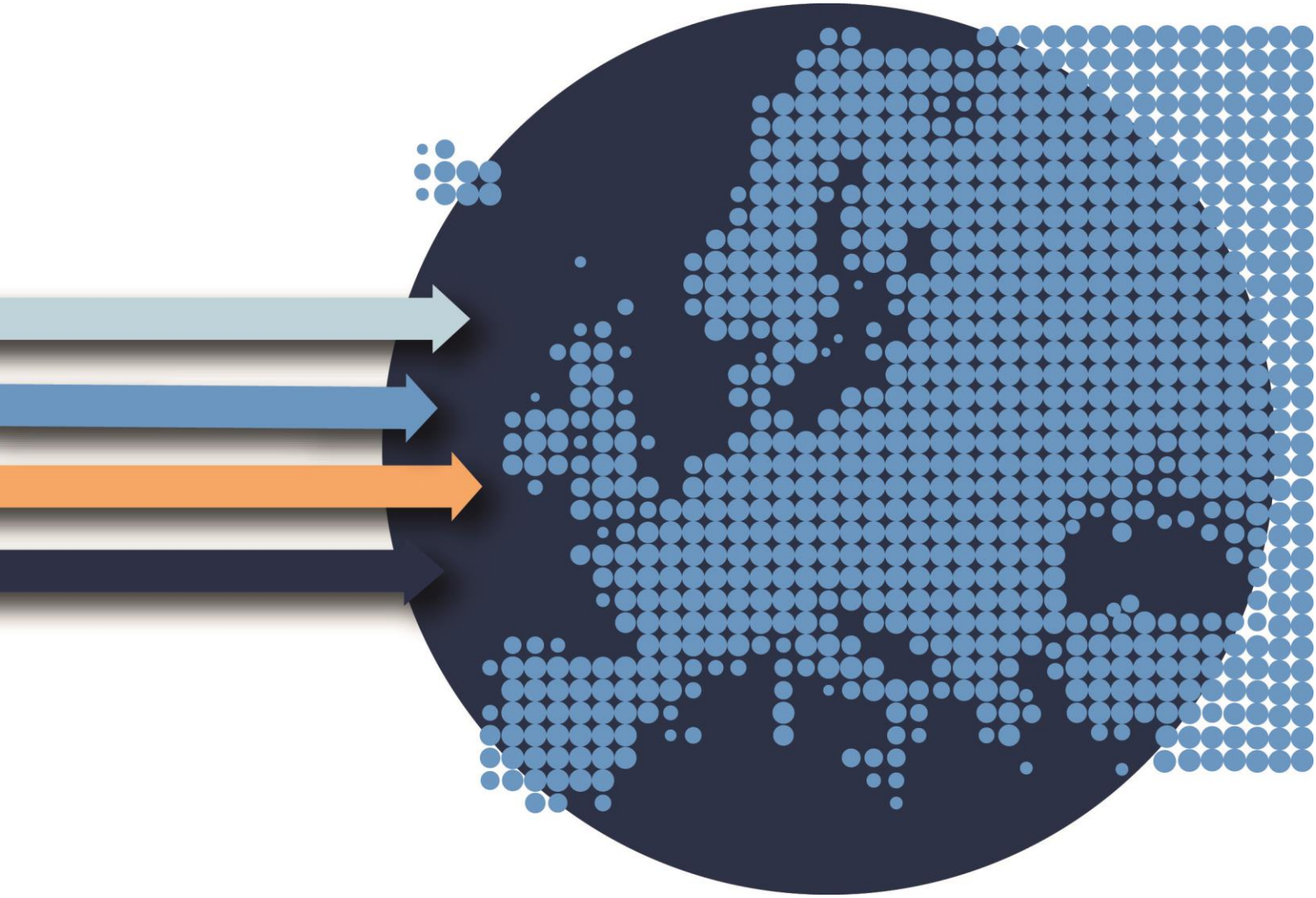
CANCER CARE IN TÜRKIYE IN A EUROPEAN CONTEXT



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Foreword

Tackling cancer is one of the major health policy issues globally and also in Türkiye. The aging societies all over the world are faced with an increasing disease burden from cancer. Yet significant scientific advancements have been made in recent decades offering improved diagnosis and treatment of cancer. The key challenge for health systems is to cater for an increasing number of patients while at the same time improving the quality of care through incorporating innovative diagnostic and treatment modalities.

This report describes the state of cancer care in Türkiye. The report builds on a comparative analysis of Türkiye with three European countries. It intends to raise awareness of the size of the burden of cancer and the need to address it comprehensively. It also provides numerous recommendations on how to improve cancer care in Türkiye based on successful examples from the European benchmark countries and international best practices.

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Lund, October 2022

Peter Lindgren
Managing Director, IHE

Acknowledgement

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Disclaimer: This report does not necessarily reflect the views of MSD or any other external experts or institutions involved.

Executive summary

Cancer is the second-leading cause of death and the leading cause of the overall burden of disease in Türkiye

Almost one in five deaths (≈18%) in Türkiye are caused by cancer. This makes cancer the second-leading cause of death, behind of cardiovascular diseases. In addition, estimations by the WHO indicate that cancer has become the leading cause of the overall burden of disease (measured using DALYs), surpassing cardiovascular diseases during the last two decades. With this development Türkiye follows in the footsteps of other countries in Western and Central Europe.

The annual number of new cancer cases in Türkiye could almost double to 400,000 cases until 2040, driven mostly by demographic changes

The latest statistics indicate that around 182,000 new cancer cases (excl. non-melanoma skin cancer) were recorded in Türkiye in 2017. The WHO estimates that this number might increase to almost 400,000 cases in 2040. This development is mostly driven by demographic factors – overall population growth and especially population aging, as cancer is an aging-associated disease. At the same time, around 78,000 cancer deaths were recorded in Türkiye in 2019. The number of deaths is also expected to nearly double in the wake of the increasing number of new cases. Improvements in all areas of cancer care are needed to lessen the expected increases in new cases and deaths.

Cancer survival has improved in Türkiye, yet if survival rates were on par with France, thousands of deaths could be avoided every year

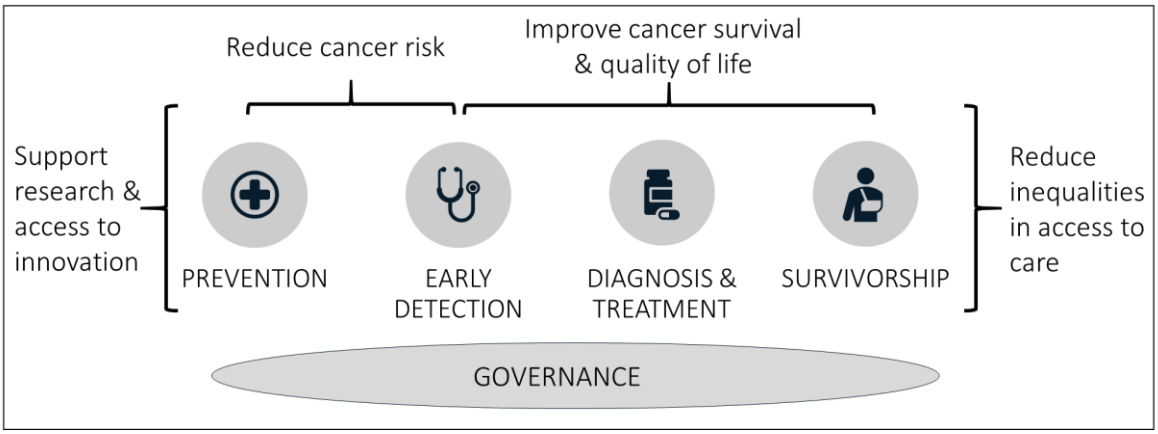
Survival rates in most major cancer types have improved in Türkiye since the early 2000s. However, the Turkish survival rates are lower than the equivalent rates in Belgium and France. Almost 5,000 additional cancer patients (equivalent to 10% of the current survivors) would survive cancer every year if Türkiye achieved the same survival rates as France in five major cancer types. This underlines the urgency to improve the quality of care delivered to patients in Türkiye.

The economic burden of cancer amounted to €2.48 billion or €30 per capita in 2019

The economic burden of cancer refers to direct costs (health expenditure on cancer care), indirect costs (productivity losses) and informal care costs. In Türkiye, the direct costs were estimated to be €1.48 billion or €18 per capita in 2019. This would equal 5% of total health expenditure. Indirect costs were estimated to be €1.00 billion or €12 per capita in 2019, whereas it was not possible to estimate the size of informal care costs. Therefore, the economic burden amounted to at least €2.48 billion (TRY 15.8 billion) or €30 per capita (TRY 192) in Türkiye in 2019.

How can Turkish cancer care be improved?

Previous examples in Europe, such as the Europe's Beating Cancer Plan launched in 2021, have shown that high-level political commitment is important to make the fight against cancer a top priority in health care. Cancer control efforts need to be comprehensive and address the whole continuum of care in order to take on the many current and future challenges, as depicted in the graph below. This report focuses on three of the five depicted areas of cancer control in Türkiye – governance, early detection (with a focus on screening), and diagnosis and treatment. It identifies key challenges and provides recommendations for improvement.



Recommendations to improve cancer care in Türkiye also need to consider the general challenges of the Turkish health care system. For the last two decades, a fundamental challenge has been the comparatively low level of health care spending. In 2019, the public part of the total health expenditure amounted to 3.4% of GDP, falling short of the informal WHO spending target of 4–5% of GDP. The comparatively low public spending level limits the quality and the range of modern health services provided through public health insurance by the SSI.

The governance of cancer care needs a revival

The governance of cancer care in Türkiye has been shaped by three NCCPs issued by the Ministry of Health since 2009, with the current NCCP covering the period 2021–2023. The NCCPs are characterized by a waning level of comprehensiveness and ambition. The current NCCP includes merely five actions and none of these actions are related to "diagnosis and treatment" and "survivorship". All three NCCPs also lacked funding plans. A new NCCP with a comprehensive set of actions across the whole continuum of cancer care should be established, and it should also include a crude funding plan for all planned actions. Such a new NCCP would need to build on cooperation between relevant stakeholders, including the ministries of health and finance, the SSI, physician organizations, patient organizations, industry, and academia.

Decision-making in cancer care should be supported by relevant local data

High-quality local epidemiological data on cancer are crucial to inform the governance of cancer care. Türkiye has a good track record in cancer registration since the establishment of the first cancer registry in the Izmir province in 1992. However, challenges remain to make the most of the collected data, in particular their use for regular performance assessment in cancer care. Main priorities are to (1) improve the functionality and the quality of the data in all provinces currently not used for official statistics by the Ministry of Health, (2) address underreporting, (3) start measuring survival, and (4) accelerate the publication of the latest data.

Screening activities need to address awareness challenges in the population

Türkiye was an early adopter of three organized, population-based cancer screening programs for breast, cervical, and colorectal cancer in line with WHO recommendations. However, all programs are characterized by low participation rates. Despite improvements between 2014 and 2019, the programs reach only around 30–40% of the target population, falling short of aim of 70% defined in the first two NCCPs.

The main challenge to be addressed is the lack of awareness in the population concerning (1) the risks to develop cancer, (2) the benefits of early detection through screening, and (3) how screening and KETEMs work. Many people are not aware that screening services are free of charge and that no appointment is required at KETEMs. The geographic accessibility to KETEMs has improved greatly and mobile teams using trucks have in recent years tried to reach remote areas. However, instead of inviting people by mail/phone to come to cervical and colorectal cancer screening at KETEMs, an invitation could be sent together with the automatic delivery of home test kits by mail.

The cancer patient pathway needs to be optimized

The patient pathway from first symptoms until treatment start can be lengthy in Türkiye due to the lack of continuity and coordination of care. The introduction of structured and standardized patient pathways, including the establishment of a better referral system with electronic transfer of patient data between primary, secondary, and tertiary care, could reduce the time to treatment, avoid the duplication of services/tests, and improve the overall quality of care.

Medical staff, treatment facilities, and diagnostic testing need to be geared to future requirements in the provision of cancer care

The availability of specialized physicians involved in the diagnosis and treatment of cancer in Türkiye is good in relation to the number of cancer patients, while the number of nurses appears to be rather low. There is also an ongoing shift in the treatment setting from inpatient care to outpatient care. The planning of new treatment facilities for cancer patients needs to consider the changing treatment setting away from inpatient care, which might also be an opportunity for future savings.

The availability of modern diagnostic imaging equipment (scanners) in Türkiye is high in relation to the number of cancer patients. Basic biomarker testing is reimbursed and tied to the availability of appropriate cancer medicines reimbursed by the SSI. It is important to maintain this link between the reimbursement of biomarker testing and medicines in the ongoing move towards personalized medicine. The introduction of multigene testing through NGS will become an increasing priority in the coming years, which will require a modernization of diagnostic laboratories and training of staff.

New developments in radiation therapy offer the opportunity to free up resources

The number of radiation therapy machines and trained professionals to operate the machines have improved in the recent decade in Türkiye. In relation to the number of cancer patients, radiation therapy machines are nowadays available at a good ratio. The adoption of hypofractionation should be prioritized. This would shorten treatment times, prevent the need for additional machines, facilitate access for patients in rural areas, and free up resources for use in other areas of cancer care.

Patient access to newer cancer medicines is limited in a European context, but could be improved by a stronger emphasis on benefits in relation to costs in decision-making

The limited availability of newer cancer medicines is a major challenge for cancer care in Türkiye. Challenges exists both in the regulatory approval by the TMMDA and the reimbursement by the Reimbursement Commission. The regulatory approval process by the TMMDA is comparatively long, often exceeding the overall approval target timelines. This process could be expedited by (1) accepting GMP inspection outcomes and certificates of manufacturing sites from other well-established regulatory bodies, and (2) postponing the pricing assessment after regulatory approval.

The reimbursement of newer cancer medicines by the SSI is comparatively limited in a European context. In the case of lung cancer, the access to treatment options in Türkiye in 2022 corresponded to the options recommended by European clinical guidelines in 2016, indicating an access delay of at least six years to new cancer medicines. The main sticking point in the reimbursement decisions of the Reimbursement Commission is the anticipated budget impact of high-priced medicines. A value-based approach calls for an assessment of the costs and the benefits of new medicines. Switching to “value-for-money” (cost-effectiveness) as the main criterion for the reimbursement decision instead of the budget impact could improve the access situation.

Opportunities to create budget headroom for new cancer medicines could be explored more actively. These include the (1) creation of a dedicated fund for new cancer medicines, (2) prioritization of cancer medicines with high clinical benefit for reimbursement, (3) use of and local production of generics and biosimilars, (4) support of clinical trials activity, (5) application of a societal perspective in the evaluation of medicines considering effects on indirect costs and informal care costs from improved treatment outcomes.

List of abbreviations

AMO	French Public Health Insurance
ASMR	Added therapeutic value scale used by the French HAS
CCC	Comprehensive Cancer Center
CT	Computed tomography
DALY	Disability-adjusted life year
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicines Agency
ESMO	European Society for Medical Oncology
FDA	Food and Drug Administration in the United States
FISH	Fluorescent in situ hybridization
FIT	Fecal immunochemical test
FOBT	Fecal occult blood test
GDP	Gross domestic product
GLOBOCAN	Global Cancer Observatory
GMP	Good manufacturing practices
HAS	French National Authority for Health
HPV	Human papillomavirus
HTA	Health technology assessment
IAEA	International Atomic Energy Agency
ICD-10	International Classification of Diseases, 10th revision
ICSS	International Cancer Survival Standard
IHC	Immunohistochemistry
INCa	French National Cancer Institute
KETEM	Cancer Early Diagnosis, Screening and Training Centers (Kanser Erken Teşhis, Tarama ve Eğitim Merkezi)
LDCT	Low-dose computed tomography
Linac	Medical linear accelerators
MCBS	ESMO's Magnitude of Clinical Benefit Scale
MoH	Ministry of Health
MRI	Magnetic resonance imaging
MV	Megavoltage
NCCP	National cancer control program
NFZ	Polish National Health Fund
NGO	Non-governmental organization
NGS	Next-generation sequencing
NIHDI	Belgian National Institute for Health and Disability Insurance
NSCLC	Non-small cell lung cancer
OECI	Organisation of European Cancer Institutes
PCR	Polymerase chain reaction
PET	Positron emission tomography
PPP	Purchasing power parity
PSA	Prostate-specific antigen
PYWLL	Potential years of working life lost
SHI	French Statutory Health Insurance
SSI	Social Security Institution in Türkiye
TMMDA	Turkish Medicines and Medical Devices Agency
UHC	Universal health coverage
UN	United Nations
WHO	World Health Organization

Country abbreviations

BEL	Belgium
EU	European Union
FRA	France
POL	Poland
TUR	Türkiye

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1. Introduction

Cancer is the collective name of a group of over 100 diseases that can occur in all parts of the body. The defining feature of the disease is the uncontrolled growth and division of abnormal cells in the body. These cells form a tumor that may invade adjoining parts of the body and spread to other organs, a process called metastasis. Metastases disrupt the normal functioning of the body and are the major cause of death from cancer (1). The most common cancer types worldwide are lung cancer, breast cancer, colorectal cancer, and prostate cancer. Globally, over 19 million new cancer cases were diagnosed in 2020 and almost 10 million people died from cancer, making cancer the second leading cause of death (2).

Cancer in Türkiye is on the rise. Population growth, population aging, and changes in lifestyles mean that the number of newly diagnosed cancer cases (incidence) and the number of cancer deaths (mortality) are predicted to rise steeply in the coming decades. Figure 1 shows projections of how the expected demographic changes[1] will affect the local situation (3). New cancer cases might increase by 67% from 227,000 cases in 2020 to 380,000 cases in 2040 (from approx. 270 to 400 cases per 100,000 inhabitants). The number of deaths might increase by 85% from 126,000 cases in 2020 to 232,000 cases in 2040 (from approx. 150 to 250 deaths per 100,000 inhabitants).

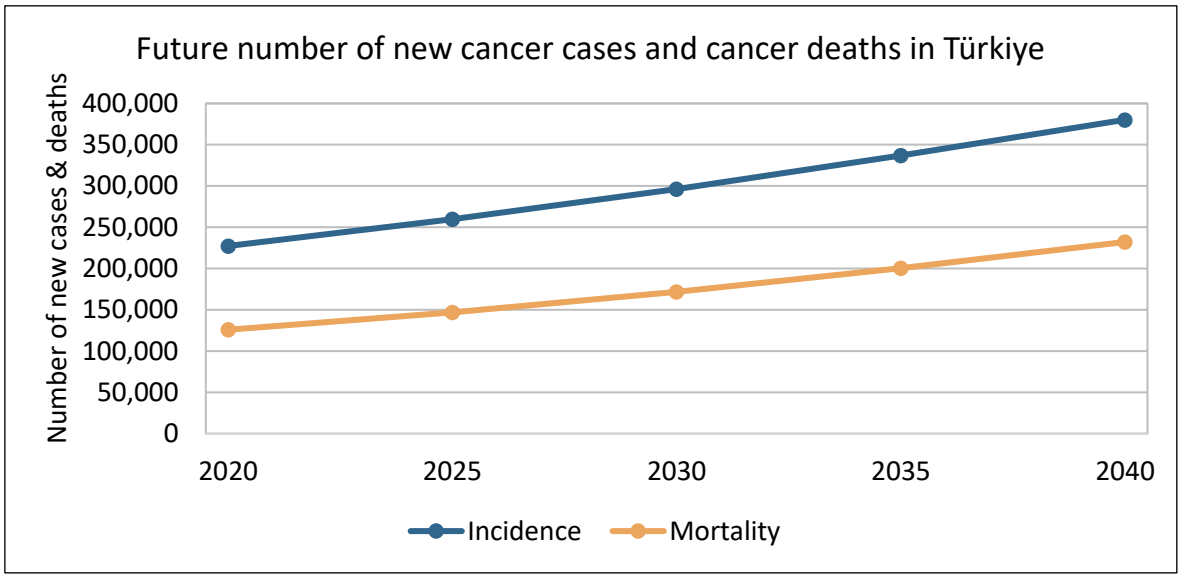


Figure 1: Projection of cancer incidence and mortality in Türkiye, 2020–2040

Notes: Cancer refers to all cancer sites but non-melanoma skin cancer (ICD-10 C00-C97/C44). Projections are based on constant age-specific rates and only driven by expected changes in the population composition (base year = 2020). Source: GLOBOCAN (3).

[1] The demographic changes only include overall population growth and shifts in the age distribution. It does not include changes in cancer-related risk factors, such as smoking or obesity. The projections show what would happen in the absence of any changes in the age-specific risk to get cancer and the age-specific risk to die from cancer.

