South-Eastern European countries, both per capita and as a percentage of gross domestic product (GDP). Spending on health as a percentage of GDP decreased from 8.9% in 2000 to 7.3% in 2019. Health expenditure per capita in North Macedonia amounted to 1 314 US$ PPP, which was below the average of South-Eastern European countries (1 649 US$ PPP) (WHO 2022, The Euro Health Observatory, p.9).

5.3.2. Direct Costs of Cancer in North Macedonia

General budget of Ministry of Health of The Republic of North Macedonia for 2024 is 5,878,688.00 million denar and 2023 is over 5,915,195.00 million denar (1 denar is 0.016 Euro).

The total health expenditures in Macedonia in the past period have been constantly growing in absolute values (measured by per capita expenditure in PPP dollars). On the other hand, as a percentage of GDP, they are constantly decreasing, and 7.3% of GDP for health is internationally far below the EU average of 9.9%.

Cancer ranks as the second most common cause of death in NM, mirroring global trends. In 2018, malignant diseases accounted for one in every five deaths in North Macedonia, compared to one in every six deaths worldwide. Approximately one-third of cancer-related deaths stem from five primary behavioral and dietary factors: high body mass index, insufficient fruit and vegetable consumption, sedentary lifestyle, and the use of tobacco and alcohol (Vasileska, 2022, p. 1).

Costs of cancer, as a disease, are almost impossible to be determined. Even if there are taking into account diagnosing, treatment, such as hospital stays, medications, and medical procedures, this endeavor encounter difficulties because of lack of data, faulty way of recording and monitoring cancer patients, their journey through disease, the complexity of the illness. Also, there is not a unitary acceptance among scholars, as well as among institutions and organization in developing a unitary, easy to use and to understand method of evaluating the direct cost of cancer. Some academic studies focused on cancer burden from the perspective of cost of cancer. However, the available data is quite old (in many cases), studies focus on specific types of cancer or on groups of diseases, or try to measure the impact of different risk factors on developing cancer. Some estimations are made, but there is a lack of literature that express the cost of cancer for North Macedonia (and not only). For example, annual economic costs generated by cardiovascular diseases and lung cancer were 232 mil. Euro (for 2011) (Meisner, Gjorgjev & Tozija, 2023, Table nr. 2, p.7).

A specific interest in the literature is devoted to the analysis of the cost of different screening programs, as the effectiveness of these programs is important in developing further public health policies and programs. As an example, the breast cancer early detection program involves costs that are divided into: 1. Costs generated by the health care system; 2. Costs generated by other sectors involved (for example, related to social protection); 3. Out of the pocket money (expenses of patients and families: personal expenses for treatment, healing consequences of the disease, family time and home care). These costs are fixed and variable. Example of fixed costs are mammography device (market price, amortization period, cost for depreciation), space, cost of the procedure itself, IT services used for the development of the program solution which is a necessary element for quality implementation of the program, administrative costs (program management costs). Variable costs depend on the number of persons caught up with the program. They are: Recording costs (number of recorded women during a period of the program), verification costs (the cost of double reading the findings), calling costs, personal expenses due to the examination which implies expenses for the patients upon arrival for a mammographic examination (out of the pocket money: transportation to the place of implementation of the mammographic examination).

For example, for the program developed in 2019 for breast cancer, the total cost was of 9.170.000,00 MKD, and more than 90% of the costs were determined by the procedure (mammography and interpretation), the logistic of the program and the updates of the software: organization of the screening program (calls, communication, data collection and interpretation, situational analysis) with a cost of 1.550.000,00 MKD, mammographic activities (recording, reading, supervision), with a cost of 6.000.000,00 MKD, interpretation of the mammography, with a cost of 1.000.000,00 MKD; Upgrade of software for screening with a cost of 500.000,00 MKD (https://iph.mk/Upload/Documents/Izvestaj-za-isplatlivost-na-Programa-za-skrining-na-dojka(1).pdf).

5.3.3. Institutional monitoring of cancer in North Macedonia

Cancer monitoring is part of the health network. The network of healthcare institutions in Macedonia consists of 118 designated institutions. Oversight of health matters is handled by the Government, the Ministry of Health, and the Health Insurance Fund (WHO 2022, The Euro Health Observatory). There are general hospitals in all major towns and three specialized hospitals in the major cities, but all tertiary health care services are provided solely in the capital city of Skopje. Most hospitals are in public ownership, but the share of private hospitals has increased, accounting for 4.3% of all hospital beds in 2019 (Eurostat, 2022). There are 67 hospitals (public and private) and 6 polyclinics, 1 dental clinical center, 34 health centers, 5 health stations. In addition, contracts have been concluded with approximately 1,500 private healthcare persons/organizations providing mostly primary health care. There are also private healthcare facilities organizations that do not have contracts with the Fund (dental offices, pharmacies and others specialized facilities). The picture for Macedonia is further complicated by the division of The University Clinical Center Skopje in 32 autonomous institutions.