The projections of the future development in Figure 1 underline the need to tackle cancer comprehensively. Actions in all areas of cancer care – prevention, screening, diagnosis and treatment, survivorship – are needed to flatten the increasing curves in cancer incidence and mortality. Providing patients with access to high-quality cancer care represents a major challenge for all health care systems. Effective strategies to balance constrained health care budgets with access to high-quality cancer care are of great importance. On the scientific front, great progress has been made in recent decades (see chapter 3 in ref. (4) and chapter 2 in ref. (5)). Our understanding of the nature of cancer has never been better. Modern technologies to detect and treat cancer are evolving continuously. A critical task for health policy makers is to ensure patient access to innovation in this quickly evolving environment.

1.1 Purpose and scope of the report

The purpose of this report is to describe the current state of cancer care in Türkiye. The report aims to provide a comprehensive assessment of key areas of cancer control, as well as provide information on the disease burden and the economic burden of cancer. It aims to identify barriers to effective, efficient, equitable, and responsive cancer care, based on which policy recommendations for improved cancer care are made. This information should support efforts to plan and take action to reduce the burden of cancer.

Türkiye is benchmarked against three selected European countries – Belgium, France, Poland – in this report. They represent different examples of providing cancer care in relation to economic strength, population size, structure of the health system, and governance of cancer care.

The report consists of seven main chapters. Chapter 2 analyzes the burden of cancer, distinguishing between the disease burden and the economic burden. Chapter 3 reviews the organization and financing of health care. Chapter 4 defines access to high-quality cancer care. Chapter 5 analyzes the governance of cancer care. Chapter 6 analyzes cancer screening. Chapter 7 analyzes the diagnosis and treatment of cancer. Chapter 8 provides recommendations to support the provision of high-quality cancer care in Türkiye.

2. Burden of cancer

This chapter describes key aspects of the burden of cancer in Türkiye. It covers the disease burden of cancer in relation to other diseases (section 2.1), cancer epidemiology (section 2.2), the future development of cancer numbers (section 2.3), and the economic burden of cancer (section 2.4).

2.1 Burden of disease

To understand the extent of the burden of cancer (here defined as malignant neoplasms, ICD-10 C00-C97, unless otherwise noted) in relation to other diseases, two measures are used. The first measure is the number of cancer deaths in comparison to the total number of deaths. The second measure is the number of Disability Adjusted Life Years (DALYs) – a measure of both premature mortality and morbidity caused by disease – caused by cancer in comparison to other diseases.

2.1.1 Deaths

Cancer is in most cases a lethal disease, if left untreated. In 2019, almost 80,000 people died from cancer in Türkiye; see Table 1. This made cancer (18% of all deaths) the second leading cause of death behind cardiovascular diseases (37% of all deaths); see Figure 2. By comparison, cancer is the leading cause of death in Belgium and France, accounting for around a quarter of all deaths. In Poland, cancer also accounts for around a quarter of all deaths, but cardiovascular deaths are even more common, similar to the situation in Türkiye.

Table 1: Total deaths and deaths by cancer

	Türkiye	Belgium	France	Poland
Year	2019	2019	2017	2019
Population (mid-year)	82.6 million	11.5 million	66.9 million	38.0 million
Median age (years)	32.0	41.7	41.4	41.0
Life expectancy at birth (years)	79.1	82.1	82.7	78.0
Total deaths	435,941	108,793	606,354	410,564
Total deaths per 100,000 inhabitants	528	947	906	1,081
Cancer deaths	77,887	26,700	164,090	100,374
Cancer deaths per 100,000 inhabitants	94	232	245	264
Proportion of cancer deaths	18%	25%	27%	24%

Notes: Cancer is defined as malignant neoplasms (ICD-10 C00–C97). Source: Eurostat and TurkStat (6-10).

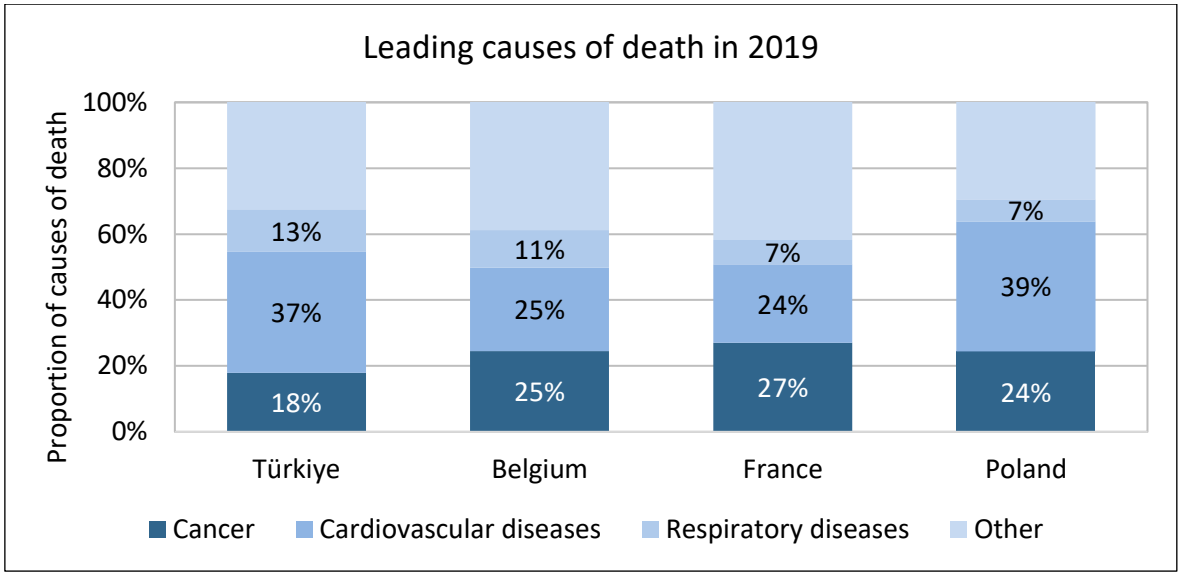


Figure 2: Leading causes of death, 2019

Notes: Cancer is defined as malignant neoplasms (ICD-10 C00–C97), cardiovascular diseases ICD-10 I00–I99, respiratory diseases ICD-10 J00–J99. Numbers for France refer to 2017. Source: Eurostat and TurkStat (6, 10).

Figure 3 shows how the 435,000 total deaths and the 78,000 cancer deaths in Türkiye in 2019 were distributed across different age groups. The absolute number of cancer deaths increases with age and is highest in the age group 65–75 years with over 23,000 deaths. Cancer deaths thus peak in a younger age group than all deaths combined, which are highest among 75–84 year-olds. The proportion of cancer deaths follows an inverted U-shape across the age distribution (illustrated by the red line in Figure 3). The proportion of people dying from cancer is highest in the age groups 45–54 and 55–64 years with over 30% of deaths.

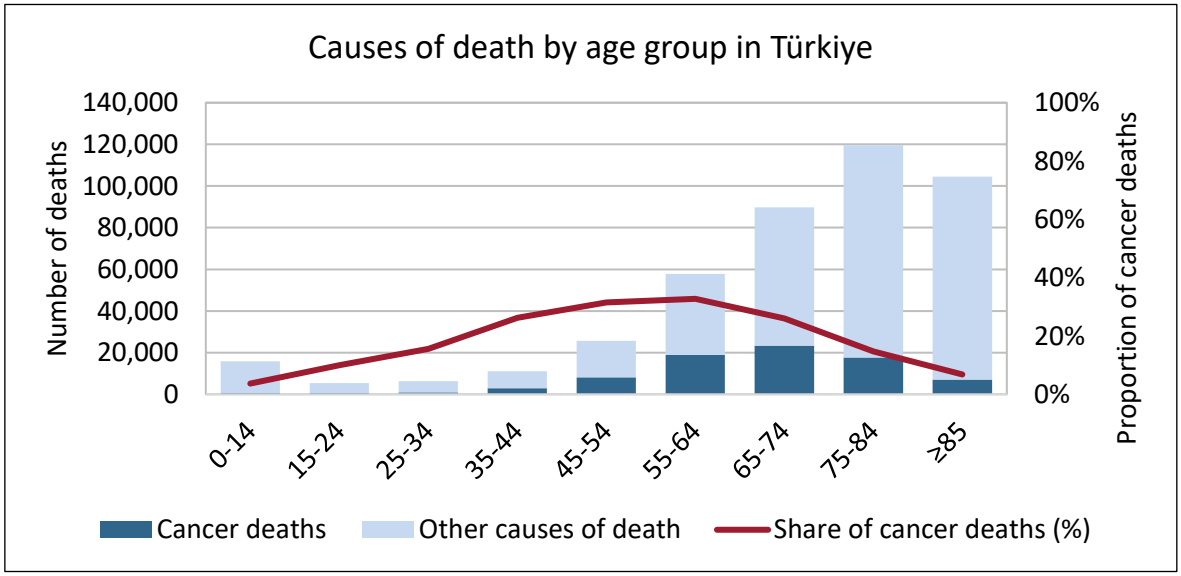


Figure 3: Number of deaths by cause (left scale) and cancer deaths as a proportion of total deaths (right scale) by age group in Türkiye, 2019

Notes: Cancer is defined as neoplasms (ICD-10 C00–D48). Source: TurkStat (10).

2.1.2 DALYs

DALYs are a comprehensive measure of the disease burden, developed by the World Health Organization (WHO) (11). They consider two aspects of a disease; the morbidity aspect (the impact of a disease on people's quality of life) and the mortality aspect (premature death due to the disease). Such a comprehensive measure is important when comparing the burden of different diseases, as many diseases are not fatal but still cause a huge burden to society and health systems. One DALY represents one lost year of healthy life. The sum of all DALYs across a country's population represents the burden of disease. It can be considered as a measure of the gap between the current health state of a population and the ideal situation in which the entire population lives to an advanced age, free of disease and disability.

Figure 4 shows the development of the disease burden measured in DALYs between 2000 and 2019 (12). The total number of DALYs per 100,000 inhabitants decreased by 20% in Türkiye during this period, while lower decreases were observed in Belgium, France, and Poland. In Türkiye, this was in large part caused by a decrease in communicable diseases and infant deaths. The lower total number of DALYs per 100,000 inhabitants in Türkiye in 2019 compared to the other countries is influenced by the greater proportion of younger, healthy people in the Turkish population.

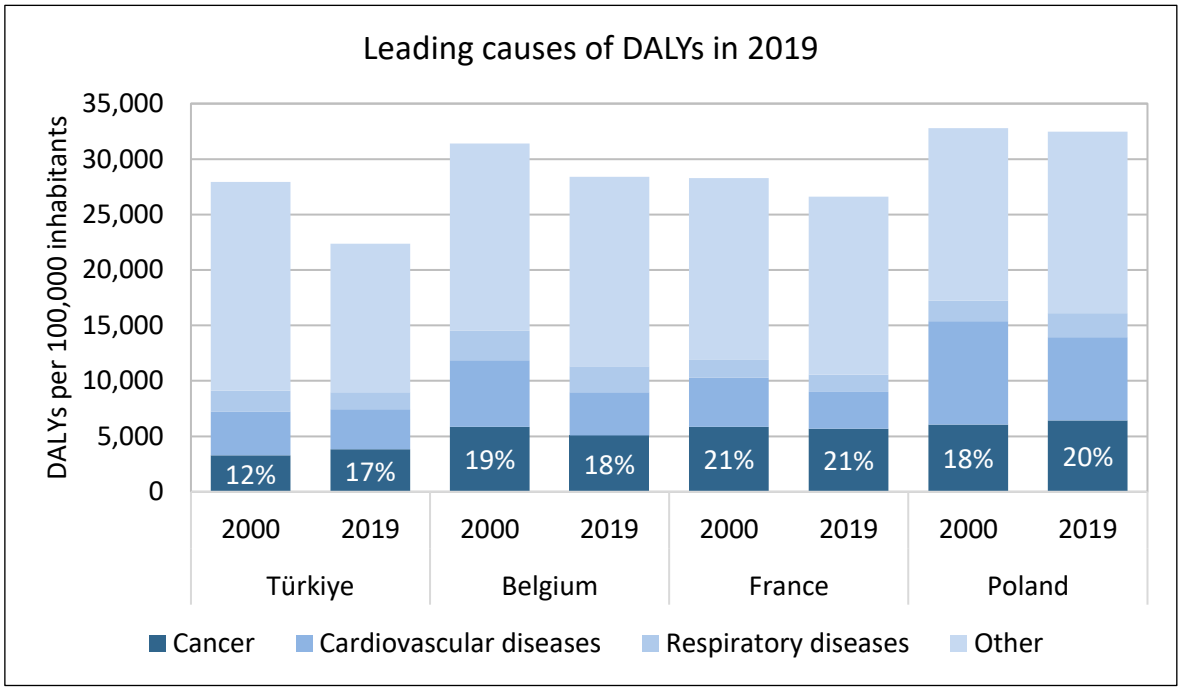


Figure 4: Leading causes of DALYs per 100,000 inhabitants, 2000 & 2019
Source: WHO (12).

Cancer caused 12% of the total DALYs in Türkiye in 2000, the second most proportion of all disease groups behind cardiovascular diseases. Until 2019, the share of cancer increased to 17% of the total DALYs. This meant that cancer overtook cardiovascular diseases and became the leading cause of

DALYs in Türkiye in 2019. By comparison, cancer was already the leading cause of DALYs in France in 2000 and remained at the top in 2019, whereas in Belgium it went from second-leading to leading cause of DALYs during this period. In Poland, cardiovascular disease remained the leading cause of DALYs, although their share declined over time while the share of cancer increased, just like in Türkiye.

2.2 Cancer epidemiology

Epidemiological measures, such as incidence, mortality, and survival, are generally used to characterize the disease burden of cancer and to monitor the development over time. Data for all of these measures are ideally collected from patient records by national population-based cancer registries. Türkiye has several regional population-based cancer registries that nowadays cover around half of the total population; see section 5.2.[2] They record newly diagnosed cases of cancer (incidence), and the Ministry of Health publishes yearly reports on the latest statistics (13). The lack of nationwide data means that the incidence data in this section should be interpreted with some caution, as the regions covered by registries are not necessarily representative of the rest of the country. Information on the number of deaths from cancer are recorded in the Turkish Statistical Institute Death Reporting System. The death registration system has gradually improved over time and provides reliable data for the whole country since reforms made in 2009 (14). Survival statistics are not available from public sources in Türkiye. Yet CONCORD, a program for worldwide surveillance of cancer survival led by the London School of Hygiene & Tropical Medicine, provides survival estimates based on data from several regional cancer registries in Türkiye (15).

2.2.1 Incidence

Cancer incidence refers to the number of new cancer cases diagnosed within a certain year in a specific geographical area. The latest estimates for cancer incidence indicated around 182,000 new cancer cases (all cancer sites except non-melanoma skin cancer) in Türkiye in 2017 (13), of which 100,000 cases in men and 82,000 cases in women.

[2] The registries cover the provinces of İzmir (established 1992), Antalya (1998), Bursa (2000), Eskişehir (2000), Samsun (2001), Trabzon (2003), Edirne (2004), Erzurum (2005), Ankara (2006), Kocaeli (2007), Gaziantep (2010), Malatya (2010), Mersin (2012), İstanbul (2012).

2.2.1.1 Crude rates and age-standardized rates

To put the latest Turkish incidence numbers into perspective – both in relation to previous years and in relation to other countries – a convenient measure is the crude rate. The total number of new cancer cases is less relevant to consider in Türkiye, because the total population is growing fast; see section 2.3. The crude rate is obtained by expressing the number of cancer cases per 100,000 inhabitants.

Figure 5 shows cancer incidence crude rates for all cancers combined (except non-melanoma skin cancer) for both sexes. In Türkiye, there has been a 70% increase in reported incidence numbers between 2002 and 2017, from 134 to 227 cases per 100,000 inhabitants. Compared to the three European comparison countries, the Turkish overall numbers are still low. Belgium and France had almost three times higher numbers than Türkiye, with increasing incidence rates of around 550 to 600 cases per 100,000 inhabitants between 2004 and 2018 (a 9% increase). Incidence numbers in Poland were about twice as high as Turkish numbers and increased by 29% from 370 to just below 480 cases per 100 inhabitants within the course of a decade only.

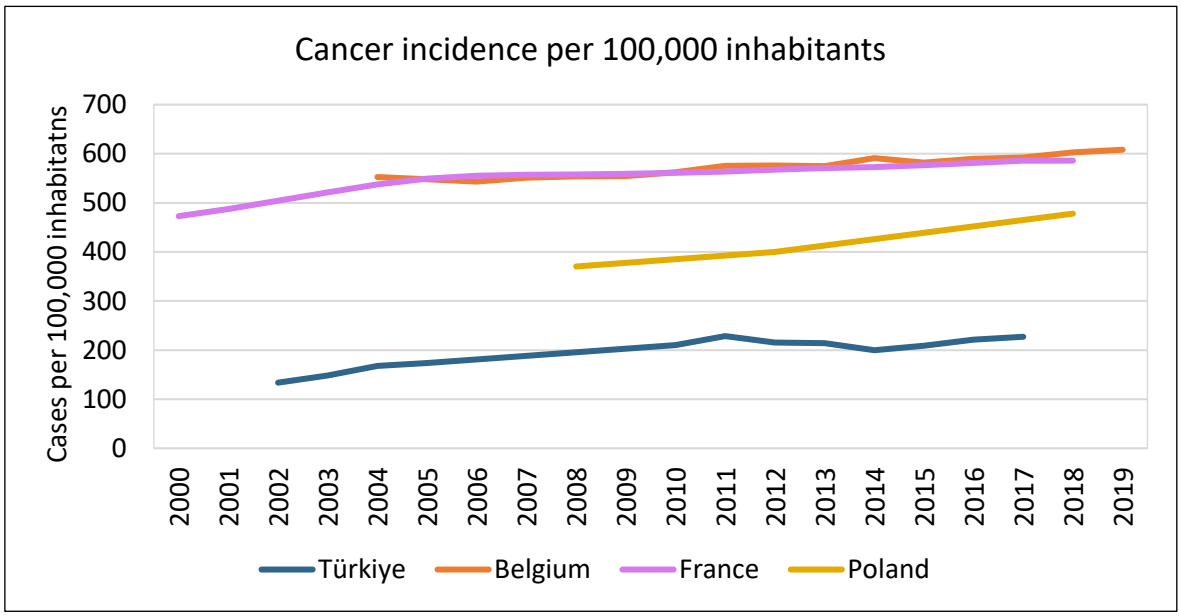


Figure 5: Cancer incidence (crude rates) per 100,000 inhabitants, 2000–2019

Notes: Cancer refers to all cancer sites except non-melanoma skin cancer (ICD-10 C00–C97/C44). Incidence rates for Türkiye combine estimates by Yilmaz et al. (2011) for 2002–2005 and the Ministry of Health for 2010–2017 (13, 16). Incidence rates for Belgium come from the Belgian cancer registry (17), for France from the network of cancer registries (Francim) (18), and for Poland from GLOBOCAN (19-21).

The numbers shown in Figure 5 pose three main questions:

(1) Why are the Turkish incidence numbers so much lower than of the other countries?

(2) Why is cancer incidence increasing in all countries?

(3) Why did Turkish cancer incidence remain stable in 2011–2017?

The following factors can help to answer all three questions.

Demographic structure: Since the risk of getting cancer increases dramatically with age (see section 2.2.1.3), a greater proportion of elderly people in the total population leads to more cancer cases. Of the four countries in Figure 5, Belgium and France had the highest proportion of elderly people between 2000 and 2020; see Figure 6. In fact, their proportion of people aged 65 years and older was between 17–21% in this period, which was more than the double of Türkiye (6–9%) and also higher than in Poland (12–19%). The younger population of Türkiye thus can partly explain why Turkish incidence rates are lower. In fact, the Turkish demographic structure in 2020 resembled the one in Poland in 1980.