Ministry of Health (MoH) is in charge of formulating and monitoring health policies, influencing broader government policies, developing annual public health programmes, collecting and using health intelligence (also through the E-health Directorate), ensuring emergency preparedness, and enforcing health legislation (WHO 2021, p.7). The strategic priorities and goals of the Ministry of Health are at the same time in the function of the priorities and goals of the Government of the Republic of North Macedonia, which are determined by the Decision on the determination of strategic priorities published in the Official Gazette of the Republic of North Macedonia.

The Institute of Public Health (IPH) is the main scientific and technical body in public health, and its core competencies include ensuring environmental health (sanitation, water, control of microbiological hazards); collecting and analysing health data; performing reference laboratory work; monitoring the performance of public health activities; and implementing annual public health programmes and activities. Another of its main functions is scientific research aimed at generating evidence for the purpose of policymaking in the area of public health; unfortunately, this is not supported by the State to a sufficient extent and mainly depends on foreign donations and projects (WHO 2021, p.8).

10 Centres of Public Health (CPHs) distributed across eight administrative regions; like the IPH, they are tasked with implementing the annual programme, and they report their activities to the IPH. However, they work independently to provide local laboratory

services and others in areas like social medicine, health protection, health education, environmental health, epidemiology and microbiology (WHO 2021, p.8).

MoH negotiates its annual budget with the Ministry of Finance, while the IPH and CPHs depend on three separate funding streams: MoH annual programmes, the Health Insurance Fund (HIF, through payments for laboratory services), and self-financing (other payments for laboratory services). The IPH and CPHs are obliged to perform the services set out in the annual programmes; however, delayed and missed payments from the MoH have led to substantial operating deficits, increasing the reliance on private sources of funding. Laboratory services may be purchased through the HIF or through agreements with private sources; purchasers are free to contract services from both public and private laboratories (WHO 2021, p.8).

As for interinstitutional collaboration and cooperation, there are difficulties and much should be done. As studies mention, the MoH, IPH and CPHs do not participate in any consensus-based processes to determine national public health priorities, which undermines programme consistency and budget negotiating power. Decisions are made within silos, so for instance, each CPH uses its own software, making it impossible to share data, and they also procure laboratory equipment independently, leading to overlaps and inefficiencies. Moreover, there are no established mechanisms for horizontal or vertical technical collaboration, complicating the development of standard operating procedures or even minimal coordination in health promotion programmes ((WHO 2021, p.17)

in February 2019 the MoH launched a national reform of the primary health care system in line with the Astana declaration, to be the basis for an overall health reform aimed at achieving universal health coverage. The success of this initiative remains a challenge considering the low public expenditure on health and the major shortage of health professionals (WHO 2021, p.9).

The need of improvements in institutional functioning is also demonstrated by some scandals. The scandal at the Oncology Clinic, which is the main hub for cancer patients for the entire country, erupted in 2023 after several media outlets published stories about an alleged well-organised scheme to steal expensive medications, by using fictional patients. The medicines then ended up on the black market.

(North Macedonia Makes Arrests over Cancer Treatment Scandal https://balkaninsight.com/2024/01/30/north-macedonia-makes-arrests-over-cancer-treatment-scandal/)

5.3.4. Cancer Registries

The Cancer Registry of the Republic of North Macedonia is managed by the Institute of Public Health of Republic of North Macedonia (IPH). Since 1995, the Register has been in electronic form. Slightly more than 165,000 individual persons were registered in the register by December 31, 2020. The IPH has developed an object-oriented software tool that is used for data entry and analysis.

At the beginning of 2023, several changes were requested in the software solution used for the Cancer Registry. The changes were initiated by the coders from the Public Health Centers, in order to improve the quality of the data, bearing in mind that they are the people who have the role of coders (IARC, 2023).

There is an inter-institutional coordination on cancer patients in terms of treatment, data collecting at the University Clinics. At the Clinic level patients are registered as cancer patients and there is available data for every patient in internal conditions, after, the date is collected by the Institute of Public Health in The Republic of North Macedonia and placed in the Cancer Registry.

5.4. Ukraine

5.4.1. General characteristics

Ukraine is the second-largest European country after Russia, which borders it to the east and northeast. The country gained independence in 1991, after the Soviet Union has dissolved. A new constitution was adopted in 1996. Ukraine became a founding member of the United Nations in 1945 as the Ukrainian Soviet Socialist Republic, together with the Byelorussian Soviet Socialist Republic. Following the Soviet Union's dissolution in 1991, Ukraine retained its membership as an independent nation (UN, 2024).