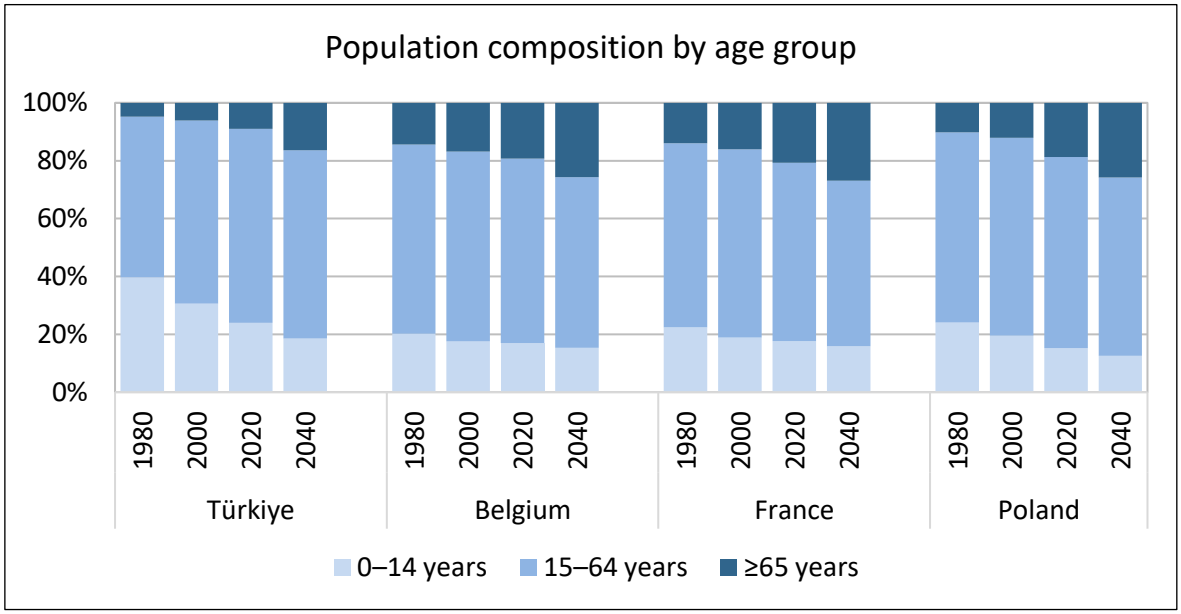


Figure 6: Population composition by age group, 1980–2040
Notes: Numbers for 2020 and 2040 are estimates based on the "medium variant". Source: UN (22).

Population aging: Figure 6 shows how the demographic structure has shifted since 1980. In all countries, the proportion of elderly people has increased. As elderly people have a higher risk of getting cancer, population aging causes increases in the number of cancer patients. Population aging thus partly explains why incidence rates have been increasing in all countries. Figure 6 also shows that the proportion of elderly people in Türkiye is expected to increase considerably between 2020 and 2040. By 2040, the Turkish demographic structure might resemble the one from Belgium and France in 2000 and from Poland in 2020. This means that the number of cancer cases can be expected to increase considerably in the coming decades in Türkiye.

Since differing demographic compositions of countries need to be taken into account in comparisons of crude rates, an alternative measure are age-standardized rates. Just as crude rates, age-standardized rates are quantified in terms of newly diagnosed cases per 100,000 inhabitants, but in addition they

are standardized according to a pre-defined age distribution. This removes the influence of different age structures between countries. Figure 7 shows estimates of the age-standardized incidence rates for 2020. The age-standardized rates for men and women in Türkiye are much closer to the three European countries than the crude rates in Figure 5. Among men, the Turkish rates are as high as the Polish rates but still about 20% lower than the Belgian and French rates. Among women, the Turkish rates are between 25–40% lower than the rates in the three European countries.

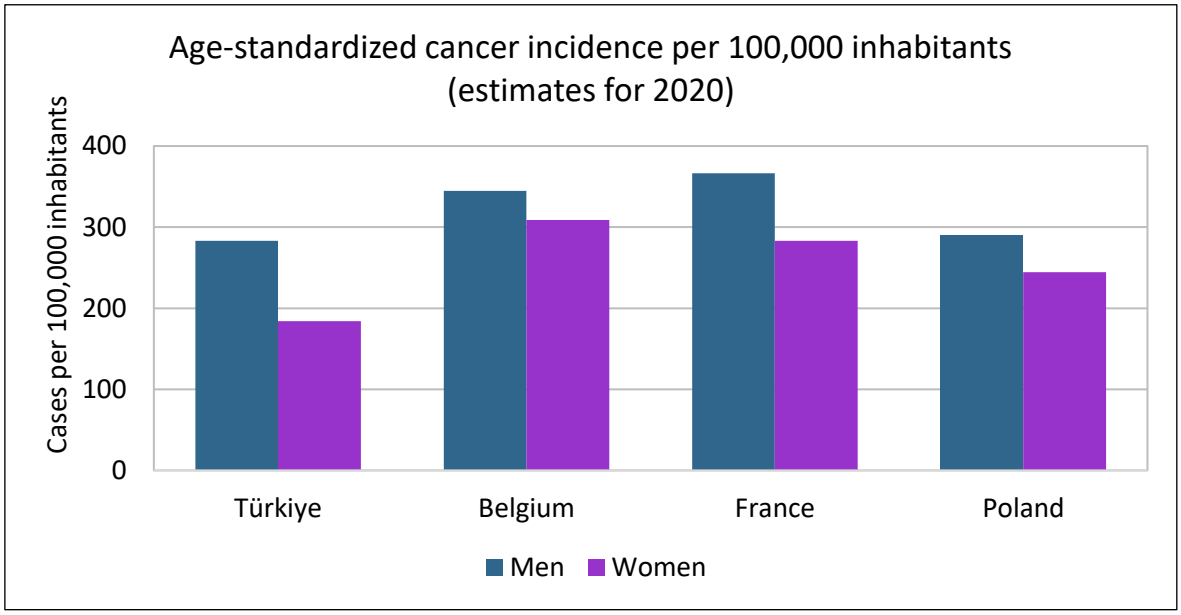


Figure 7: Cancer incidence (age-standardized rates) per 100,000 inhabitants, estimates for 2020

Notes: Cancer refers to all cancer sites except non-melanoma skin cancer (ICD-10 C00–C97/C44). Source: GLOBOCAN (23).

The following factors can help to explain why Turkish age-standardized rates are mostly lower than those of the other European countries and why Turkish crude rates seemed to have been stable in recent years.

- **Risk factors**: Many lifestyle factors (e.g., smoking), infections (e.g., human papillomavirus, HPV), and environmental factors (e.g., air pollution) are linked to cancer (24). The adoption of and exposure to some of these factors has been increasing in many countries around the world in recent decades, but also differs between countries and men and women. For example, the daily smoking rate among women in Türkiye was 14% compared to 41% in men, whereas the gender gap was much smaller in Belgium (12% vs. 18%), France (15% vs. 20%), and Poland (14% vs. 23%) (25).
- **Screening**: Screening programs for certain cancer types have been implemented to varying extent in Türkiye as well as the other countries; see chapter 6. Breast cancer screening and especially prostate cancer screening can lead to the detection of cases of latent disease that

never would have become symptomatic (26, 27). These detected asymptomatic cases are artificially increasing incidence numbers, especially in Belgium and France. The absence of certain screening programs (e.g., for prostate cancer) in Türkiye as well as low participation rates compared to the other countries might lead to lower incidence numbers, as more cancer cases remain undiagnosed.

- **Cancer registration**: The registration of cancer in local registries has become better over time in all countries; see section 5.2. Some of the reported increases in cancer incidence in Belgium, France, and Poland might reflect more complete coverage of all patient records rather than true increases in the number of cancer cases. In Türkiye, the whole population is nowadays covered by cancer registries, but only information of around half of the population is used for official statistics. However, the regions covered by official statistics in Türkiye tend to be more urban (e.g., İstanbul, Ankara, İzmir, Bursa) with younger populations than the ones not covered, which might underestimate the true number of cancer cases.
- **Epidemiological development in other diseases** (competing risks of death): Cardiovascular diseases are the leading cause of death in Türkiye and Poland; see Figure 2. Great declines in the number of people dying from heart attacks and strokes have been observed in the past decades due to improvements in medical treatment (28). This means that people live longer. As people live longer and grow older, this leaves more people at risk of getting cancer (29).

2.2.1.2 Incidence by cancer type

The development of a sound cancer control strategy requires knowledge about the distribution of different cancer types in a country. Figure 8 shows the ten most common types in men and Figure 9 in women for each country. There are four to five cancer types that account for more than half of all newly diagnosed cancer cases.

Lung cancer is by far the most common cancer type in men in Türkiye. This might be explained by the exceptionally high smoking rates among Turkish men (25). Lung cancer is also the most common type in men in Poland, but it is closely followed by prostate cancer. In Belgium and France, prostate cancer is the most common type and lung cancer comes in second place. The larger share of prostate cancer can be explained by the larger proportion of elderly people in the population in these countries, as prostate cancer is very uncommon below age 65, and also by more prostate cancer screening. Colorectal cancer is the third most common type and bladder cancer is the fourth most common type in men in all countries.

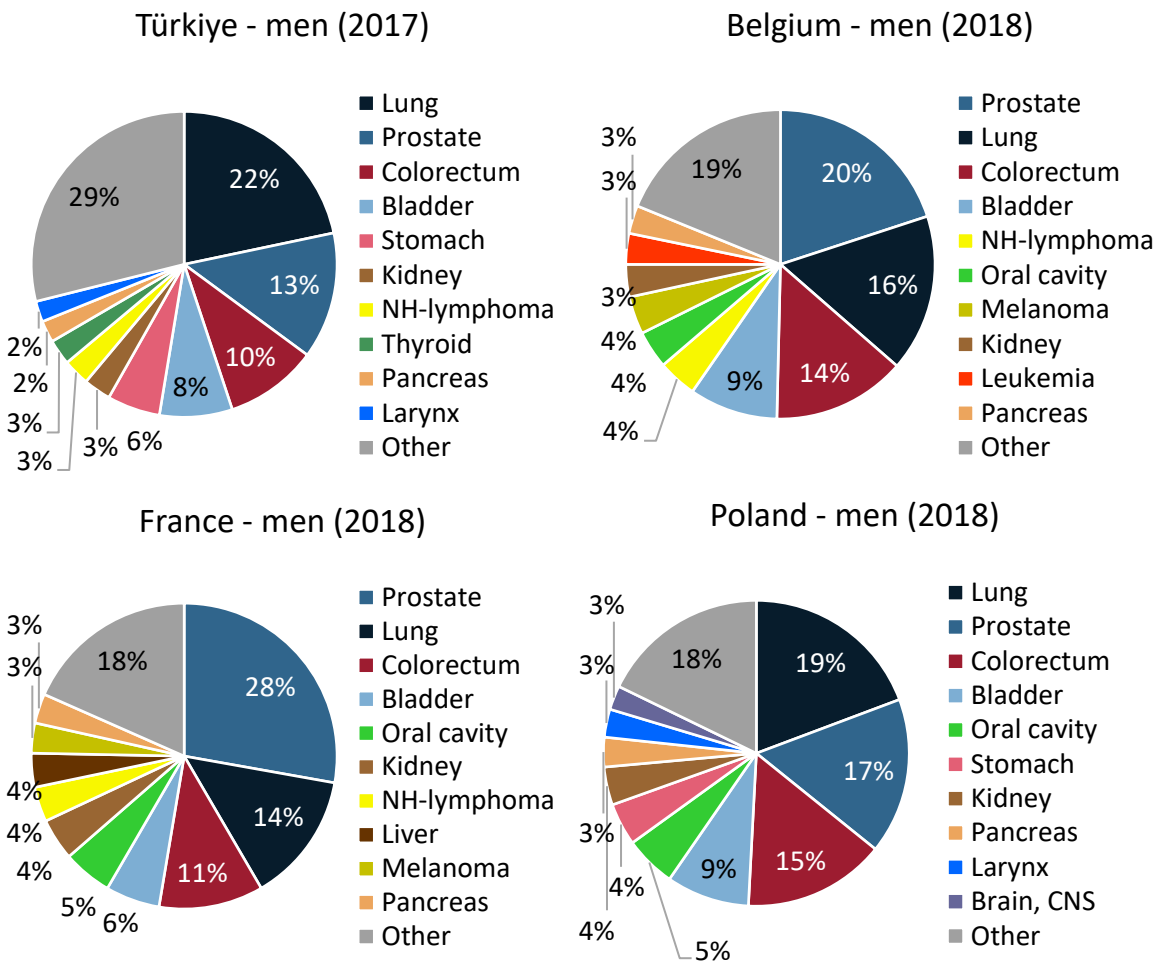


Figure 8: Most commonly diagnosed cancer types in men

Notes: NH = Non-Hodgkin. CNS = Central nervous system. Source: Turkish Ministry of Health (13), and GLOBOCAN (19).

Among women, breast cancer is by far the most common cancer type in all countries, accounting for a quarter or more of all new cancer cases. Thyroid cancer was the second most common type in women in Türkiye, while it was much less common in the other European countries. On a worldwide level, women are about three times as likely as men to be diagnosed with thyroid cancer, but the reason for this disparity is unclear and, importantly, there are no differences by sex in mortality from thyroid cancer (24). In addition, only 159 women and 128 men died from thyroid cancer in Türkiye in 2018, corresponding to 0.6% and 0.2% of all cancer deaths, respectively (6). Colorectal cancer and lung cancer are the third and fourth most common cancer types in women in Türkiye, whereas they are in second and third place in the other European countries. Cancer of the corpus uteri (endometrial cancer) is the fourth or fifth most common cancer type in all countries.

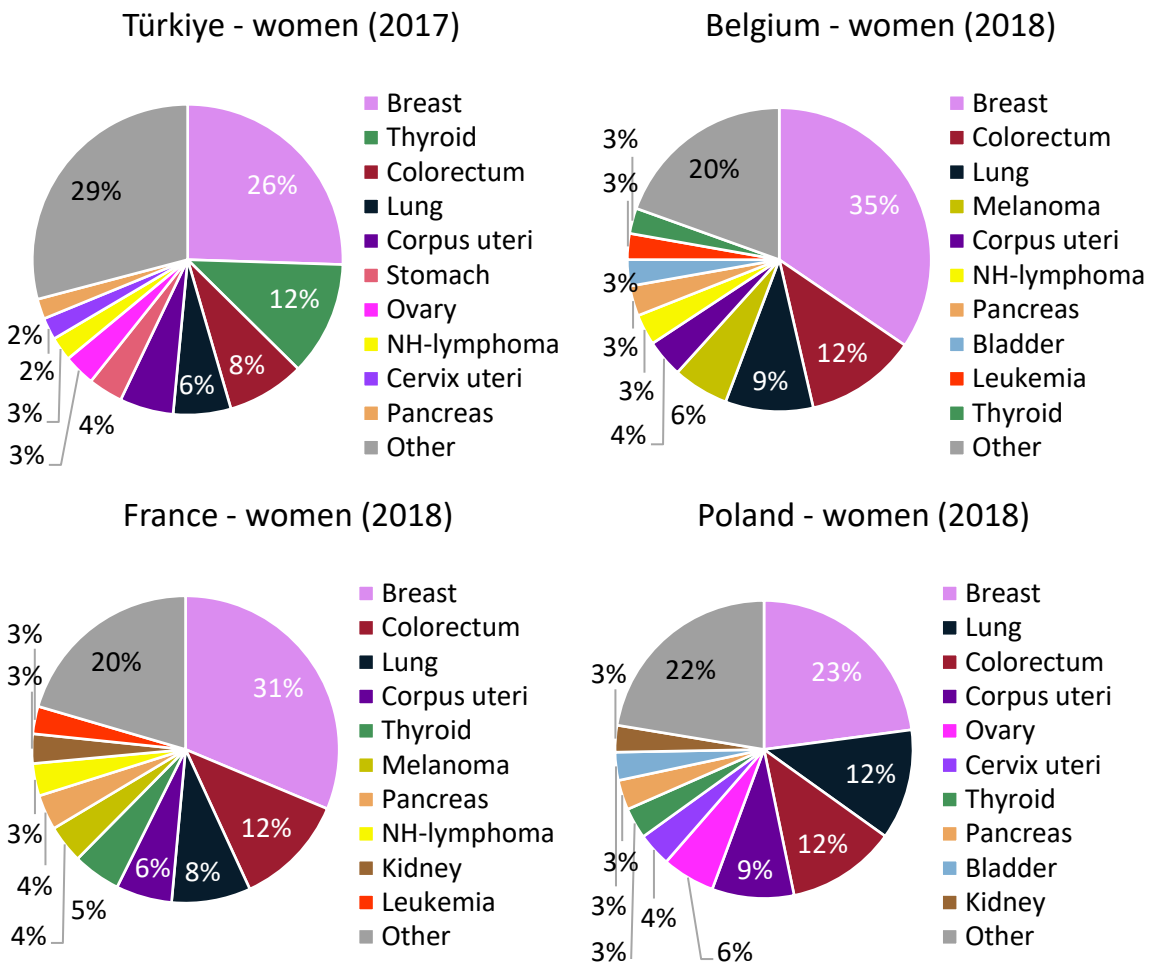


Figure 9: Most commonly diagnosed cancer types in women

Notes: NH = Non-Hodgkin. Source: Turkish Ministry of Health (13), and GLOBOCAN (19).

2.2.1.3 Incidence by age

Cancer affects people of all ages. The risk of getting cancer is very low in younger ages but increases dramatically in older ages. This is because the cellular repair mechanisms become less effective as a person grows older. Aging is therefore a key factor in the development of cancer and cancer is considered an aging-associated disease. This is visible in Figure 10 where the number of newly diagnosed cases rise with age. What looks like a decrease in the numbers (bars in Figure 10) after the age group 65–69 is simply a reflection of fewer people living at those ages. The risk of getting cancer at a particular age (lines in Figure 10) keeps increasing until the age group of 75–79 and remains at a high level after that.

Figure 10 also shows that the number of cancer cases and also the risk to get cancer is higher among women than among men in middle age (30–54 years). This is driven by the comparatively early onset

of breast cancer, which is the most common cancer type among women. At older ages (≥54 years), the number of cancer cases and also the risk to get cancer is much higher among men than among women. This is driven by lung cancer which often occurs in men in their sixties and seventies and even more so by prostate cancer which often occurs in men in their seventies. The median age of women to get cancer is in the age group 55–59 years and for men in the age group 60–64 years.

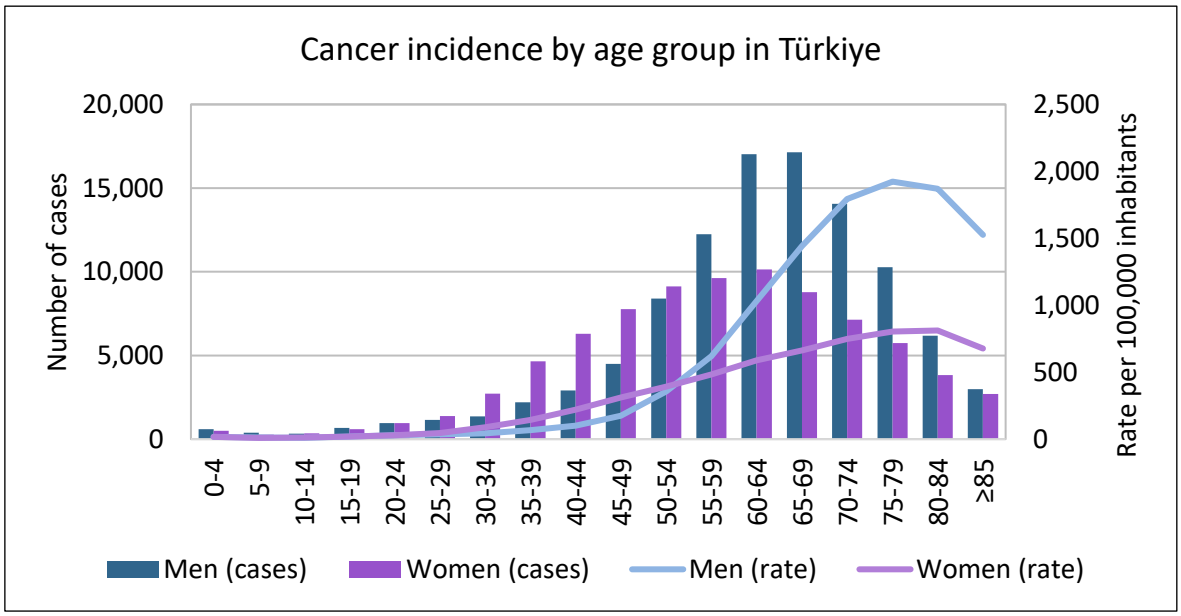


Figure 10: Cases of cancer incidence by age group in Türkiye, 2017

Notes: Cancer refers to all cancer sites but non-melanoma skin cancer (ICD-10 C00–C96/C44). Source: Ministry of Health (13).

2.2.2 Mortality

Cancer mortality refers to the number of deaths caused by cancer in a certain year in a specific geographical area. The latest estimates for cancer mortality indicated around 78,000 cancer deaths in Türkiye in 2019 (10), of which 50,000 deaths in men and 28,000 deaths in women.

Similar to cancer incidence above, this section presents crude rates and age-standardized rates of cancer mortality per 100,000 inhabitants. This ensures that numbers are comparable between countries and within countries over time, as the influence of the demographic structure is removed. When interpreting numbers on cancer mortality the close connection to cancer incidence is important to keep in mind. A high cancer mortality rate in a country does not automatically imply poor quality of cancer care – it could rather be a result of the country's high incidence rate. Thus, two countries with different mortality rates might still be equally good at providing cancer care, and two countries with identical mortality rates might still provide very different levels of quality of cancer care.