According to the World Bank data (WB, 2024), the major concern for Ukraine remains the Russian invasion, as the war entering in the third year. Consequences on the Ukraine affect the entire society. As World Bank underlines, it is remarkable that Ukraine, with the help of donors and the support of allies, managed to keep a functional society: schools remain open, education continues for children aged 6-18 through in-person, remote or blended learning, including in the regions under hostilities; health clinics remain open. Nine out of 10 people say community health clinics remain open, including 8 out of 10 people in the regions under hostilities. Companies adapt by adjusting their product mix, embracing ITC use or relocating internally and international firms remain committed to working in Ukraine. In 2023, the Government of Ukraine, with the support of its partners, has met some of the most urgent needs, according to government data: repairing and reconstruction of damaged building, motorways, highways and other national roads.

Despite efforts, economic situation of Ukraine is at a high uncertainty. European Parliament (2024) appreciates that in 2022, as a result of Russia's full-scale invasion, Ukraine's GDP fell by almost 30%. In 2023, economic growth exceeded expectations, with the National Bank of Ukraine (NBU) putting the latest estimate of the annual real GDP growth rate at 5.7% (at the beginning of 2023, the NBU's forecast was 0.3%). According to the NBU and the International Monetary Fund (IMF) baseline forecasts, growth in the coming years is expected to be above 4%. Nominal GDP of Ukraine was USD 159 billion in 2022, GDP per capita was of USD 4,005 compared to the global average of USD 10,589., and average real GDP growth of 3.1% over the last decade (https://www.focus-economics.com/countries/ukraine/).

As for the health situation, Dr. Hans Kluge, the World Health Organization's regional director for Europe commented in Politico, "the number of internally displaced persons is currently estimated at 3.5 million; over 6 million refugees have been recorded, mostly in neighboring countries; and almost 8 million people are in need of health assistance within government-controlled territory. Currently, two-thirds of those seeking care encounter barriers that are primarily related to cost, time and transportation. In areas close to the front lines, 22 percent of households delay seeking medical care, with 7 percent struggling to acquire essential medications. Family doctor access is also significantly reduced in these regions where financial constraints are more acute, and almost 25 percent cannot afford medicines, while 51 percent are unable to pay for medical services. Moreover, noncommunicable diseases (NCDs) — like cardiovascular disease, diabetes, cancer —

these don't simply disappear in a conflict zone. On the contrary, in Ukraine, NCDs cause 84 percent of all deaths, often exacerbated by factors stemming from the war. Ukraine also continues to experience one of the highest burdens of HIV, tuberculosis and maternal mortality ratios in the WHO European Region. And the risk of infectious disease and outbreaks of food and water-borne disease is constant. This applies to the unprecedented threat of a chemical, biological, radiological and nuclear emergency as well".

5.4.2. Direct Costs of Cancer in Ukraine

Nearly 80% of all deaths in Ukraine are attributable to circulatory system diseases, cancer and respiratory diseases. Although Ukraine's health system theoretically guarantees a comprehensive array of publicly funded health services, the actual availability of resources at public facilities, where care is intended to be free at the point of service, dictates whether individuals must bear the cost of care or medications (WHO Ukraine,2021, p. 7). At US$ 683 PPP in 2018, health expenditure per capita in Ukraine ranks well below the WHO European Region average. As a percentage of Ukraine's GDP, expenditure on health increased from 5.3% in 2000 to 7.7% in 2018, just slightly below its high mark in 2015. The share of public spending on health as a percentage of total government expenditure was 8.9% in 2018, an increase from its lowest point of 6.8% in 2008. As a share of Ukraine's GDP, public spending on health stood at 3.7% in 2018, which was below the WHO European Region average of 4.9% and the EU average of 5.9%. Levels of private spending as a percentage of current health expenditure reached 51% in 2018, up from 39.1% in 2006 and almost exactly where it was in the early 2000s. This high share of private spending (almost entirely in the form of out-of-pocket payments) can lead to households becoming impoverished and to patients not accessing necessary care (WHO Ukraine,2021, p. 9).

The National Health Service of Ukraine (NHSU), established in 2018, is the single purchaser of health services, replacing the former input-based financing of health care facilities. The NHSU is funded from general taxation through the state budget and is subordinate and accountable to the Cabinet of Ministers through the Ministry of Health (MoH) (WHO Ukraine,2021). In the law on the 2024 budget, general healthcare expenditures are planned as 5576.7 mil UAH (3.28% GDP) (https://zakon.rada.gov.ua/laws/show/3460-20#Text).