2.2.2.1 Crude rates and age-standardized rates

Figure 11 shows cancer mortality crude rates for all cancers combined for both sexes. In Türkiye, there has been an 23% increase in cancer mortality rates between 2009 and 2014, after which the rates have stabilized at around 100 deaths per 100,000 inhabitants. In the other three European countries, the mortality rates were about 2.5 as high as in Türkiye. In France, the rates have been mostly flat during the last 20 years. In Belgium, there has been a slight downward trend since 2011, whereas in Poland there has been a slight upward trend since 2000. The close connection between cancer incidence and cancer mortality means that factors explaining the observed increases in incidence (population aging, risk factors, screening, the epidemiological development in other diseases) indirectly influence trends in cancer mortality. The treatment of cancer and also screening have a direct influence on mortality trends.

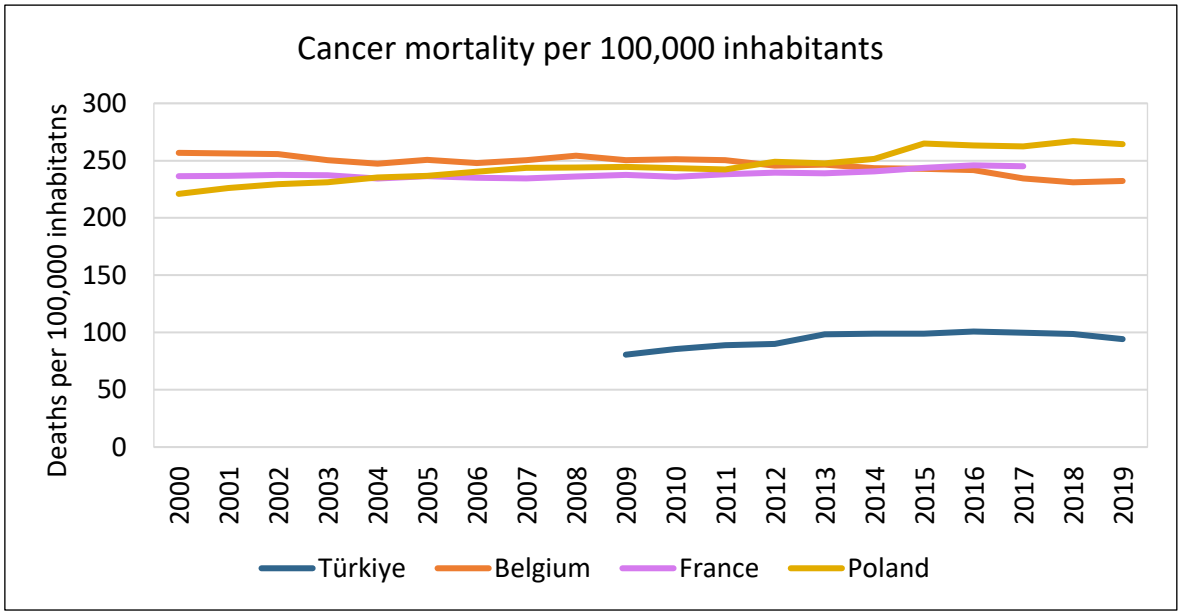


Figure 11: Cancer mortality (crude rates) per 100,000 inhabitants, 2000–2019
Notes: Cancer refers to all cancer sites (ICD-10 C00-C97). Source: TurkStat, WHO, Eurostat (6, 10, 30).

The fact that the gap in the mortality crude rate (Figure 11) between Türkiye on the one hand and Belgium and France on the other hand seems to be smaller than the corresponding gap for the incidence crude rate (Figure 5) indicates lower chances of cancer patients to survive in Türkiye. This is also true for Poland. This observation is supported by Figure 12, which shows age-standardized mortality rates. The mortality rates for men in Türkiye and Poland are higher than in Belgium and France. For women, the mortality rates in Türkiye are as high as in Belgium and France, which stands in stark contrast to the big gap that was observable for the corresponding incidence rates (Figure 7).

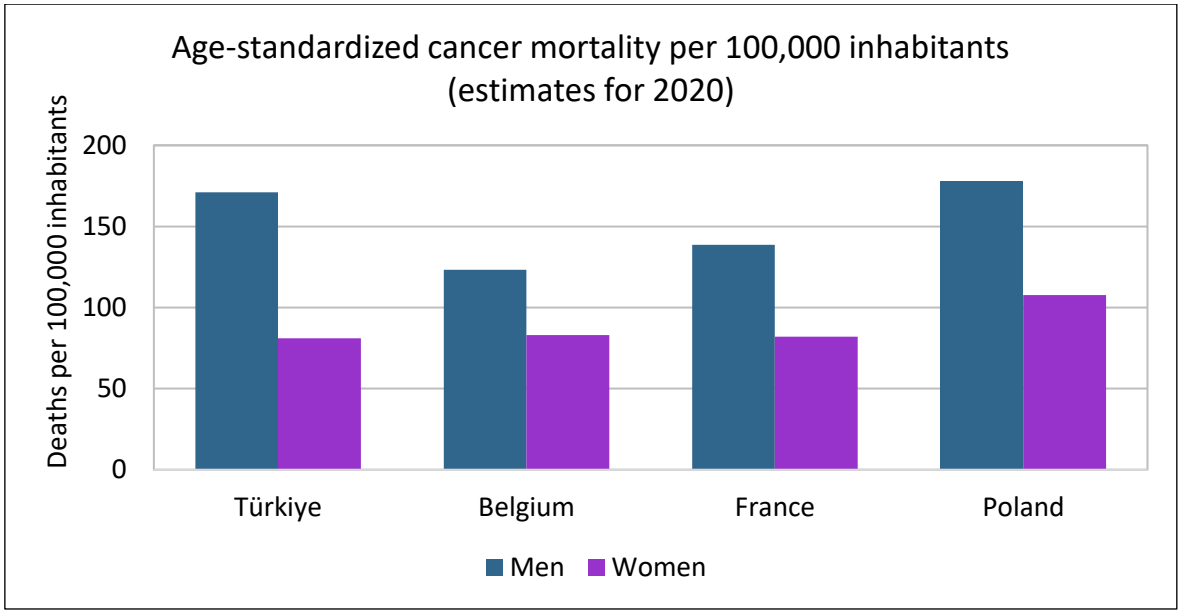


Figure 12: Cancer mortality (age-standardized rates) per 100,000 inhabitants, estimates for 2020

Notes: Cancer refers to all cancer sites except non-melanoma skin cancer (ICD-10 C00–C97/C44). Source: GLOBOCAN (23).

2.2.2.2 Mortality by cancer type

Figure 13 shows the ten cancer types causing the most deaths in men and Figure 14 in women for each country. Only four cancer types account for more than half of all cancer deaths.

Among men in Türkiye, almost 40% of cancer deaths are due to lung cancer. This is the result of both a high incidence of lung cancer in Türkiye and a low survival rate (see section 2.2.3). In the other European countries, lung cancer is also the leading cause of cancer death, but at a smaller share of around 25%. Colorectal cancer is the second leading cause of cancer death among men in all countries, except in Belgium where it is in third place. Prostate cancer is almost causing as many deaths as colorectal cancer in all countries and ranks fourth in Türkiye. The fact that prostate cancer accounts for a much smaller share of deaths than of incidence cases is explained by its high survival rate (see section 2.2.3). Stomach cancer is the third leading cause of cancer death in Türkiye, whereas it is less common in the other European countries.

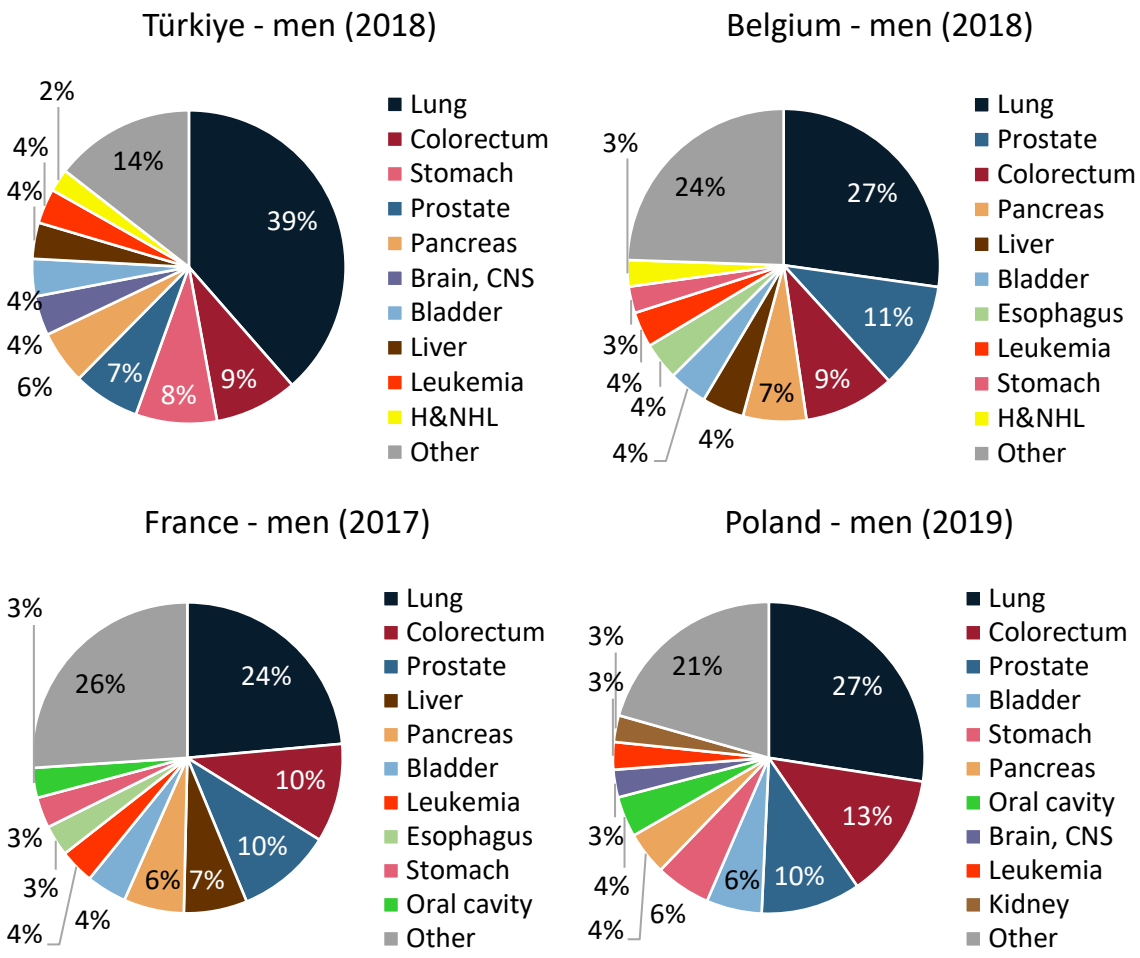


Figure 13: Cancer types causing the most deaths in men

Notes: H&NHL = Hodgkin and non-Hodgkin lymphoma. CNS = Central nervous system. Source: Eurostat (6).

Breast cancer is the leading cause of cancer death among women in all countries, except in Poland, accounting for around 15–20% of all cancer deaths. This proportion is smaller than for incidence cases because survival rates in breast cancer are typically higher than in most other cancer types (see section 2.2.3). Lung cancer was the second leading cause death in Türkiye, Belgium, and France and the leading one in Poland. Colorectal cancer ranked in third place in all countries. Pancreatic cancer and ovarian cancer ranked in fourth or fifth place in Belgium, France, and Poland, whereas stomach cancer caused slightly more deaths in Türkiye, ranking in fourth place.

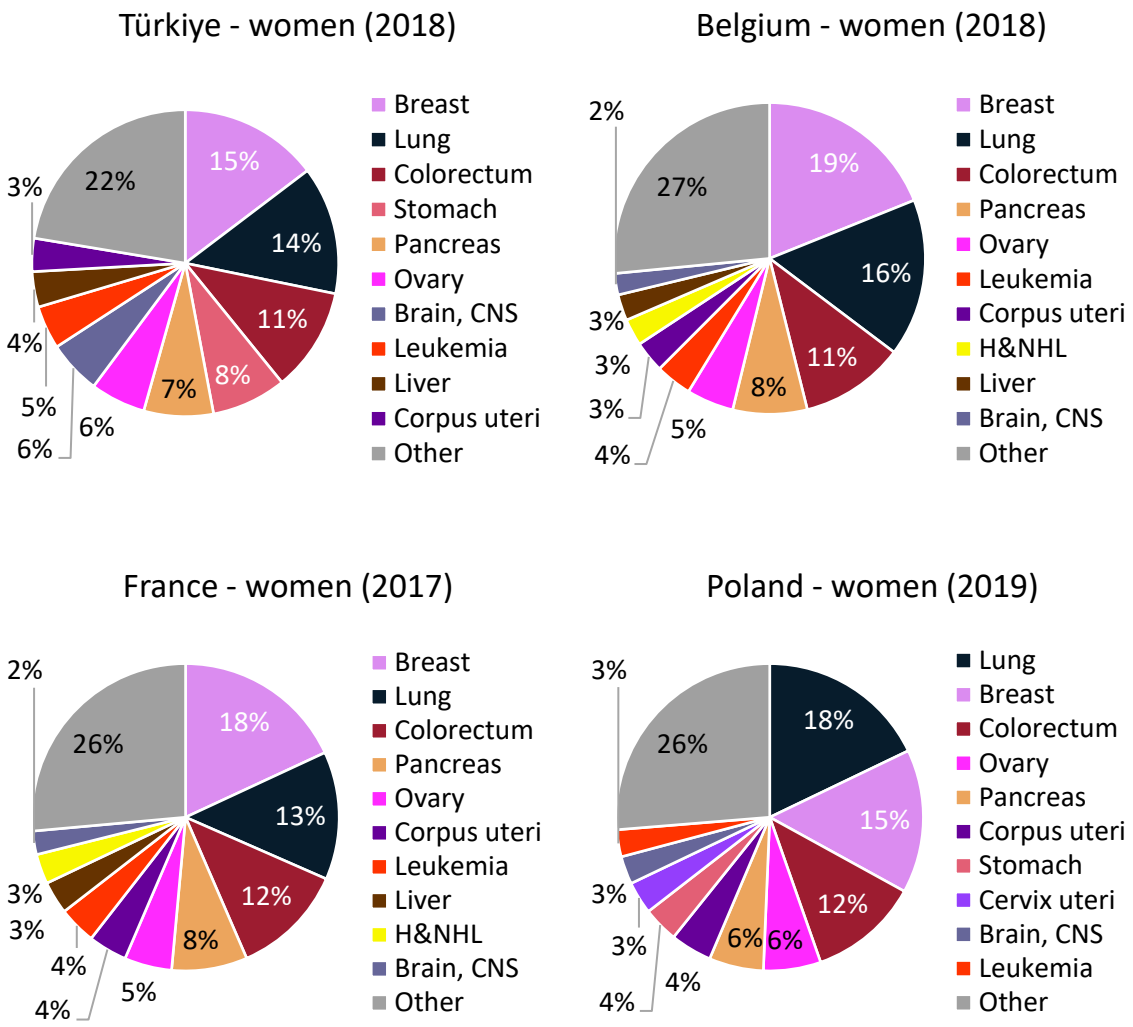


Figure 14: Cancer types causing the most deaths in women

Notes: H&NHL = Hodgkin and non-Hodgkin lymphoma. CNS = Central nervous system. Source: Eurostat (6).

2.2.2.3 Mortality by age

As cancer affects people of all ages, people at all ages may die from cancer. Among children and younger people, the number of deaths is low in Türkiye; see Figure 15. The death toll starts to increase in the age group 35–44 years. This is the only age group in which slightly more women than men die, which is mainly driven by breast cancer. In all older age groups, more men than women die from cancer. In fact, twice as many men die than women in the age groups 55–64 and 65–74 years, which is mainly driven by lung cancer. Figure 15 also shows that the risk of dying from cancer increase continuously with age. The median age of both men and women to die from cancer is in the age group 65–74 years.

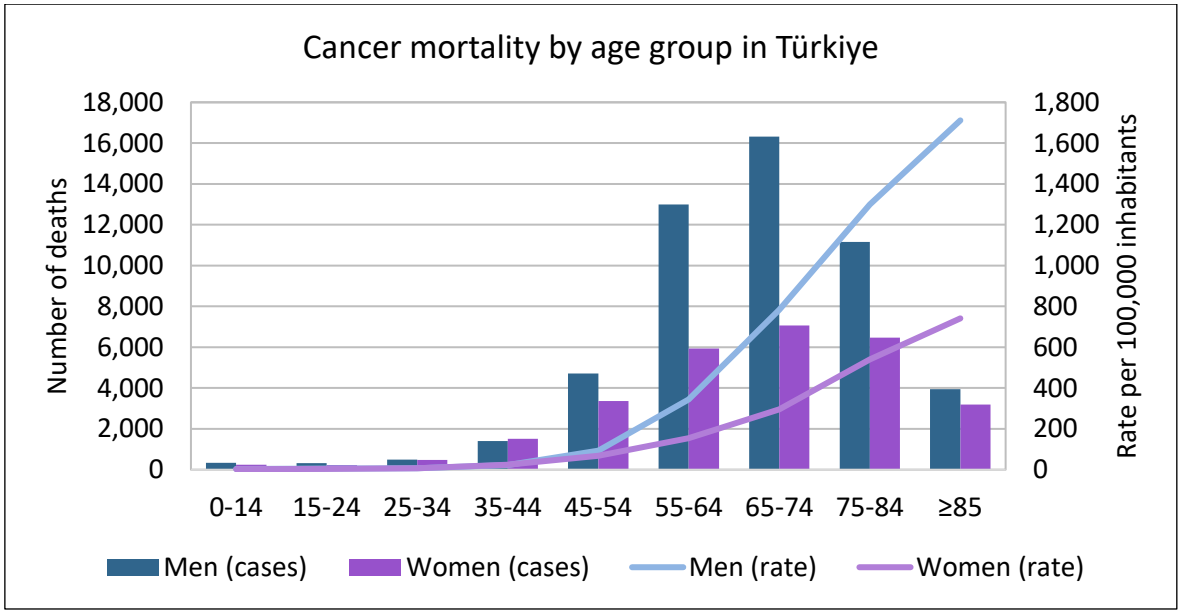


Figure 15: Cases of cancer mortality by age group in Türkiye, 2019

Notes: Cancer is defined as neoplasms (ICD-10 C00–D48). Source: TurkStat (10).

2.2.3 Survival

Survival is the epidemiological concept that links the measures of incidence and mortality. It measures the share of people that have been diagnosed with cancer in a certain year and that are still alive after a specified period of time, ranging from 0% (no one survives cancer) to 100% (everyone survives cancer). Survival rates are commonly measured as 5-year survival rates, i.e., the share of people diagnosed with cancer in year t that is still alive in year t+5.[3,4]

The accuracy of survival estimates depends on the quality of cancer registration, both for incidence and cause-of-death registration in cancer registries. A joint analysis of survival rates from existing regional cancer registries carried out by the Turkish authorities is not available. The international

[3] This means that data on the 5-year survival rate of cancer patients diagnosed in 2022 can only be calculated for sure after 2027. The method to do this is called "cohort analysis". There are alternative methods, "period analysis" and "mixed analysis", which can provide a good approximation of the likely result already before 2026 (31, 32).

[4] Two adjustments are routinely made to survival rates to receive comparable rates across time and countries. Firstly, net (also called "relative") rates rather than absolute ("gross") rates are compared. The net survival rate is the ratio of two survival rates: the absolute survival rate of cancer patients divided by the expected survival rate of people in the general population with similar age and sex in the same country and calendar year (33). This adjusts survival rates for the effect of competing causes of death (background mortality) that would otherwise bias comparisons across time and between countries. Thus, net survival rates indicate the hypothetical situation in which cancer is the only cause of death (31). Secondly, the age structure of cancer patients differs across countries and within countries across time. Since survival rates for most cancer types vary by age (typically they decrease with age), they are adjusted for age at diagnosis (15). The International Cancer Survival Standard (ICSS) is usually used to this end.

CONCORD-3 program[5] aims to calculate comparable survival estimates for countries around the world (15). The latest round of this program also includes an analysis of nine regional cancer registries in Türkiye, covering almost a quarter of the population.

Figure 16 shows 5-year survival rates of the five most commonly diagnosed cancer types in Türkiye for which data are available from the CONCORD-3 program.[6] In general, survival rates of lung cancer are very low, with less than 20% of patients still alive five years after diagnosis. Survival rates of breast cancer and prostate cancer are high, with 80% or more patients still alive five years after diagnosis. All survival rates in Türkiye are lower than the equivalent rates in Belgium and France, whereas they are higher than in Poland (for which the data cover the entire population, however). Figure 16 also shows that the survival rates have generally improved between the periods 2000–2004 and 2010–2014, except for breast cancer in Türkiye. This means that more and more people survive cancer.

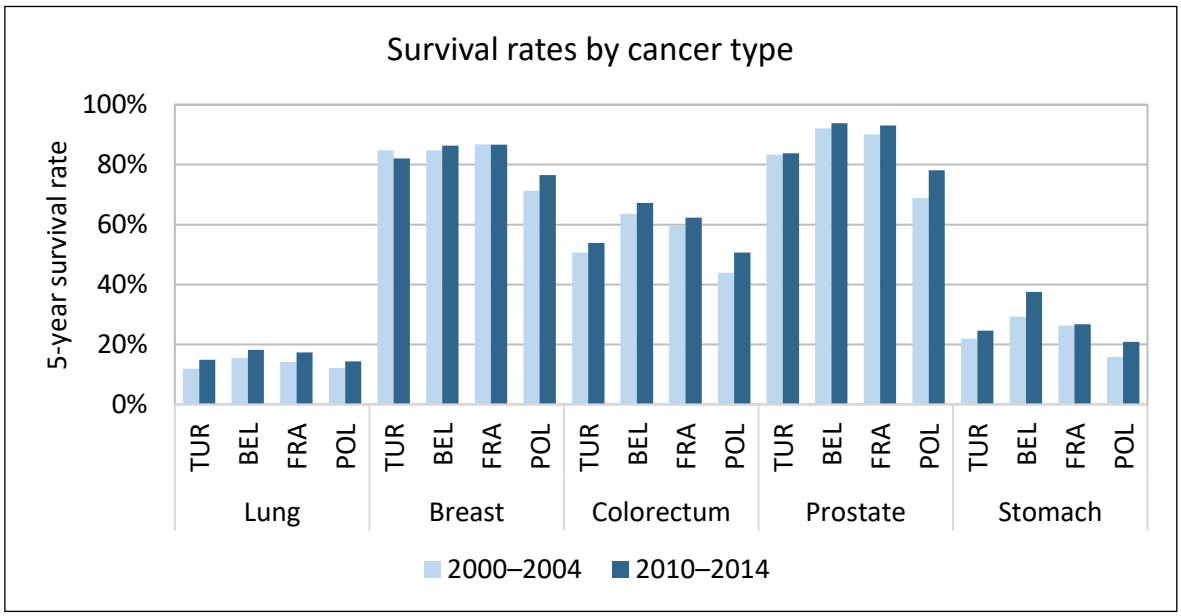


Figure 16: 5-year age-standardized net survival rates for selected cancer types in adult patients (15–99 years), 2000–2014

Notes: The underlying registry data cover the whole country in Belgium and Poland, whereas in Türkiye they only cover 23.4% of the total population from 9 registries and in France 21.7% of the total population from 23 registries. Survival rates of colorectal cancer were calculated as the average of the survival rates of colon cancer and rectal cancer. Source: CONCORD-3 (15).

[5] The CONCORD program is the largest international project to provide 5-year age-standardized (according to ICSS) net survival rates for countries around the world. The latest CONCORD-3 release estimated survival rates for 18 cancer types diagnosed during the 15-year period 2000–2014 and followed up to Dec 31, 2014.

[6] Survival rates for all cancer types are highly dependent on the disease stage at which they are diagnosed; see Info Box 5. Early diagnosis improves the chances to survive considerably. For prostate cancer, screening with PSA testing generally leads to the detection of minor malignancies that would not have led to death, which drives up the survival rates.

Info Box 1 – How many lives of cancer patients could be saved ever year if Türkiye achieved the same survival rates as France?

Method: Patient numbers of newly diagnosed cancer cases in Türkiye 2017 were calculated from official numbers from the Ministry of Health (13). 5-year survival rates from CONCORD-3 for the period 2010–2014 for Türkiye and France were applied to the Turkish patient numbers (15). The differences in the higher survival rates in France and the lower rates in Türkiye were used to calculate a crude estimate of lives that could be saved per year in Türkiye.

Results: Across five major cancer types, the number of cancer survivors in Türkiye would increase by almost 5,000 people (or 10%) from around 48,000 to 53,000 per year, if Türkiye achieved the same survival rates as France.

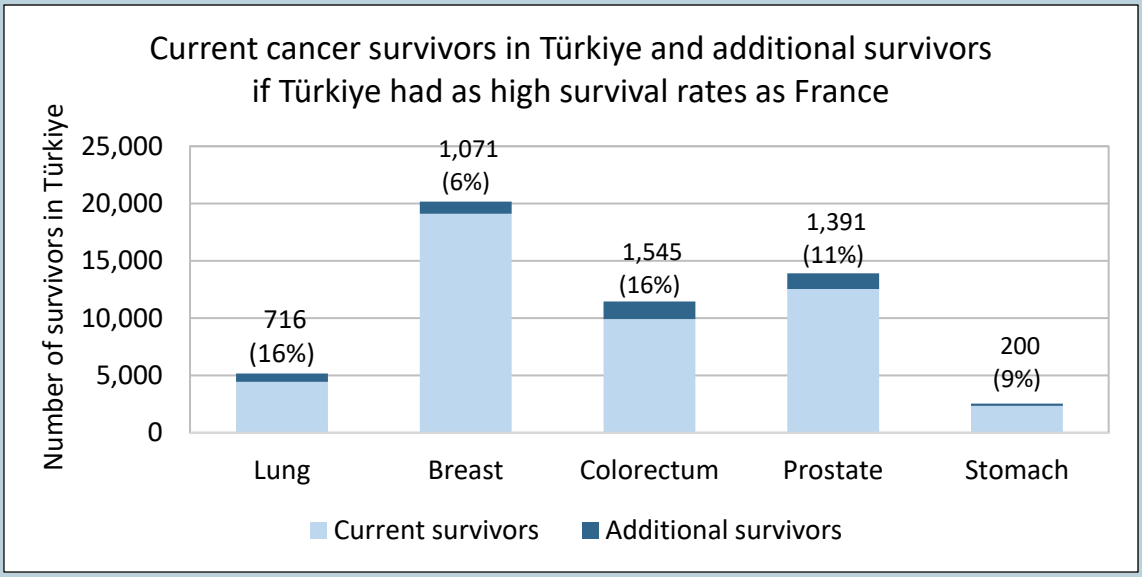


Figure 17: Estimated current number of cancer survivors in Türkiye and additional survivors if Türkiye had as high survival rates as France

Source: own calculations based on incidence (see section 2.2.1) and survival rates from CONCORD-3.

2.3 Future cancer numbers

Overall population growth and population aging are key trends for future cancer numbers in Türkiye. Figure 18 shows how the total population has been steadily increasing from about 63 million in 2000 to 84 million in 2020 and how it might further increase to 94 million until 2040. A growing population means that more people will get cancer, all else equal. The age structure of the population has also been changing. The share of children (0–14 years) has been decreasing from 31% in 2000 to 24% in 2020 and might fall below 20% in 2040 due to decreasing fertility rates. The share of working-age people (15–64 years) has been increasing in the past and might remain mostly stable in the two coming decades. The biggest challenge ahead is the rising share of elderly people (65 years and older), who have the highest risk of getting cancer. While the share of elderly people only was 6% in 2000, it increased to 9% in 2020 and might reach 16% in 2040. In sum, both overall population

growth and population aging will exert a distinctive upward pressure on future cancer numbers in Türkiye.

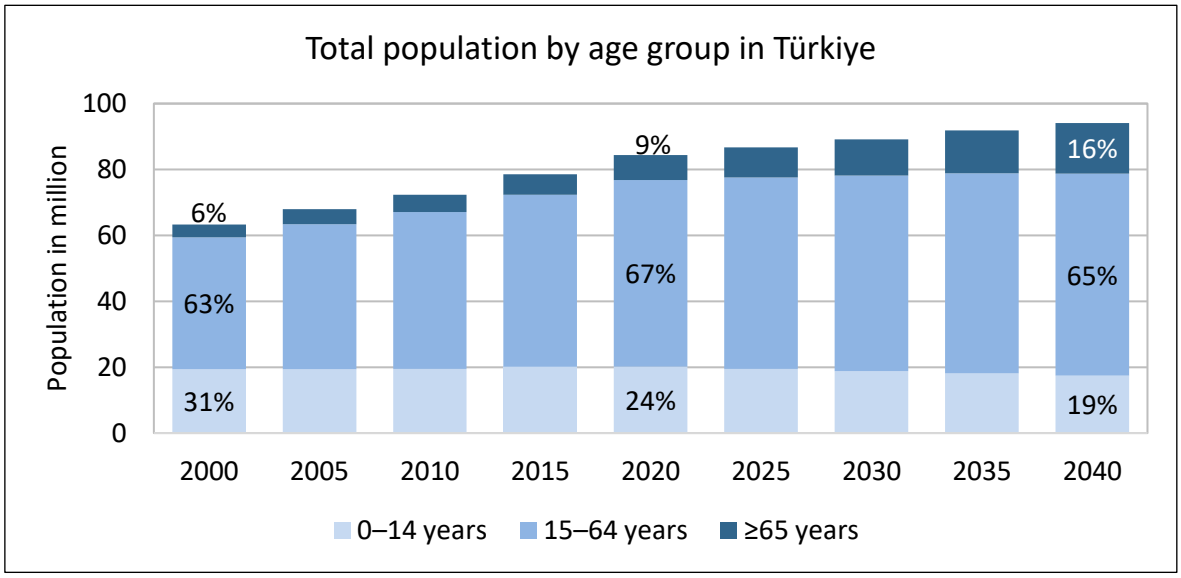


Figure 18: Population (in millions) in Türkiye by age group, 2000–2040
Notes: Numbers for 2020–2040 are estimates based on the "medium variant". Source: UN (22).

Future cancer numbers are naturally uncertain, but predictions based on the status quo and past developments in other countries can provide some guidance. Figure 19 shows different scenarios of future cancer numbers in Türkiye until 2040. The base case scenarios are based on the current age-specific risk to get cancer and the age-specific risk to die from cancer.

- **Base case scenario:** New cancer cases would almost double from 227,000 cases in 2020 to 380,000 cases in 2040 (from ≈270 to 400 new cases per 100,000 inhabitants). The number of deaths would increase from 126,000 cases in 2020 to 232,000 cases in 2040 (from ≈150 to 250 deaths per 100,000 inhabitants).
    - The Turkish incidence in 2040 would be as high as in Poland in 2010 (see Figure 5)
    - The Turkish mortality in 2040 would be as high as in all three European countries in 2010 (see Figure 11)
- **Scenario 1 - The risk to get cancer increases slightly by 1% every year (e.g., due to more unhealthy lifestyles)**: The yearly number of new cases would reach over 470,000 cases (≈500 new cases per 100,000 inhabitants) in 2040.
    - The Turkish incidence in 2040 would be as high as in France in 2002 and in Poland in 2020 (see Figure 5)

- **Scenario 2 - The risk to die from cancer decreases slightly by 1% every year (e.g., due more early detection and better treatment)**: The yearly number of deaths would reach over 186,000 cases (≈200 deaths per 100,000 inhabitants) in 2040.
    - The Turkish mortality in 2040 would be slightly lower than in Belgium in 2020 (see Figure 11)

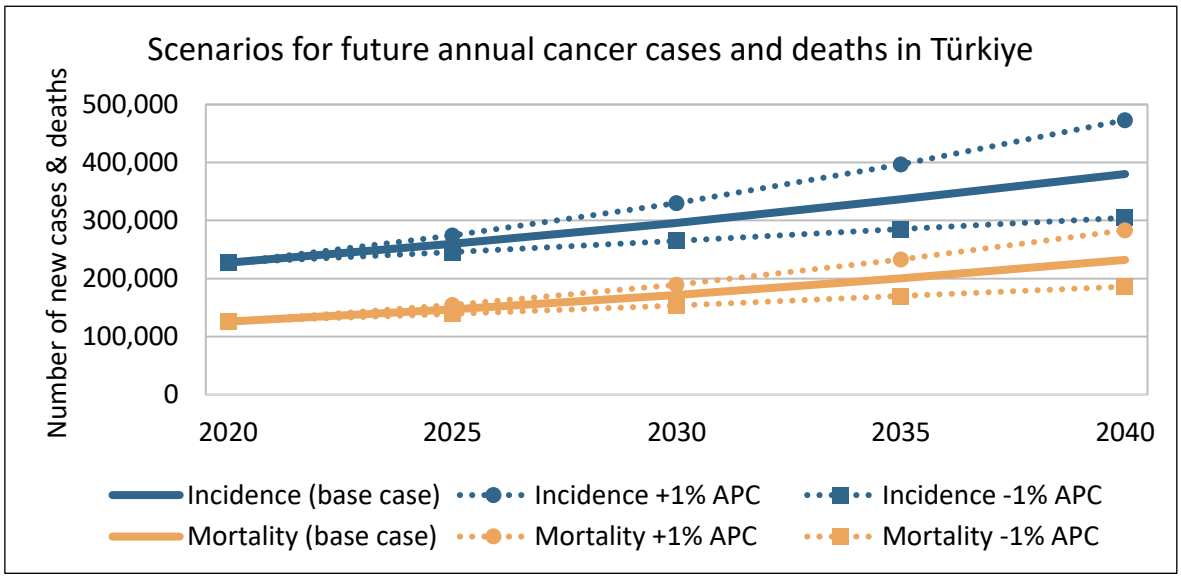


Figure 19: Different scenarios of future cancer incidence and mortality in Türkiye, 2020–2040

Notes: Cancer refers to all cancer sites but non-melanoma skin cancer (ICD-10 C00–C97/C44). APC = annual percent change. Projections in the base case scenario are based on constant age-specific rates and only driven by expected changes in the population composition (base year = 2020). Source: GLOBOCAN (3).

Despite the challenge that cancer represents in Türkiye in the coming decades, there is a silver lining. The general demographic structure with a mostly stable share of the population in working age in the coming decades (Figure 18) is favorable for building a strong economy. This era, sometimes called the "demographic window of opportunity", should be used to invest in health care and cancer care. This investment can yield health returns that reinforce the economy.

The notion that public spending on cancer care is thus not just a cost but also an investment needs to be embraced in the coming decades. To draw a parallel with the COVID-19 pandemic, public funds were cleared quickly so that testing equipment and protective equipment could be purchased, while lockdowns of societal life severely hit the economy. The close connection between a disease and consequences for the whole economy has never been so salient as with COVID-19. The fact that a similar connection exists for cancer is important to recognize. Premature death, sick leave, and early retirement of cancer patients, who otherwise would have been working, represent a big loss to the economy. Informal caregivers who must stay at home and care for cancer patients instead of pursuing

their regular work are another source of loss to the economy. Not investing in cancer care and improving patient outcomes thus has far-reaching implications for the whole economy.

Info Box 2 – Impact of the COVID-19 pandemic on cancer numbers in Türkiye

During 2020, the start of the COVID-19 pandemic affected cancer patients in Türkiye in various ways, as summarized in a recent report (34).

Delays in diagnosis of cancer

- Health care seeking behavior of patients declined out of fear of contracting COVID-19 at health care facilities.
- Screening activities for breast cancer, cervical cancer, and colorectal cancer were greatly decreased, leading to significant drops in the screening participation rates from 2019 to 2020.
- Towards the end of 2020, an increase in the proportion of patients with advanced stage disease was observed, due to the decrease in screening activities.

Consequences: The delays in the diagnosis of cancer, which led to a larger proportion of late-stage diagnoses, means that overall survival of patients is likely to have decreased. This is because the survival rates of late-stage disease are lower than of early-stage disease.

Delays in treatment of cancer

- The large number of hospitalized COVID-19 patients led to capacity shortages at hospitals for other patient groups, including cancer patients. Cancer patients faced disruptions in radiation therapy services, because many public hospitals with radiation therapy clinics were turned into pandemic hospitals.
- In order to keep the stays at hospitals a short as possible, various strategies have been used, such as the implementation of shorter treatment durations, the postponement of adjuvant treatments, the suspension of the follow-up visits in outpatient clinics, and the postponement of surgical procedures.

Consequences: The disruptions and delays in the treatment process of cancer patients is likely to have resulted in worse treatment outcomes and decreased overall survival of patients.

2.4 Economic burden

The burden of cancer to society can also be measured in monetary terms. The economic burden of cancer refers to the costs that cancer imposes on society. Costs are here defined more broadly than in an everyday meaning (35). Three types of costs can be distinguished:[7]

- Direct costs are costs of resource consumption arising from the disease. These are expenditures made for services within the health care system, such as for oncologists, hospital beds, radiation therapy machines, medicines, etc. Formally provided social support services, such as by non-governmental organizations (NGOs), are also direct costs. Private

[7] Another cost component that is sometimes included in cost-of-illness studies are intangible costs. These costs refer to a valuation of reduced quality of life due to a disease. Unlike direct, indirect, and informal costs, these costs have no direct connection to the use of or lack of production of resources. Cost-of-illness studies often exclude intangible costs, as they are difficult to measure and cannot be valued with existing (market) prices. Omitting intangible costs is nonetheless unsatisfactory, as the implicit assumption would be that the economic value of quality of life is zero (36).

costs of travelling to receive treatment, fees for health care visits, and prescription fees for medicines borne by the patient are also direct costs.

- Indirect costs are costs of patients' productivity loss arising from the inability to work due to the disease. They consist of the temporary or permanent inability to work in the formal labor market and from premature death of people in working age.
- Informal care costs arise from the time forgone by relatives and friends to provide unpaid care, such as help with transportation to a health care facility and support at home with household chores.

The economic burden of cancer is linked to the disease burden of cancer in various ways. The greater the number of cancer patients is, the larger the direct costs for diagnosis and treatment will be. If the quality of cancer care is low, survival rates will be low, and the number of cancer deaths will be high. If these deaths occur in patients in working age, mortality-caused productivity loss will be high. Progress in cancer care, such as new imaging techniques for diagnosis, new treatment modalities, and additional screening programs may entail an extension (rather than a replacement) of health care services, which increases direct costs. Yet more effective diagnosis and treatment might enable more patients to go back to work and might decrease the need for help from family members, thus decreasing morbidity-caused productivity loss and informal care costs.

Info Box 3 – The financial burden of cancer for patients in Türkiye

Residents that are part of the social security system are entitled to cancer care free of charge at hospitals owned by the Ministry of Health and university hospitals (37). There are no co-payments for cancer care services, including cancer medicines as long as they are reimbursed in Türkiye. However, if cancer patients access services at private hospitals or receive non-reimbursed medicines, they have to pay themselves. In addition, the financial burden for the individual patient consists of costs for travelling to health care facilities as well as lost earnings due to time taken off from work while receiving care.

This section aims to estimate the economic burden of cancer in Türkiye in 2019. A prevalence-based cost-of-illness approach was adopted to estimate the costs (38). This method entails the estimation of costs incurred during a given year – 2019 in this report. A societal perspective was adopted to estimate the total costs of cancers. The results are expressed in euros (€) to facilitate a comparison across countries using exchange rates in 2019 (39). Costs were also adjusted for price differentials between countries (purchasing power parities, PPP) in 2019 unless otherwise noted (39); see Table A1 in the Appendix for the exchange rates and PPP conversion factors used.

2.4.1 Direct costs

The direct costs of cancer are in this report defined as the sum of the costs of all resources used within the health care system. This includes costs for prevention, screening, diagnosis, and treatment. Direct costs include both publicly paid resources, financed by tax money and/or social security contributions, and privately paid resources, including out-of-pocket payments for health care visits and medicines as well as fees for private health insurance. Direct costs of resources outside the health care system (e.g., private costs for transportation) could not be included in any country.

2.4.1.1 Methodology

Direct costs were calculated in a top-down manner, in line with previous studies on the cost of cancer (4, 40). In a first step, estimates of gross domestic product (GDP) and total health expenditure[8] for 2019 were obtained for Türkiye, Belgium, France, and Poland from Eurostat and the WHO (39, 41); see Table 2. In a second step, a pragmatic literature search was performed to obtain information on the proportion (or the absolute size) of the total health expenditure spent on cancer in Türkiye.[9] Two studies provided some relevant information:

- A report by Wilking et al. (2010) cites a report from the Turkish Ministry of Health that indicated that in the year 2007 around €1.8 billion were spent on cancer out of total health expenditure of €30 billion (PPP-adjusted) (42). This indicates that around 6.0 percent of total health expenditure were spent on cancer that year.
- Cicin et al. (2021) estimate the economic burden of lung cancer in Türkiye in 2018 (43). Using a bottom-up costing approach, they estimate that the direct costs of lung cancer amounted to almost €500 million (not PPP-adjusted). This would correspond to around 1.8 percent of total health expenditure that year.
- Abdul-Khalek et al. (2020) estimate the direct costs of cancer care among the Syrian refugee population residing in Türkiye in 2017 (44). Their estimates range from €25 million to €118 million (not PPP-adjusted). This would correspond to around 0.1–0.4 percent of total health expenditure that year.