Cancer related costs are represented in aggregated numbers for the whole healthcare sector. Some specific numbers related to the oncological services can be found in the Program of medical guarantees (https://zakon.rada.gov.ua/laws/show/1394-2023-%D0%BF#Text). After approving the budget, the government adopts the Procedure for implementing the medical guarantee program for the relevant year (e.g., for 2024 – https://zakon.rada.gov.ua/laws/show/1394-2023-%D0%BF#Text). It defines the specific cost provision for oncological services, which is reimbursed to healthcare institutions. For example, the tariff for medical services for chemotherapeutic treatment and support of patients with oncological diseases in inpatient and outpatient conditions, provided by the specifications, is defined as a global rate. The global rate per month is calculated as 1/12 of the sum of the products of the number of unique patients, the capitation rate per year, which is 36,807 UAH, to which the following adjustment factors are applied depending on the age of the patient: 3,555 - for willingness to provide medical services to patients under 18 years of age; 0.97 - for willingness to provide medical services to patients aged 18 and older in inpatient and outpatient settings; 0.7 - for the willingness to provide medical

services to patients aged 18 and over exclusively in outpatient settings. There are also budget program passports for each year, created by the Ministry of Health of Ukraine.

During the period of operation of state programs such as the State Program "Oncology" for 2002-2006, the State Program "Children's Oncology" for 2006-2010, the National Program for the Fight against Oncological Diseases for the period until 2016, funds for their implementation were allocated directly from the central budget, and it was possible to track this on the basis of the National Health Accounts of Ukraine (https://www.ukrstat.gov.ua/druk/publicat/Arhiv_u/15/Arch_nroz_bl.htm), which were carried once per 2 years.

Partially, costs for cancer care might be coming from donors, like in the example of EU4Health program that can support cancer care in forms of grants or procurement.

5.4.3. Institutional monitoring of cancer in Ukraine

The National Cancer Institute, in Kyiv, established in 1920, stands as a pivotal institution for cancer patients. Its significance extends through various initiatives, including the creation of the Ukrainian Cancer Registry in 1966 and advocacy for the National Programme Control of Cancer until 2016. Prior to February 24, 2022, the institute boasted a workforce of over 1,000 employees, including 95 researchers, and provided care for up to 400 cancer patients daily across its 600 swing beds. Collaboration flourishes with the Ukrainian Society of Surgical Oncology, counting at least 150 active members and maintaining strong ties with the National Cancer Institute. Ukraine houses approximately 40 radiotherapy centers equipped with 133 gamma therapy units and 24 electron accelerators. As of 2018, the nation employed 1,935 clinical oncologists, with a ratio of 73.20 new cancer cases per clinical oncologist. Additionally, the Kavetsky Institute of Experimental Pathology, Oncology, and Radiobiology of the National Academy of Sciences of Ukraine (IEPOR) in Kyiv proudly represents Ukraine as a member of the Organization of European Cancer Institutes (OECI) (Caglevic et al. 2022, p.3).

War provoked by Russia altered dramatically the situation of cancer patient in Ukraine. It exists a deficit in access to the essential conditions necessary for ensuring proper diagnosis and treatment. Focusing solely on the five most prevalent types of cancer among Ukrainian residents, with a delay of four months for initial diagnosis and/or treatment commencement, studies projected a minimum of 3,600 additional deaths attributable to cancer in the coming years (Caglevic et al. 2022, p.2).

6.4.4. Cancer Registry

There is a National Registre of Cancer in Ukraine (NCRU), member of the European Network of Cancer Registries (ENCR). According to the official data (http://www.ncru.inf.ua/info_en.htm), NCRU database is used in such WHO publications as "Cancer Incidence in Five Continents" (Vol. X, Vol. XI and Vol. XII), "International Incidence of Childhood Cancer", Vol. III, as well as in a number of international projects, such as the European Cancer Information System, Global Cancer Observatory, Global Cancer Facts & Figures, Global Burden of Disease Study and others.

NCRU is the structure that aggregates the data from regional cancer registries. The principle of organization of the NCRU database is aggregation (consolidation) of information about the oncological diagnoses of the patient, all episodes of the treatment

and observation into a single electronic registration card. The content of this card is determined by the form No 030-6/o "Registration card of a patient with cancer".