[8] The total health expenditure correspond to "current expenditure on health" and are defined as the final consumption of health goods and services. Expenditure from both public and private sources are included.
[9] Search terms used were ["economic burden" OR "cost of illness"] AND "cancer" AND "Turkey".

Table 2: GDP and health expenditure in 2019

Country	Gross domestic product (GDP)				Total health expenditure		
	Total (M €)	Per capita (€)	Per capita (PPP €)	% of GDP	Total (M €)	Per capita (€)	Per capita (PPP €)
Türkiye	679,132	8,224	18,852	4.3%	29,502	357	819
Belgium	478,161	41,619	37,691	10.7%	50,953	4,435	4,016
France	2,437,635	36,248	34,081	11.1%	269,541	4,008	3,769
Poland	533,600	14,055	23,473	6.4%	34,400	906	1,513

Notes: M = million. PPP = purchasing power parity. Source: Eurostat and WHO (39, 41).

In the absence of any suitable up-to-date information, the proportion of total health expenditure spent on cancer in Türkiye was estimated. The estimations were based on an assumed proportionality between the cancer disease burden and the costs of cancer in a country, using the two following approaches:[10]

1. The proportion of cancer deaths in Türkiye (18% of all deaths in 2019; see section 2.1.1) was put in relation to the corresponding proportion in a sample of 31 European countries (Europe-31) (25% of all deaths in 2019, according to Eurostat (6)) and the estimated direct costs of cancer in Europe-31 (6.2% in 2018, according to the most recent estimates (45)). This yields an estimate of 4.4% of cancer-specific health expenditure in Türkiye in 2019.
2. The proportion of the DALYs caused by cancer in Türkiye (17% of all DALYs in 2019; see section 2.1.2) was put in relation to the corresponding proportion in Europe-31 (19% of all DALYs in 2019, according to the WHO (12)) and the estimated direct costs of cancer in Europe-31 (6.2% in 2018, according to the most recent estimates (45)). This yields an estimate of 5.7% of cancer-specific health expenditure in Türkiye in 2019.

As it is not clear which of the two estimates represents a better reflection of the reality in Türkiye in 2019, the average of the two estimates (5.0%) was used.

For Belgium and Poland, the same proportion (6.9%) and (7.0%) as in the most recent estimates for 2018 were used (45). For France, the National Health Insurance Fund publishes annual reports on public health expenditures by disease group (46). The latest available report for 2019 indicates that public health expenditure on cancer amounted to €20.1 billion, which corresponds to 7.5% of total health expenditure (41).[11]

[10] This method was also used in a previous international cancer report in the Middle East and Africa (40). Similarly, the study on the direct costs of cancer of Syrian refugees in Türkiye in 2017 based its estimations on epidemiological and economic data observed in 27 European countries (44).
[11] The estimates by the National Health Insurance Fund do not include out-of-pocket payments, which leads to an underestimation of the health expenditure on cancer.

2.4.1.2 Results

The estimated direct costs of cancer in Türkiye amounted to €1.48 billion (TRY 9.43 billion; unadjusted for PPP differences) or €18 per capita (TRY 114) in 2019. A comparison of the direct costs of cancer is shown in Figure 20. After adjusting for differences in purchasing power, the direct costs of cancer amounted to €41 per capita in Türkiye. This is about half as much as the costs in Poland (€106) and only about a seventh of the costs in Belgium and France. An obvious reason for the large differences is the number of cancer patients, which are – in per capita terms – much lower in Türkiye (see section 2.2.1). Therefore, Figure 20 also shows the direct costs of cancer per newly diagnosed cancer case (incidence). This brings cancer spending in Türkiye (around €18,600 per new cancer case; PPP-adjusted) almost in line with spending in Poland (€22,200), whereas Belgium and France still spend more than twice as much as Türkiye per new cancer case.

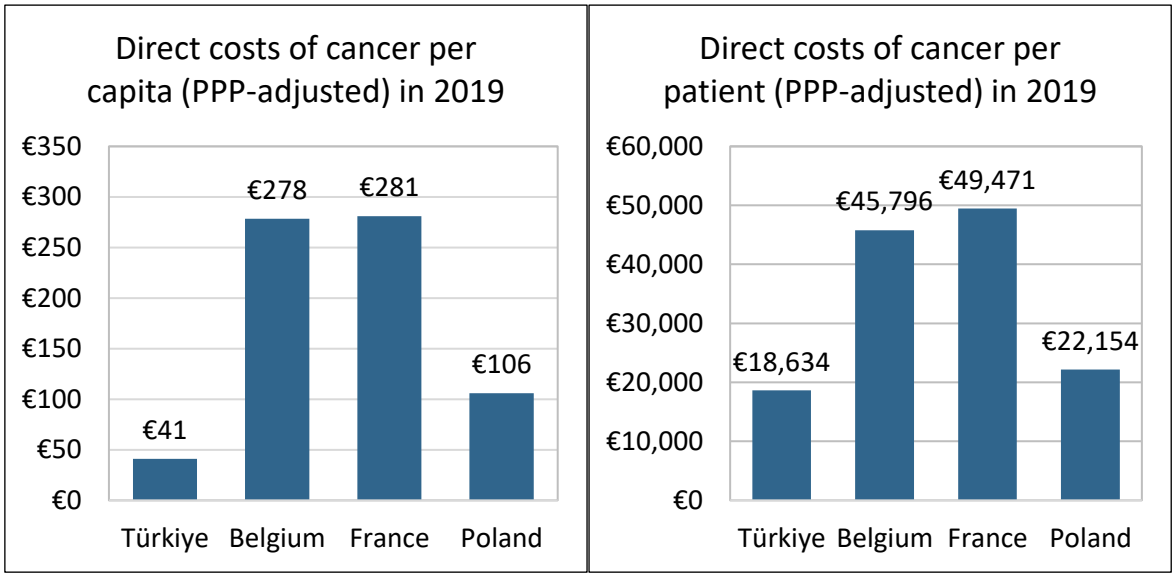


Figure 20: Direct costs of cancer per capita and per cancer patient (PPP-adjusted), 2019
Notes: A "cancer patient" is here defined as the number of newly diagnosed cases (total cancer incidence) in the latest available year with information.

It is also important to emphasize the link between health spending on cancer in Figure 20 and survival rates of patients (Figure 16). Belgium and France – the countries with the highest spending – achieve higher cancer survival rates – than Türkiye and Poland. A positive correlation between survival and per-capita spending on health/cancer care has also been previously documented in samples of countries in Europe and the Asia-Pacific region (4, 47). Nonetheless, when comparing the direct costs of cancer between countries, it is important to remember that these costs only represent a single number of the monetary value of all resources used. For the monetary inputs to yield the highest benefits to patients, the allocation and organization of resources is pivotal (48).

2.4.2 Indirect costs

From an economic perspective, it is costly when patients of working age are forced to be on sick leave to receive treatment and recover from the disease, are forced to retire early due permanent incapacity/disability, and die. An indirect cost to society arises if these patients could have been expected to work in the absence of disease.[12] Their foregone labor market earnings represent a productivity loss caused by morbidity (i.e., sick leave and early retirement) and premature mortality.

2.4.2.1 Methodology

Indirect costs were calculated using the human-capital method, in line with previous studies on the cost of cancer (4, 40). This method takes the patient's perspective and counts any hour not worked as an hour lost. The indirect costs of cancer were defined as productivity loss attributable to premature mortality and to morbidity.

The productivity loss from premature mortality represents the present value of the future earnings that a working-age person who dies would have been expected to generate throughout her/his working life.[13] Potential years of working life lost (PYWLL) were calculated based on age-specific and sex-specific data on cancer deaths from Eurostat for the latest available year (6). As data on deaths were grouped into five-year age intervals, all deaths in an age interval were assumed to occur in the middle of that interval, and working age was defined to range from age 15 to the official retirement age in each country (Türkiye: 60 years for men, 58 years for women; Belgium 65/65; France 62/62; Poland 65/60; (50, 51)). PYWLL were combined with country-specific data on sex-specific mean annual earnings and sex-specific employment rates from Eurostat (52, 53). Future lost earnings were discounted with a 3.5% annual discount rate and a zero real growth rate in future earnings was assumed.

The estimation of the productivity loss from morbidity is more challenging as no detailed data on disease-specific sick leave and early retirement are available and no previous results in the literature were found for Türkiye. In order to provide a ballpark estimate of the possible size of this type of productivity loss, a similar strategy as for the direct costs was applied. The size of the productivity loss from morbidity in Türkiye was estimated based on the ratio between the loss from morbidity

[12] The fact that individuals' time is a limited resource for which there is an alternative cost is widely accepted in economic theory (49). One hour of lost production thus corresponds to the value of the work that would have been carried out. Transfer payments within the social security system (sick leave benefits, disability benefits, widower's/widow's pensions, etc.) should not be included to avoid double counting of costs.
[13] The value of paid work in the informal sector, the unpaid work of homemakers, or work done as volunteering is thus not included.

and the loss from premature mortality observed in Europe-31 in 2018 in a previous study (45). This ratio (0.41) was applied to the estimated cost of the productivity loss from premature mortality in Türkiye. In Belgium, France, and Poland the productivity loss from morbidity was taken from the same previous study and extrapolated from 2018 to 2019.

2.4.2.2 Results

The estimated indirect costs of cancer, defined as the sum of productivity loss from premature mortality and morbidity, amounted to €1.00 billion (TRY 6.33 billion; unadjusted for PPP differences) or €12 per capita (TRY 78) in Türkiye in 2019. A comparison of the indirect costs of cancer is shown in Figure 21. After adjusting for differences in purchasing power, the indirect costs of cancer amounted to €28 per capita in Türkiye. This is about a fourth of the costs in Poland (€97) and only about a seventh of the costs in Belgium (€189). The lower number of cancer patients per capita as well as the lower retirement ages, employment rates, and earnings levels in Türkiye compared to the other countries are all reasons for the large differences. When considering the indirect costs of cancer per newly diagnosed cancer case (incidence), the differences between Türkiye and the other countries become smaller.

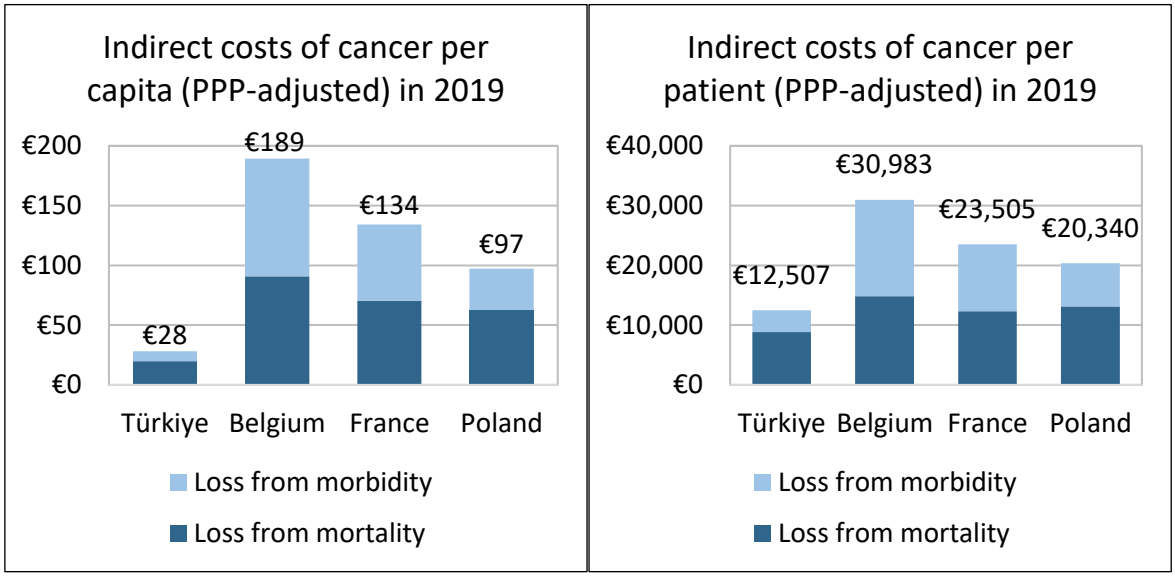


Figure 21: Indirect costs of cancer per capita and per cancer patient (PPP-adjusted), 2019
Notes: A "cancer patient" is here defined as the number of newly diagnosed cases (total cancer incidence) in the latest available year with information.

2.4.3 Informal care costs

Informal care refers to the services and help provided to the patient by informal caregivers in the form of relatives and friends (54). These services are very important complements but also substitutes to formal care services. They include accompanying and transporting the patient to the hospital to

receive treatment and providing support and care for the patient at home. Most palliative care is essentially provided by informal caregivers (55). If these services had not been provided informally, formal services would have been needed to replace them. This means that the work and time spent by informal caregivers entail an opportunity cost, which should be assigned an economic value.

Cancer patients in low-income and middle-income countries are more likely to have an informal caregiver (a family member) living permanently in the same household than patients in high-income countries (56). The high presence of multi-generational households in Türkiye compared to other European countries might in this regard be beneficial for cancer patients (57).

A systematic assessment of the extent of informal care for cancer patients in Türkiye is not available, even though previous studies emphasize the importance of family caregivers in Türkiye (58). It is also difficult to estimate the approximate magnitude of the informal care costs in Türkiye based on results in other European countries, which have fewer multi-generational households and potentially more formal care services. Nonetheless, previous results for many European countries indicate that informal care costs are about as large as morbidity-caused indirect costs (45).

2.4.4 Total costs

The sum of direct costs, indirect costs, and informal care costs represent the economic burden that cancer imposes on society. A societal perspective on the costs of a disease is important for decision making in health care, if the aim is to ensure value-for-money for patients, taxpayers, and society at large. Essentially every new intervention made in the health care system (e.g., use of a new medicine, use of an improved surgical procedure, implementation of a screening program) will always also affect costs outside the health care system. If these costs are not taken into account, decisions might be misguided and will not maximize value-for-money for society.

In this report, only direct costs and indirect costs were possible to estimate for Türkiye. The total costs amounted to €2.48 billion (TRY 15.75 billion; unadjusted for PPP differences) or €30 per capita (TRY 192) in Türkiye in 2019. A comparison of the total costs of cancer is shown in Figure 22. After adjusting for differences in purchasing power, the total costs of cancer amounted to €69 per capita and €31,000 per cancer patient in Türkiye. Indirect costs accounted for around 40% of the total costs of cancer in Türkiye, which was similar to the other European countries.

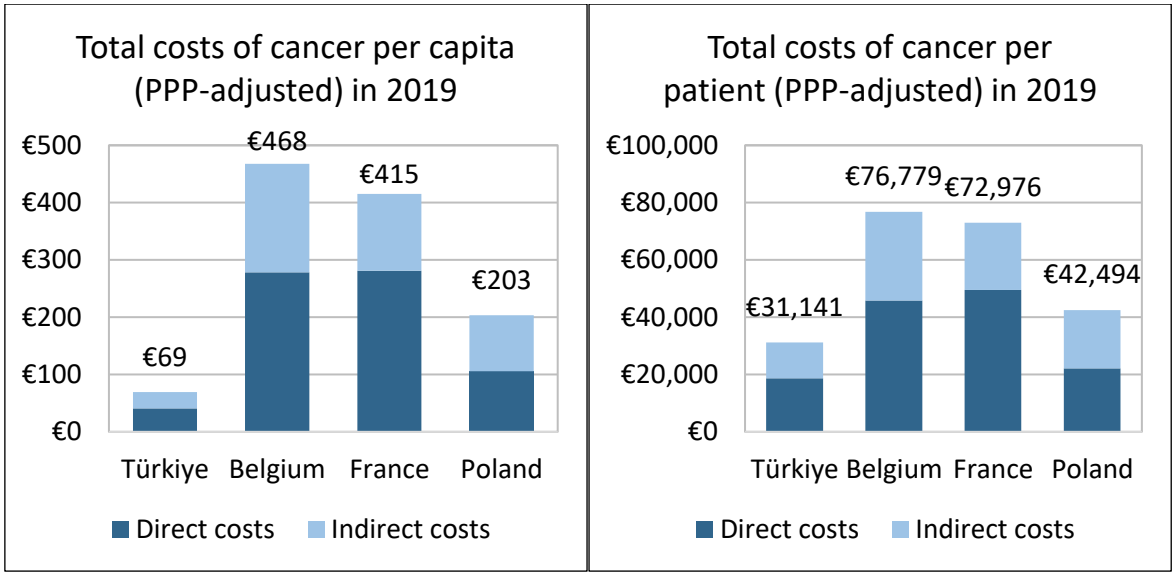


Figure 22: Total costs of cancer per capita and per cancer patient (PPP-adjusted), 2019

Notes: A "cancer patient" is here defined as the number of newly diagnosed cases (total cancer incidence) in the latest available year with information.

3. Health systems overview

This chapter provides a brief overview of the health system in Türkiye as well as of the three benchmark countries. It starts with a description of universal health coverage (UHC). This is followed by a description of the regulation and organization as well as the financing of the health system. The information presented in this chapter was mainly sourced from the WHO.

The main take-away points of the comparison of the health systems are the following:

- Türkiye and the three benchmark countries have all achieved UHC through as system of compulsory public health insurance.
- Health care provision consists of a mix of public and private health services. In all countries, public health insurance grants access to public providers as well as private providers contracted by the public health insurance.
- Primary care is the main entry point to the health care system in three benchmark countries, with free choice of general/family physicians in all countries. In Türkiye, the gatekeeping role of primary care is less pronounced, and patients may directly go to secondary care or hospitals.
- Public health insurance is financed through income-based contributions from employees and employers in all countries.

3.1 Population coverage

Türkiye: Türkiye has universal public health insurance administered by the Social Security Institution (SSI) which covers 99% of the population (59). All citizens have an identification number (T.C. Kimlik No.) that grants free access to health services within the public sector. The transformation towards universal and compulsory health coverage began in 2003 and was completed around 2008 (60). Despite the public coverage, a growing number of people purchase complementary private health insurance to cover some costs of treatment in private hospitals (59). The private health insurance usually covers costs for examinations but not newer medicines that are not yet reimbursed by the SSI.

Info Box 4 – Health care access of Syrian refugees in Türkiye

After the start of the civil war in neighboring Syria in 2011, Türkiye became the country that received the highest number of refugees. Over 3.6 million Syrian refugees were registered in Türkiye until 2018 (61). Their legal status was systematized in 2014 with the establishment of the Temporary Protection Regulation, which granted free access to health care (61). The financial costs of these health benefits were

covered by the Disaster and Emergency Management Authority (62). The access to health care services was initially limited by language barriers and the mobility of the refugees. To address the access challenges, migrant health centers staffed with Syrian physicians were established with support from European Union funds in 2016 (61).

Belgium: Belgium has a system of compulsory health insurance that covers around 99% of the population. All residents must be affiliated to a sickness fund of their choice or to the public auxiliary fund. The remaining 1% of people not formally covered may still access care services through the public center for social assistance of their municipality (63).

France: France has a statutory health insurance (SHI) system providing universal coverage for all residents. Public health insurance (AMO) consists of three compulsory schemes that provide SHI to different segments of the population depending on their professional status (employees & self-employed, agriculture, others). Almost 95% of the population have complementary private health insurance that supplements the public health insurance and that covers most out-of-pocket payments for public health services (64).

Poland: Poland has a system of universal and compulsory public health insurance, introduced in 1999. In 2003, the health insurance system was centralized, with the creation of the National Health Fund (NFZ) that replaced a system of 17 regional sickness funds. The role of voluntary private health insurance is limited and mostly comes in the form of medical subscription packages offered by employers to employees (65).

3.2 Health care regulation and organization

Türkiye: The Ministry of Health is responsible for the regulation of health policy and the delivery of health care. The Ministry of Finance sets the financial framework through the governmental budget and the SSI administers the budget pertaining to health care. Health care provision consists of a mix of public and private health services. The SSI sets prices for health services and contracts with both public and private health care providers (59). The Ministry of Health owns over half of all hospitals and hospital beds, while the rest are university hospitals and private hospitals (66). As part of the introduction of universal health insurance, the role of primary care with family physicians was enhanced to unburden secondary care. However, family physicians do not act as gatekeepers to the rest of the health care system and patients may seek care directly at secondary or tertiary care, even for minor complaints (67). Citizens have the right to choose among family physicians contracted by the SSI (59).