The organizational fundamentals for the National Cancer Registry in Ukraine (NCRU) were:

(1) the oncological service system, which exists in Ukraine since the 1950s and consists of the oncological health care institutions in each oblast, and

(2) the state cancer registration system with its well-established ways of informing through paper notifications on each diagnosed and/or treated cancer case (is currently regulated by the Orders of Ministry of Health of Ukraine No 845 of 01.10.2013, No 1 of 10.01.2006 and No 629 of 10.10.2007), as well as obtaining of data on deaths of cancer patients in the local bodies of state registration of civil status (http://www.ncru.inf.ua/info_en.htm).

Also, in the central Ehealth database there is the following data:

- Registry of patients, which contains information about persons, who are the subjects of guarantees according to the Law of Ukraine "On State Financial Guarantees of Medical Services of the Population";
- Registry of declarations on the choice of a doctor who provides primary medical care, containing information about the declarations;
- Registry of business entities in the field of health care, which contains information on health care institutions who have a license to carry out business activities in medical practice, and laboratories that have signed a contract under the medical guarantee program (or intend to do so) or involved to the provision of medical services by medical service providers;
- Registry of medical specialists, containing information on persons who have received education in the field of health care;
- Registry of medical workers, containing information on professionally trained persons who, in accordance with the law, have the right to provide medical care;
- Registry of contracts for medical care of the population, containing information about contracts for medical care of the population under the medical guarantee program concluded with the National Health Service;
- Registry of reimbursement contracts, which contains information on reimbursement contracts under the medical guarantee program concluded with the National Health Service;
- Registry of medical records, referral records and prescriptions;
- Registry of medical reports and others.

Complete data on cancer mortality in whole Ukraine are available in NCRU since 2002. Until 2014, the NCRU database had annually increased by 150-160 thousand of new cancer cases. After 2014 the NCRU does not receive data from the Autonomous Republic of Crimea, and Donetska and Luhanska oblasts are covered by the NCRU unified information technology only partially, that is why the annual number of new cancer cases in this period was about 140 thousand. At the beginning of 2023, the NCRU database contained more than 4 million records on cancer patients, of which more than 1 million

were registered as supposed to be under follow-up (http://www.ncru.inf.ua/publications/ucr_db_today.pdf).

There is a registry of medical-technological documents on the standardisation of medical care, which operates in accordance with the Regulation on the Register, (MoH Order, #751 from 28/09/2012 "On the creation and implementation of medical-technological documents on the standardisation of medical care in the system of the Ministry of Health of Ukraine" and registered with the Ministry of Justice of Ukraine on 29/11/2012 under #2004/22316. Current industry standards and clinical guidelines in Ukraine, including cancer medical care, are presented on the special website of the State Expert Center of the Ministry of Health of Ukraine. Standards and guidelines, the cancer care including, are available on the website of State Expert Center of the Ministry of Health of Ukraine (https://www.dec.gov.ua/cat_mtd/galuzevi-standarti-ta-klinichni-nastanovi/, example), and on the website for Ukrainian legislation. Latest data are available for 2023 (http://www.ncru.inf.ua/publications/BULL_24/index_e.htm).

5.5. Conclusions

There are several common characteristics of all these four countries, characteristics that can be identified in the case of other former communist countries. Major improvements have been made in the health system in these countries, and their efforts in complying with the guidelines elaborated by the WHO and the EU. However, there are still some lags behind the developed European countries. The health expenditures are lower than in western countries, they there is a focus on hospital treatment instead of ambulatory (in all countries there is a generous number of hospitals beds), face, in different degrees, a shortage of human resources for the health system (including for cancer pathology), encounter difficulties in implementing health policies that are both efficient and generous. All in one, it seems that things in the health system, including cancer, looks much better on paper than they look on the field!

For cancer patients, despite many improvements, important challenges are still in place:

- Insufficient financial resources. Cancer patients grow in number and the pressure on the health system increase. As the burden of the disease manifest on multiple plans, the governments need to look for efficiency in designing health policies and programmes.
- All these countries face a shortage in professionals working in health, as many of these retired or emigrated. A sustainable human resource for health system is a critical issue.
- There is an institutional fragmentation, an inefficient coordination among health institutions, overlapping among institutions, and inefficient coordination.
- Mostly for cancer patients, high inequalities that exist between rural and urban area in these countries create major obstacles. Access for diagnosis, treatment (radiotherapy, for example) is diminished by the lack of health infrastructure, poor infrastructure in terms of transportation and lack of many other amenities.

- There is a lack of adequate equipment in these countries and a lack of personnel trained to use moder equipment. These countries need to invest more in technical facilities and in training more personnel.
- Informal payments to doctors, nurses and other health workers are still a problem in these countries. Together with out of the pocket money, these informal payments weaken the access to health care, delay the diagnose and worsen patient situation.
- Out of the pocket money remains a big problem for these countries. High level of out of the pocket money led to households becoming impoverished.
- Corruption in these countries is still a problem and for health care, also. For cancer patients, as for other patients, corruption means inefficiency of a system which already function with some difficulties.
- There is a need to increase and to improve the capacity to collect population health data using different methods. Without accurate data, it is difficult to increase the efficiency of cancer policies and programmes. National and regional strategies need to be developed in order to organized reliable screening programs for early cancer detection, campaigns for preventing cancer, adequate state-of-the-art diagnostic, and treatment equipment, advanced treatment modalities that can serve as a base for data analysis and strategic planning (Ristova et al. 2021, p.2).

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Annex 1

Health Status in Moldova

Indicator	Value/Year*	Value/Year*	Value/Year*
General Health Selected Indicators			
Life expectancy at birth[a]	71/2019	70/2020	69/2021
Infant mortality rate per 1000 live births[b]	13/2019	13/2020	12/2021
Mortality from the cardiovascular diseases, cancer, diabetes or cardio respiratory diseases[c]	24.4/2017	24.5/2018	24.1/2019
Diabetes prevalence[d] (% population ages 20 – 79)			
Depression prevalence[e]			
Hospital beds per 10,000 inhabitants[i]	62/2012	58/2013	57/2014
Doctors per 10,000 inhabitants[j]	41/2017	33/2019	41/2020
Nurses and midwives per 10,000 inhabitants[k]	62/2018	51/2019	61/2020
Health expenditure per capita (US$)[l]	276.47/2018	284.31/2019	306.65/2020
Health expenditure (%GDP)[m]	6.59/2018	6.37/2019	6.78/2020
CANCER Related indicators			
Cancer incidence[1]			
Smoking rate (% of all population)[n]	28.7/2018	28.7/2019	29/2020
Obesity rate (%)[o]	18.3/2015	18.7/2016	20.6/2019
Alcohol consumption per capita/year (liters)[p]	11.4/2010	11.3/2015	11.4/2019
Air pollution levels based on annual average PM2.5 concentration (μg/m³)[r]		22.6/2022	15.7/2023

Value/Year* express the value according to the year that value was available

1 Incidence rates are calculated as the number of cancers diagnosed (numerator) divided by the number of persons or person-years at risk for the cancer (denominator) (Marcus, 2022, p. 39).

a) Available at: https://data.worldbank.org/indicator/SP.DYN.LE00.IN?locations=MD

b) Available at: https://data.worldbank.org/indicator/SP.DYN.IMRT.IN?locations=MD

c) Available at: https://data.worldbank.org/indicator/SH.DYN.NCOM.ZS?locations=MD

i) Available at: https://data.worldbank.org/indicator/SH.MED.BEDS.ZS?locations=FR-MD

j) Available at: https://data.worldbank.org/indicator/SH.MED.PHYS.ZS?locations=FR-MD

k) Available at: https://data.worldbank.org/indicator/SH.MED.NUMW.P3?locations=FR-MD

l) Available at: https://data.worldbank.org/indicator/SH.XPD.CHEX.PC.CD?locations=MD

m) Available at: https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS?locations=MD

n) Available at: https://www.macrotrends.net/global-metrics/countries/MDA/moldova/smoking-rate-statistics

o) Available at: https://globalnutritionreport.org/resources/nutrition-profiles/europe/eastern-europe/republic-moldova/

p) Available at: https://data.worldbank.org/indicator/SH.ALC.PCAP.LI?end=2019&locations=MD&start=2000&view=chart

r) Available at: https://www.iqair.com/world-most-polluted-countries

Annex 2

Health Status in Montenegro

Indicator	Value/Year*	Value/Year*	Value/Year*
General Health Selected Indicators			
Life expectancy at birth[a]	77/2019	76/2020	74/2021
Infant mortality rate per 1000 live births[b]	2/2019	2/2020	2/2021
Mortality from the cardiovascular diseases, cancer, diabetes or cardio respiratory diseases[c]	22.8/2017	22.5/2018	22.3/2019
Diabetes prevalence[d] (% population ages 20 – 79)	8.7/2016		9.1/2021
Depression prevalence[e]			
Hospital beds per 10,000 inhabitants[i]	39/2015	39/2016	39/2017
Doctors per 10,000 inhabitants[j]	27/2019	27/2020	28/2021
Nurses and midwives per 10,000 inhabitants[k]	52/2019	54/2020	57/2021
Health expenditure per capita (US$)[l]	727.26/2018	732.35/2019	866.17/2020
Health expenditure (%GDP)[m]	8.34/2018	8.33/2019	11.42/2020
CANCER Related indicators			
Cancer incidence[1]			
Smoking rate (% of all population)[n]	31.8/2018	31.8/2019	31.4/2020
Obesity rate (%)[o]	22.8/2015	23.2/2016	25.6/2019
Alcohol consumption per capita/year (liters)[p]	8/2016	11.47/2018	10.34/2019
Air pollution levels based on annual average PM2.5 concentration ($\mu g/m^3$)[r]	35.2/2021	15.7/2022	21.3/2023