Belgium: The Ministry of Health is responsible for the general organization of the health system. The Federal Authorities are responsible for the national compulsory health insurance (managed by the National Institute for Health and Disability Insurance, NIHDI), hospitals and other regulations, while the Federated Entities are responsible for primary care. Reimbursed health care services are provided by both public and private health care facilities. There is free choice of physicians and of health care facilities (63).

France: The Ministry of Health has control over the governance of the health system. The SHI schemes reimburse both public and private health care providers. Primary care is mostly provided in private practices of general physicians who are reimbursed by the SHI schemes. There is free choice of general physicians. Hospital care is predominantly provided by public or private nonprofit providers (64).

Poland: The Ministry of Health shares governance and responsibility for health care with three administrative levels; municipalities responsible for primary care, counties responsible for smaller county hospitals, and voivodeships for larger regional hospitals. The NFZ is responsible for providing access to health services by contracting public and private health care providers. The NFZ also contracts general physicians from which the insured residents can choose freely for primary care. Private facilities provide mainly outpatient care, while most hospitals are public (65).

3.3 Health care financing

Türkiye: There is a joint public budget for health care and pensions that is financed from social insurance premiums (66). Social insurance premiums paid to the SSI are financed through a combination of employer and employee contributions, with those on low incomes exempt. The SSI pays hospitals via bundled prices within predetermined global budgets. The SSI contracts family physicians and pays them on the principle of capitation. Patients pay different levels of co-payments for primary, secondary, and tertiary care services (59).

Belgium: The public health system is predominantly financed by compulsory health insurance with contributions proportional to income paid by employers and employees. Patients typically pay fees for outpatient services in advance and then request reimbursement from their sickness fund. A third-party payment system applies for the purchase of prescribed medicines and hospital care (63).

France: The SHI system is financed through income-based contributions from employees and employers, and increasingly by earmarked taxes on a broad range of revenues. While SHI covers over 90% of costs for hospital care, it only covers 44% of the costs for non-pharmaceutical medical

goods in outpatient care. The co-payment required by the patient is usually covered by the complementary private health insurance (64).

Poland: The major public source of health care funding are earmarked payroll taxes received by the NFZ. Out-of-pocket spending is relatively high for prescribed medicines compared to other European countries (65).

A fundamental question is how much to spend on health. This question has mainly been discussed in the context of achieving UHC, which Türkiye and the three benchmark countries already have achieved. Nonetheless, the question of what defines an *adequate level* of public health spending has engaged scholars and the WHO in recent decades (68). The 2010 World Health Report of the WHO notes in relation to public health spending that it is "*difficult to get close to universal health coverage at less than 4–5% of GDP* [p.98]" (69). This informal target is thus not officially endorsed but the 5%-of-GDP reference keeps being used as a benchmark by the WHO (70).

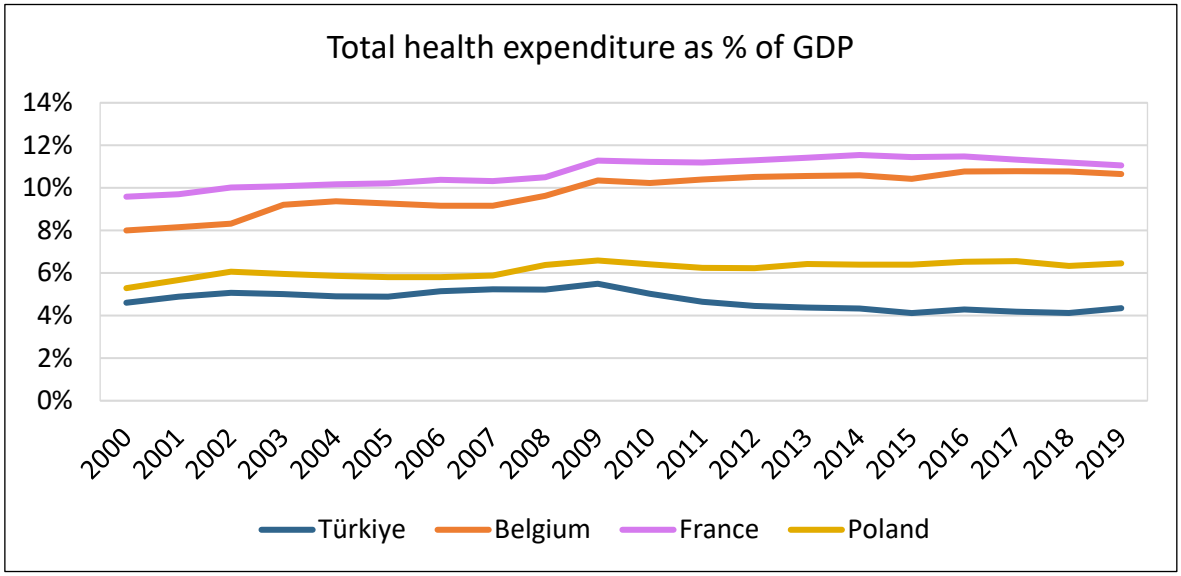


Figure 23: Total health expenditure as % of GDP, 2000–2019
Notes: GDP = gross domestic product. Source: WHO (41).

The health system in Türkiye has been characterized by comparatively low spending levels for the last two decades; see Figure 23. In the 2000s, the spending level was around 5% of GDP, and declined to around 4% in 2010s. In the three benchmark countries, spending levels increased slightly during the last two decades, widening the gap between them and Türkiye.

According to the latest comparable information from 2019, total health expenditure (financed from public and private sources) in Türkiye stood at 4.3% of GDP; see Figure 24. The public part of the total health expenditure was only 3.4% of GDP, falling short of the 5%-WHO-benchmark. In

comparison, public health expenditure in Poland amounted to 4.6% of GDP and in Belgium and France they just exceeded 8% of GDP.

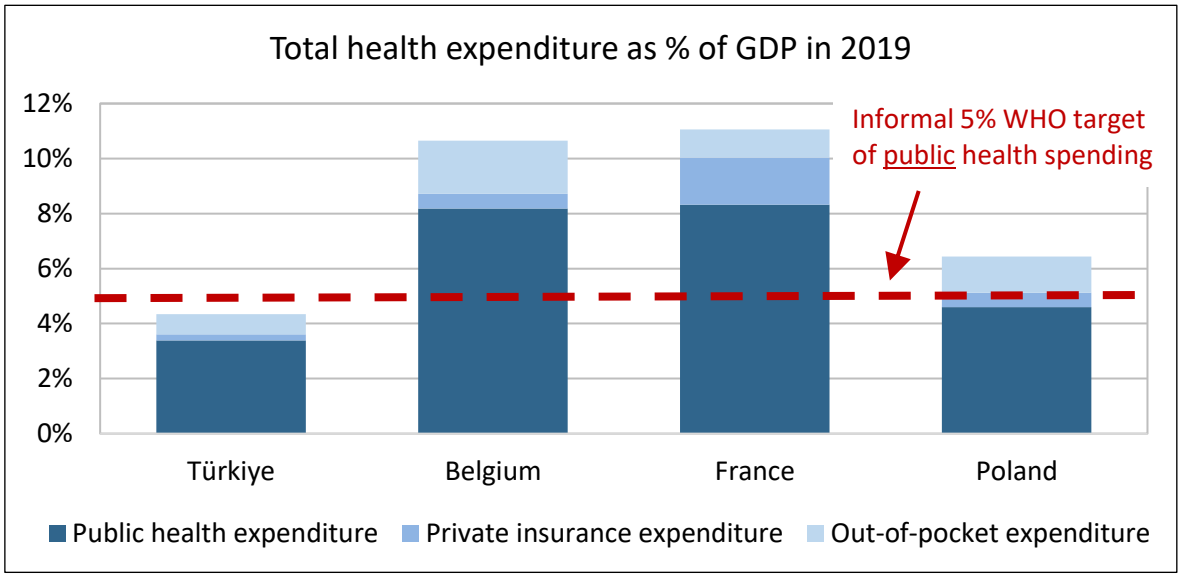


Figure 24: Total health expenditure as % of GDP, 2019

Notes: GDP = gross domestic product. Source: WHO (41).

The comparatively low level of public spending in Türkiye is worrisome. As emphasized above, the level of public health spending matters for being able to provide comprehensive and adequate coverage to the whole population. In relation to Türkiye's health system, the WHO notes that there are challenges to equitable access, exacerbated, for example, by a nationwide shortage of physicians (59). This is similar to the situation in Poland, where the WHO notes that there are key gaps in the scope and depth of public coverage of modern health services despite UHC (65).

4. Defining access to high-quality cancer care

The chapter provides a conceptual description of how to define access to cancer care and how to define quality of care in oncology.

4.1 Defining access to cancer care

UHC is the most basic prerequisite for patients to gain access to health care and cancer care. Figure 25 shows the dimensions of UHC as described by the WHO (69). The three dimensions are the population covered, the services covered, and the proportion of costs covered. These dimensions apply to health care in general but also to cancer care. As described in chapter 3, Türkiye already succeeded in implementing UHC. Yet there are still challenges such as including additional population groups (e.g., Syrian refugees), covering more modern cancer care services (e.g., positron emission tomography (PET) scans, next-generation sequencing (NGS) testing, immunotherapy medicines), and reducing out-of-pocket payments for these services. Managing a health care system with limited resources requires policy makers to take critical decisions about which dimension to prioritize and to what extent.

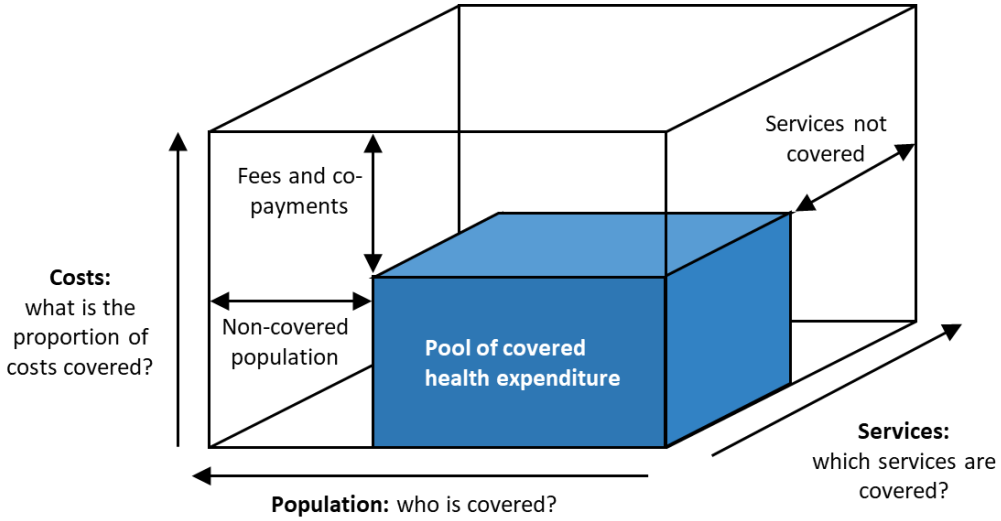


Figure 25: Dimensions of Universal Health Coverage
Source: Adapted from WHO (69).

The dimensions of UHC cover the first layer of access to health/cancer care. They define the basic availability (supply) of health care services that people could theoretically have access to in a country. They are mostly a question of adequate public financial resources spent on health care (71).

The second layer is a question of actually being able to gain access to existing health care services (matching patient demand with supply) (71). There are several barriers that prevent patients from gaining access to health care:

- **Geographic accessibility**: This denotes the geographic barrier that patients have to overcome to get from their homes to the health care facility. This is linked to the availability of a means of transportation, distance, travel time, and cost (72). In cancer care, the spatial concentration of specialized cancer care facilities is detrimental to accessibility but might increase the quality of care provided for those gaining access.
- **Timely accessibility**: This denotes contact accessibility, describing the ease of contacting providers for appointments, and appointment accessibility, indicating the length of time it takes to get an appointment (73). Waiting lists are a result of appointment inaccessibility and indicate a mismatch between the demand and supply of health care services.
- **Affordability**: This denotes the financial barrier and is about patients' ability to pay for health care services taking into account any health insurance scheme that the patient might have signed or is included in (72).
- **Acceptability**: This denotes the social and cultural barrier that stands in between patients and the health care system. It describes patients' attitudes, beliefs, and trust in the ability of the health care system to deliver the help that they need (72). This is also a question of health literacy.

4.2 Defining quality of care in oncology

Any discussion about access to cancer care needs to consider the quality aspect of cancer care. A conceptual way to think about quality of care is the Donabedian model (74). This model postulates that quality of care is composed of three components: quality of structure, quality of process, and quality of outcome; see Figure 26 for an illustration. Quality of structure refers to contextual factors or inputs (such as human resources, physical facilities, equipment) for the care process as well as organizational factors. Quality of process refers to all actions in health care provision (such as diagnosis and treatment) and is, among other things, shaped by clinical and health policy guidelines. Quality of outcome refers to the effects of health care provision on the patient (such as health status, health-related quality of life, patient satisfaction).

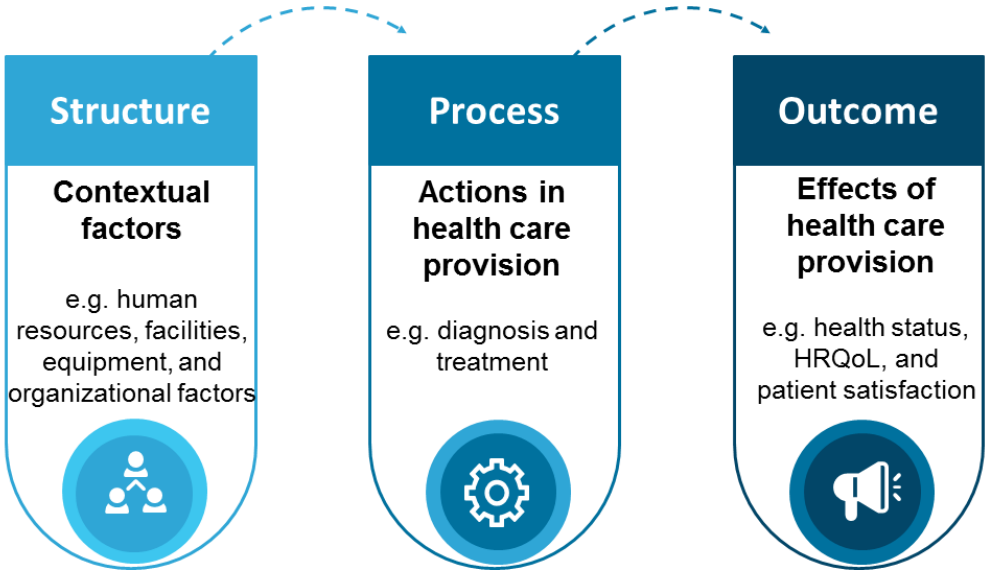


Figure 26: Donabedian model of quality of health care

An oversimplified but useful interpretation of the Donabedian model is to think of the three dimensions in terms of inputs, outputs, and outcomes (75). This interpretation alludes more to the notion of efficiency in care provision. The aim of an efficient care provision is essential to ensure value-for-money. "Quality of care" would here be interpreted as "value", and value would be defined as the "health outcomes achieved per euro spent" (76).

4.3 Assessing cancer care

Five different areas of cancer control can be distinguished; see Figure 27. Four areas – prevention, early detection, diagnosis and treatment, survivorship – follow a life-course approach whereas the fifth area – governance – is a cross-cutting area that affects the other four.

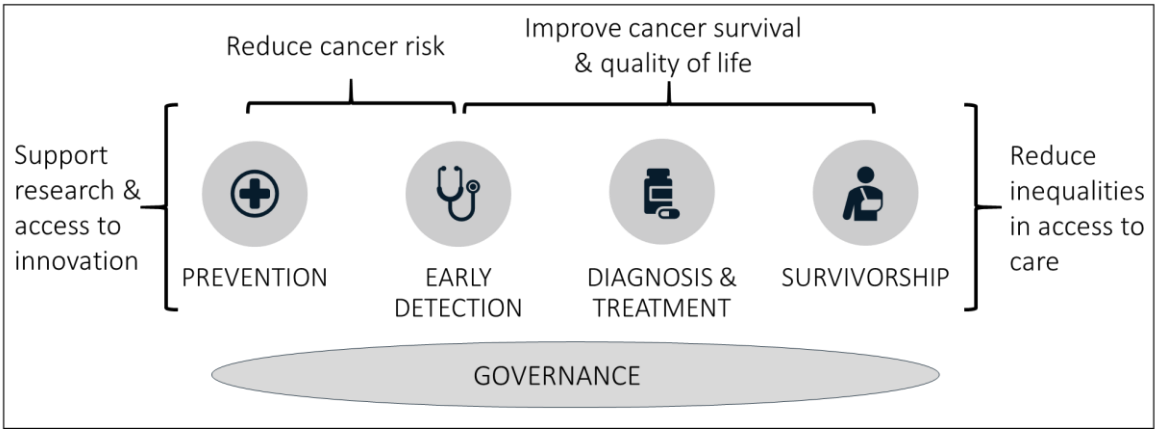


Figure 27: Areas of cancer control and overarching goals

Overarching goals of cancer control are also included in Figure 27. This includes:

- **Reduce the risk to get cancer**: Through prevention measures, lifestyles that increase the risk of developing cancer should be reduced. Early detection of pre-cancer (cancer in situ) through screening can help to reduce the risk of developing cancer.
- **Improve cancer survival and quality of life**: For people who develop cancer, early detection together with high-quality treatment is imperative for improving survival. Palliative care in the end-of-life setting and psychosocial care for survivors can increase patients' quality of life.
- **Reduce inequalities in patient access to all areas of cancer control**: This includes protection from the financial burden of cancer, but also overcoming geographic barriers (urban vs. rural), socio-economic barriers (men vs. women, high-income/educated vs. low-income/educated people, local citizens vs. refugees), and cultural barriers (ethnic groups).
- **Support cancer research and enable access to innovation**: To advance the quality of care, innovative diagnostic and treatment modalities need to be incorporated in the care process.

The remainder of the report focuses on three of the five areas of cancer control – governance, early detection (with a focus on screening), and diagnosis and treatment. A number of key indicators have been collected for each of these areas to assess the status of patient access to high-quality cancer care in Türkiye.

5. Governance of cancer care

Effective cancer control requires a strategy that facilitates the coordination between all areas of cancer control; see Figure 27. Many times, this strategy takes the form of a national cancer control program (NCCP) (section 5.1). A designated institution, such as the Ministry of Health, with a clear leadership and responsibility for cancer control is important for governance, irrespective of whether a formalized NCCP exists or not. In order to monitor the burden of cancer and the effectiveness of the implementation of cancer control measures, reliable and up-to-date data are essential. These data should come from cancer registries (section 5.2).

5.1 National cancer plans

NCCPs, often simply called "national cancer plans", are formalized plans by governments to address cancer. The WHO endorses them as the best available method to control both the causes and the consequences of cancer in a strategic and comprehensive way (77). They are "*designed to reduce cancer incidence and mortality and improve the quality of life of cancer patients, through the systematic and equitable implementation of evidence-based strategies for prevention, early detection, diagnosis, treatment and palliation, making the best use of available resources.*" (78).

Türkiye

Cancer control in Türkiye is coordinated by the Ministry of Health. The first NCCP was released in 2009 (79). It defined multiple actions for the period 2009–2015, covering the following areas:

- **Prevention**: Actions to address four priority risk factors (tobacco use, infections, environmental and occupational factors, obesity and lack of physical activity)
- **Early detection**: Actions to (1) educate the society about cancer, early diagnosis, and screening programs, as well as training of medical personnel on cancer, early diagnosis, and screening programs; (2) improve cooperation and coordination among institutions responsible for screening (covering breast, cervical, and colorectal cancer)
- **Treatment**: Actions to improve cancer treatment services by (1) improving human resources, (2) improving the technological and physical infrastructure, (3) development of a national policy in diagnosis, treatment, and medicament applications, (4) establishment of a national organization structure in cancer care, (5) establishment of a delivery chain structure in diagnosis, treatment, and scientific research concerning cancer

- **Palliative care**: Actions to (1) develop awareness about palliative care among medical professionals and the public, (2) extend palliative care services throughout the country, (3) ensure that all cancer patients requiring palliative care can get that service

The planned actions covered all four core areas of cancer control shown in Figure 27. All planned actions had "indicators of progress" to be able to measure the success of their implementation. Most of the planned actions required major investments in infrastructure, human resources, training, equipment, medicines, etc. However, the plan did not include a funding plan.