Value/Year* express the value according to the year that value was available

1 Incidence rates are calculated as the number of cancers diagnosed (numerator) divided by the number of persons or person-years at risk for the cancer (denominator) (Marcus, 2022, p. 39).

a) Available at: https://data.worldbank.org/indicator/SP.DYN.LE00.IN?locations=ME

b) Available at: https://data.worldbank.org/indicator/SP.DYN.IMRT.IN?end=2021&locations=ME&start=1984&view=chart

c) Available at: https://data.worldbank.org/indicator/SH.DYN.NCOM.ZS?locations=ME

d)Available at: https://data.worldbank.org/indicator/SH.STA.DIAB.ZS?locations=HU-ME

i) Available at: https://data.worldbank.org/indicator/SH.MED.BEDS.ZS?locations=ME

j) Available at: https://data.worldbank.org/indicator/SH.MED.PHYS.ZS?locations=ME

k) Available at: https://data.worldbank.org/indicator/SH.MED.NUMW.P3?locations=ME

l) Available at: https://data.worldbank.org/indicator/SH.XPD.CHEX.PC.CD?locations=ME-TR

m) Available at: https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS?locations=ME

n) Available at: https://www.macrotrends.net/global-metrics/countries/MNE/montenegro/smoking-rate-statistics

o) Available at: https://globalnutritionreport.org/resources/nutrition-profiles/europe/southern-europe/montenegro/

p) Available at: https://tradingeconomics.com/montenegro/total-alcohol-consumption-per-capita-liters-of-pure-alcohol-projected-estimates-15-years-of-age-wb-data.html

r) Available at: https://www.iqair.com/world-most-polluted-countries

Annex 3

Health Status in North Macedonia

Indicator	Value/Year*	Value/Year*	Value/Year*
General Health Selected Indicators			
Life expectancy at birth[a]	77/2019	74/2020	75/2021
Infant mortality rate per 1000 live births[b]	5.96/2019	5.20/2020	4.65/2021
Mortality from the cardiovascular diseases, cancer, diabetes or cardio respiratory diseases[c]	23.6/2017	23.2/2018	22.7/2019
Diabetes prevalence[d] (% population ages 20 – 79)	7.7/2011		6.1/2021
Depression prevalence[e]	5.0/2015		
Hospital beds per 10,000 inhabitants[i]	44/2015	44/2016	43/2017
Doctors per 10,000 inhabitants[j]	27/2012	28/2013	28/2015
Nurses and midwives per 10,000 inhabitants[k]	41/2012	42/2013	37/2015
Health expenditure per capita (US$)[l]	387.47/2018	421.39/2019	452.97/2020
Health expenditure (%GDP)[m]	6.46/2018	7.07/2019	7.89/2020
CANCER Related indicators			
Cancer incidence[1]	7,392/2020[f]		7,563/2022[g]
Smoking rate (% of all population)			
Obesity rate (%)[o]	21.95/2015	22.35/2016	24.5/2019
Alcohol consumption per capita/year (liters)[p]	4.3/2010	4.3/2015	4.6/2019
Air pollution levels based on annual average PM2.5 concentration (μg/m^3)[r]	25.4/2021	25.6/2022	25.2/2023

Value/Year* express the value according to the year that value was available

1 Incidence rates are calculated as the number of cancers diagnosed (numerator) divided by the number of persons or person-years at risk for the cancer (denominator) (Marcus, 2022, p. 39).

a) Available at: https://data.worldbank.org/indicator/SP.DYN.LE00.IN?end=2021&locations=MK&name_desc=false&start=1960&view=chart

b) Available at: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/infant-mortality-rate-(probability-of-dying-between-birth-and-age-1-per-1000-live-births)

c) Available at: https://data.worldbank.org/indicator/SH.DYN.NCOM.ZS?end=2019&locations=MK&name_desc=true&start=2000&view=chart

d) Available at: https://data.worldbank.org/indicator/SH.STA.DIAB.ZS?end=2021&locations=MK&start=2011

e) Available at: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/estimated-population-based-prevalence-of-depression

f) Available at: https://www.wcrf.org/cancer-trends/global-cancer-data-by-country/

g) Available at: https://gco.iarc.who.int/media/globocan/factsheets/populations/807-north-macedonia-fact-sheet.pdf

i) Available at: https://data.worldbank.org/indicator/SH.MED.BEDS.ZS?locations=MK&name_desc=false

j) Available at: https://data.worldbank.org/indicator/SH.MED.PHYS.ZS?locations=MK

k) Available at: https://data.worldbank.org/indicator/SH.MED.NUMW.P3?locations=MK

l) Available at: https://data.worldbank.org/indicator/SH.XPD.CHEX.PC.CD?locations=MK

m) Available at: https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS?locations=MK

o) Available at: https://globalnutritionreport.org/resources/nutrition-profiles/europe/southern-europe/north-macedonia/

p) Available at: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/total-(recorded-unrecorded)-alcohol-per-capita-(15-)-consumption

r) Available at: https://www.iqair.com/world-most-polluted-countries

Annex4

Health Status in UKRAINE

Indicator	Value/Year*	Value/Year*	Value/Year*
General Health Selected Indicators			
Life expectancy at births[a]	72/2020	71/2021	72/2022
Infant mortality rate per 1000 live births[b]	7.28/2019	7.15/2020	7.24/2021
Mortality from the cardiovascular diseases, cancer, diabetes or cardio respiratory diseases[c]	25.1/2017	26.1/2018	25.5/2019
Diabetes prevalence[d] (% population ages 20 – 79)	2.9/2011		6.6/2021
Depression prevalence[e]	6.3/2015		
Hospital beds per 10,000 inhabitants[i]	89 (2012)	88/2013	75/2014
Doctors per 10,000 inhabitants[j]	35/2012	35/2013	30/2014
Nurses and midwives per 10,000 inhabitants[k]	75/2012	76/2013	67/2014
Health expenditure per capita (US$)[l]	221.47/2018	246.91/2019	269.73/2020
Health expenditure (%GDP)[m]	7.52/2018	7.09/2019	7.62/2020
CANCER Related indicators			
Cancer incidence[1]	157,275/2020[f]	160,00/2021[g]	155,239/2022[h]
Smoking rate (% of all population)[n]	26.2/2018	26.2/2019	25.8/2020
Obesity rate (%)[o]	23.5/2015	23.85/2016	26/2019
Alcohol consumption per capita/year (liter)[p]	11.7/2010	9.7/2015	8.7/2019
Air pollution levels based on annual average PM2.5 concentration (μg/m^3)[r]	18.5/2021	9.7/2022	8.6/2023

Value/Year* express the value according to the year that value was available

[1]Incidence rates are calculated as the number of cancers diagnosed (numerator) divided by the number of persons or person-years at risk for the cancer (denominator) (Marcus, 2022, p. 39).

[a)] Available at: https://data.worldbank.org/indicator/SP.DYN.LE00.IN?end=2021&locations=UA&most_recent_year_desc=false&start=1960&view=chart

[b)] Available at: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/infant-mortality-rate-(probability-of-dying-between-birth-and-age-1-per-1000-live-births)

[c)] Available at: https://data.worldbank.org/indicator/SH.DYN.NCOM.ZS?end=2019&locations=UA&most_recent_year_desc=false&start=2000&view=chart

[d)] Available at: https://data.worldbank.org/indicator/SH.STA.DIAB.ZS?end=2021&locations=UA&start=2011&view=chart

[e)] Available at:

https://www.who.int/data/gho/data/indicators/indicator-details/GHO/estimated-population-based-prevalence-of-depression

[f)] Available at: https://www.wcrf.org/cancer-trends/global-cancer-data-by-country/

[g)] Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9270614/

[h)] Available at:https://gco.iarc.who.int/media/globocan/factsheets/populations/804-ukraine-fact-sheet.pdf

[i)] Available at:https://data.worldbank.org/indicator/SH.MED.BEDS.ZS?locations=UA

[j)] Available at:https://data.worldbank.org/indicator/SH.MED.PHYS.ZS?locations=UA

[k)] Available at:https://data.worldbank.org/indicator/SH.MED.NUMW.P3?locations=UA

[l)] Available at:https://data.worldbank.org/indicator/SH.XPD.CHEX.PC.CD?locations=UA

[m)] Available at:https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS?locations=UA

[n)] Available at: https://www.macrotrends.net/global-metrics/countries/UKR/ukraine/smoking-rate-statistics

[o)] Available at:https://globalnutritionreport.org/resources/nutrition-profiles/europe/eastern-europe/ukraine/

[p)] Available at:

https://www.who.int/data/gho/data/indicators/indicator-details/GHO/total-(recorded-unrecorded)-alcohol-per-capita-(15-)-consumption

[r)] Available at: https://www.iqair.com/world-most-polluted-countries