In 2013, the Ministry of Health renewed the cancer plan (80). The second NCCP covered the period 2013–2018. It defined multiple actions in the following areas:

- **Prevention**: Actions to (1) create Turkey Asbestos Control Program, (2) create a Turkey Radon Map, (3) monitor effects of electromagnetic fields on health and raising awareness of the public
- **Early detection**: Actions to (1) create awareness for cancer, (2) improve and extend the scope of national population-based screening programs for breast, cervical, and colorectal cancers, (3) use of HPV tests in screening for cervical cancer
- **Palliative care**: Actions to improve palliative care through (1) procurement of palliative care policies to be formal governmental policies, (2) giving palliative care educations, (3) establishment of palliative care centers, (4) increasing the use of opioids in cancer patients
- **Cancer registration**: Actions to (1) establish an active cancer registration center in 81 cities, (2) increase quality of cancer registration data

The planned actions covered three core areas of cancer control but omitted actions relating to "diagnosis and treatment" (see Figure 27). As in the first NCCP, all planned actions had "indicators of progress" to be able to measure the success of their implementation until 2018. The NCCP did not include a funding plan for the financing of all planned actions.

In August 2021, the Ministry of Health launched the third NCCP (81). The NCCP contains a detailed description of cancer registration and the epidemiological situation in Türkiye. It also reviews the areas of prevention and screening. Diagnosis and treatment of cancer is not described, except for a section on – global but not Türkiye-specific – standard of care in breast cancer treatment. The NCCP defines the following five actions:

- **Prevention**: (1) Turkey Asbestos Control Strategic Plan, (2) Turkey Radon Mapping and National Radon Control Program

- **Early detection**: Improvement and increasing the coverage of breast, cervical, and colorectal cancer screening
- **Cancer registration**: (1) Ensuring the functionality of cancer registry centers established in 81 provinces, (2) Improving cancer registry data quality

The third NCCP contains the shortest list of actions and no actions related to "diagnosis and treatment" or "survivorship". As with the first and second NCCP, all planned actions have "indicators of progress" to be able to measure the success of their implementation until December 2023. A funding plan for the financing of all planned actions is lacking.

Belgium

Belgium has only had one national cancer plan in the past. The background to the plan was a report published by a group of Belgian oncologists in 2007 on the status of all aspects of cancer care in the country, including proposals for improvement and anticipation of new challenges (82). The Ministry of Social Affairs and Public Health, after consultation with stakeholders, published a national cancer plan in 2008 for the period 2008–2010 (83). This plan effectively addressed many of the issues raised in the 2007-report (82).

The primary objectives of the NCCP were to reduce mortality and morbidity and to enhance quality of life of patients and their families. The NCCP contained 32 actions (83). The actions covered three main areas to be implemented by the Federal Service of Public Health and the NIHDI:

- **Prevention and screening** (6 actions): such as tobacco control, HPV vaccination program, screening programs
- **Treatment and support** (20 actions): such as introduction of multidisciplinary consultations, establishment of clear care pathways, recognition of the title of oncology nurse, reimbursement of selected cancer medicines, improvement of rehabilitation services
- **Research, innovative technologies, and evaluation** (6 actions): such as creation of a tumor bank, support for translational research, strengthening cancer registration

These actions were supported by a dedicated budget of €380 million for the period 2008–2010 (83), corresponding to €12 per capita per year. The budget was created based on a budgetary evaluation for each of the planned actions. By 2010, half of all actions had been implemented (82), and by 2015 nearly all actions had been structurally implemented (84).

There were plans for a follow-up, second Belgian Cancer Plan for the period 2011–2015 (82), but these were ultimately not pursued. Instead, there was a shift in cancer control policy towards

"targeted interventions based on needs" (84). Two examples are the introduction of NGS in routine diagnostics in oncology, and the concentration of complex surgery for pancreatic and esophageal cancer to larger treatment centers (84).

France

France has a long tradition of governing cancer control by NCCPs (85). The first NCCP (2003–2007) included 71 actions related to prevention and screening, care and patient support, upgrading care facilities, access to innovative treatment, and research and training. Notably, it established the National Cancer Institute (INCa) in 2004, which has been in charge of coordinating and evaluating cancer care in France ever since (85). The second NCCP (2009–2013) emphasized the personalization of care and the deployment of therapeutic innovations (85). As a part of the first two NCCPs, large investments were made in diagnostic and therapeutic equipment to improve quality of care (86, 87).

The third NCCP (2014–2019) aimed to cure more patients, maintain continuity and quality of life, invest in prevention and research, and optimize management and arrangements in the fight against cancer (85). It contained 17 operational objectives, which were supported by 208 actions. Every year, the INCa published a report on the progress made with the implementation of the actions (88).

The latest NCCP was published in 2021 and covers the period 2021–2030 (89). The plan was drafted by the INCa based on an evaluation of the third NCCP. It was subject to a wide consultation that brought together all stakeholders in oncology to define priorities and actions in fight against cancer for the next ten years. A roadmap for the first half (2021–2025) defines 234 actions that will be implemented until 2025. The NCCP focuses on four strategic goals:

- **Improve prevention** (13 objectives): such as putting an end to tobacco use; improving access to screening and preparing future screening programs
- **Limit negative consequences and improve the quality of life** (14 objectives): such as facilitating patient access to diagnostic and therapeutic innovations; preventing, identifying, and treating negative disease-related or treatment-related consequences; supporting carers to protect their health and retain their quality of life
- **Fight against cancers with poor prognosis** (7 objectives): such as guaranteeing seamless care pathways; ensuring patient access to innovative therapies within the scope of clinical trials

- **Ensure that progress benefits everyone** (7 objectives): such as taking action to reduce cancers in children, adolescents, and young adults; enabling remote regions to provide high-quality tailored care

The plan includes a funding plan of €1.7 billion, corresponding to €5 per capita per year, that has been earmarked by the government to support the implementation of the first half of the plan until 2025 (90). Of this amount, €634 million will be spent on research, mostly coordinated by the INCa (91).

Poland

The first NCCP was adopted by the Ministry of Health in 2005 and covered the period 2006–2015 (92). The plan contained a strong focus on early detection through screening programs, but also on prevention, and enhancing treatment effectiveness as well as monitoring the effectiveness of the fight against cancer. The government earmarked PLN 3 billion (ca. €750 million, corresponding to around €2 per capita per year) in funds to support the implementation of planned actions over the whole ten-year period (92). In 2014, a white paper by different stakeholders in oncology was published (93), which included 30 objectives, covering the organization and management of the cancer care system, cancer science and research, prevention, screening, diagnosis and treatment, and quality of life during and after treatment. It influenced the adoption of the second NCCP in 2015, covering the period 2016–2024 (94). The second NCCP defined actions covering prevention, early detection including screening, improving treatment, oncological education of medical staff, and supporting the cancer registration system. It contained a yearly budget of PLN 250 million (ca. €58 million, corresponding to around €1.5 per capita per year) to support the implementation of planned actions (94).

The latest NCCP was published in 2020 and covers the period 2020–2030, replacing the second NCCP (95). The NCCP defines 23 main goals with multiple supporting actions in five areas:

- **Human resources**: such as improving the staffing situation and the quality of oncological education of medical staff
- **Prevention**: such as health education in schools, public campaigns to adopt a healthy lifestyle, introduction of an HPV vaccination program for girls and boys
- **Screening**: such as stronger involvement of primary care to motivate people from high-risk groups to undergo screening, social campaigns to increase participation in screening
- **Science and innovation**: such as increasing the number of patients participating in clinical trials, establishing a network of tumor banks, shortening the patient's access time to innovative therapies and expanding the list of reimbursed medicines

- **Cancer care system**: such as the implementation of quality criteria for key diagnostic procedures, development of guidelines for conducting diagnostics and treatment, modernization of infrastructure, improving the quality of life of cancer patients during and after treatment

The implementation of the actions in the NCCP is monitored in annual reports (96). The NCCP also specifies earmarked funding for the implementation of all actions, PLN 250 million (around €1.5 per capita) in 2020, PLN 150 million per year (around €1 per capita) in 2021–2023, and PLN 71.43 million per year (around €0.5 per capita) in 2024–2030 (95).

Overview

The description above highlights several important differences in the NCCPs of Türkiye and the three benchmark countries. Table 3 provides an overview. The latest NCCP in Türkiye was published in 2021 and only establishes five actions until 2023, whereas France and Poland both work with 10/11-year long strategies that contain several dozens of actions.

As opposed to the first NCCP in Türkiye, the two latest NCCPs did not include actions to address the whole continuum of care (see Figure 27). Actions for improving "diagnosis and treatment" and also "survivorship" are missing. By contrast, the three benchmark countries all defined a comprehensive set of actions across the continuum of care, which prevents arbitrariness and improves coordination between different actors involved in cancer control.

The Turkish NCCP lacks annual monitoring of the implementation of its five actions, whereas this is done in France and Poland. The NCCPs of all three benchmark countries contain a funding plan for the planned actions, whereas the Turkish NCCP lacks a funding plan. Having at least a crude funding plan included in the cancer plan can serve as reality check for whether all planned actions are financially viable. The fact that the current (and also the past) Turkish NCCP does not include this information casts some doubt on the feasibility to implement the actions, because they require additional funding.

Table 3: National cancer plans

	Plan and time period	Publisher of the plan	Actions across the continuum of care	Annual monitoring of implementation	Funding plan
Türkiye	Plan for 2021–2023	MoH	No	No	No
Belgium	Plan for 2008–2010	MoH	Yes	No	Yes
France	Plan for 2021–2030	INCa	Yes	Yes	Yes
Poland	Plan for 2020–2030	MoH	Yes	Yes	Yes

Notes: MoH = Ministry of Health.

5.2 Cancer registries

To mount the challenge with cancer, policy-makers need reliable and up-to-date local data on the cancer burden. A population-based cancer registry is the best tool to collect such data (97). A registry is ideally covering the entire country, but it can also be enough to cover one or multiple regions within the country that are representative of the rest of the country. A description of the state of cancer registration in Türkiye and the three benchmark countries is provided below.

The first cancer registry in Türkiye was established in İzmir province in 1992 (98). This registry became a member of the International Association of Cancer Registries in 1995 and the European Network of Cancer Registries in 1997, demonstrating that this registry was meeting international standards. Subsequently, other Turkish provinces established cancer registries with İzmir as its model. However, many provinces struggled initially to achieve the necessary level of data quality (98). Over the years, more and more cancer registries in all parts of the country have been established. Figure 28 shows how the population coverage of active cancer registries used for official statistics by the Ministry of Health has steadily increased from around 16% in 2004 to 50% in 2017. Since 2013, cancer registration is ongoing in all 81 provinces, but the functionality and quality of the data in many provinces is still inadequate to be used for policy purposes (81). The latest NCCP from 2021 aims to improve this situation until the end of 2023 (81).

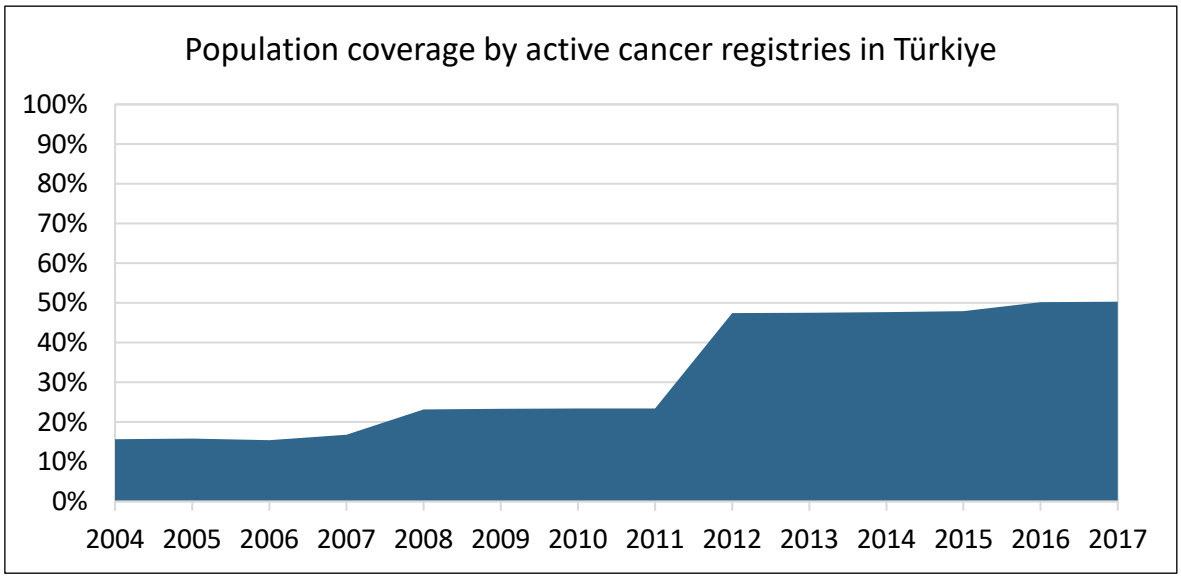


Figure 28: Population coverage by active population-based cancer registries in Türkiye
Notes: The graph includes the cancer registries used for official statistics by the Ministry of Health. The addition of Ankara causes the jump from 2007 to 2008 and the addition of Istanbul the jump from 2011 to 2012. Ministry of Health (13).

In Belgium, cancer registration started already in 1950, but the development of a population-based cancer registry covering the entire country was not achieved until 2005 (99). In France, the oldest

regional cancer registry started collecting data in 1975 (100). Currently, the French population-based cancer registries (Francim network) cover 19 to 22 districts, depending on the cancer site, equal to 21 to 24% of the metropolitan population (100). In Poland, cancer registration started in 1952, but was for many decades plagued by poor quality and completeness of data (101). Since 1999, a network of 16 regional cancer registries covering all voivodeships of the country report data into the national cancer registry, yet underreporting is still occurring in some regions (102).

Despite the progress with cancer registration made in Türkiye, there are still persistent challenges. Without good local data from cancer registries, it is difficult to develop, assess, and monitor concrete cancer control measures. The main areas for improvement are:

- **Comprehensiveness and relevance of the data**: The annual reports by the Ministry of Health only provide data on incidence. Without also including information on mortality (which is already collected by TurkStat), it is impossible to trace out improvements in the treatment of cancer. There are also no statistics on survival rates, which is the best metric to measure the effectiveness of cancer care. There is only one published study about survival rates of gynecological cancers that used information from several regional registries (103).
- **Reliability of the data**: Underreporting of the number of cancer patients is happening. This is mainly a result of Turkish registries not collecting data on non-nationals. The mobility of the refugee population within the country results in the absence of accurate information (104).
- **Up-to-dateness of the data**: Information on the latest data on incidence is published with considerable delay by the Ministry of Health. As of May 2022, only data for 2017 are available. Belgium and Poland publish similar data two years faster; see Table 4.

Table 4: Cancer registries

	Is there a population-based nationwide cancer registry?	Are there annual publications of the cancer registry in publicly available reports/websites? °	What is the latest year of publicly available data (as of May 2022)?
Türkiye	No, but 14 active regional population-based registries*	Yes, for incidence	2017
Belgium	Yes	Yes, for incidence and survival	2019
France	No, 14 regional general population-based registries and 9 regional specialized population-based registries	No, only irregular updates on incidence, mortality, and survival	2018 (2015 for survival)
Poland	Yes	Yes, for incidence and mortality; Survival is only published at an irregular basis	2019

Notes: * In principle, all provinces are covered by registries, but only data from 14 registries are used by the Ministry of Health, covering the provinces of İzmir, Antalya, Bursa, Eskişehir, Samsun, Trabzon, Edirne, Erzurum, Ankara, Gaziantep, Malatya, İstanbul, Mersin, Kocaeli. ° Mortality data based on cause of death statistics are regularly published by the national statistical authorities in all countries.

6. Screening

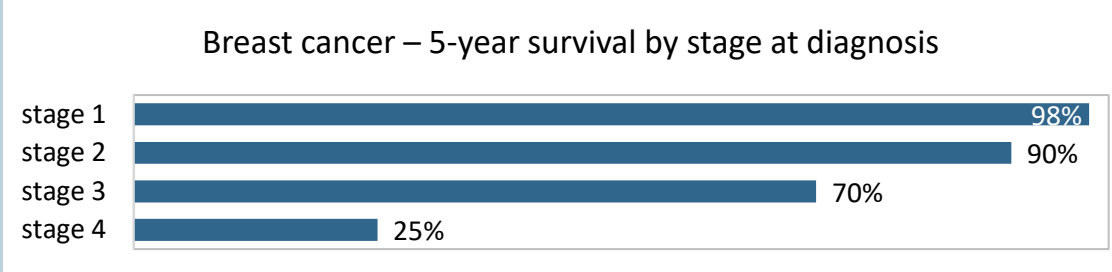
This chapter describes the current state of screening in Türkiye. It describes general key elements of a high-quality screening program (section 6.1), reviews screening programs for breast cancer (section 6.2), cervical cancer (section 6.3), and colorectal cancer (section 6.4), and potential future screening programs (section 6.5).

Screening is an essential part of the cancer control area "early detection"; see Figure 27. Screening for cancer aims to detect abnormal cells among healthy, asymptomatic people as early as possible (105). The ideal situation would be to detect abnormal cells at the earliest possible stage (stage 0, also known as cancer in situ or pre-cancer) when there is only a group of abnormal cells localized at limited site. These abnormal cells may become cancer and spread to nearby normal tissue. They can usually be removed by surgery. The detection and treatment of in-situ (i.e., non-invasive) cases can help to reduce the cancer incidence in a population, because in-situ cases are usually not counted as real (i.e., invasive) cases of cancer.

In reality, screening will most often detect cancer when it has already turned into a malignant tumor (invasive cancer). The tumor might be localized at the site of origin (stage 1), have started to spread to nearby tissue (stage 2 and stage 3), or metastasized and spread to other parts of the body (stage 4). Screening can help to increase the share of people diagnosed with early-stage cancer (stage 1) and decrease the share diagnosed with late-stage cancer (stage 4). This will improve survival of patients (and thereby reduce the number of people dying from cancer), because the earlier stage at diagnosis, the better the chances to survive; see Info Box 5.

Info Box 5 – The benefits of early cancer diagnosis

The chances to survive cancer vary by stage at diagnosis. Survival chances are far greater when the cancer is diagnosed at an early stage when the tumor is still small and not spread. At a late stage, when the tumor has started to spread to other parts of the body, survival chances are smaller. The figure below illustrates 5-year survival rates for breast cancer, cervical cancer, and colorectal cancer by stage at diagnosis. For all three cancer types, survival rates in stage 1 are 90% or higher, whereas for stage 4 they are 25% or lower.



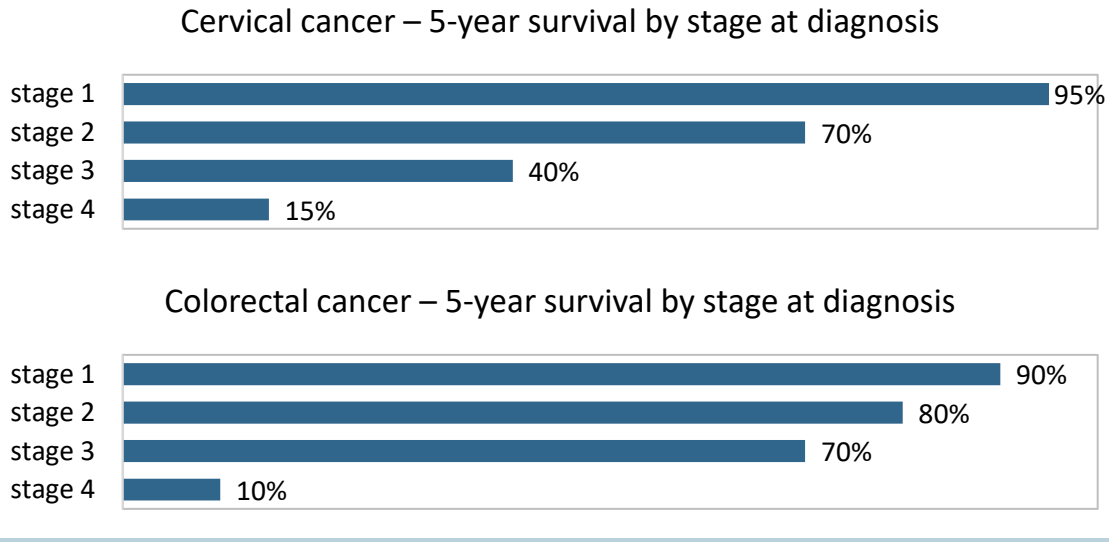


Figure 29: 5-year net survival rates for selected cancer types by stage at diagnosis of adult patients (15–99 years) diagnosed in England in 2013–2017

Notes: Stage 1 ("localized") = tumor is small and is localized to its primary site. Stage 2 ("locally spread") = tumor has grown and may have spread into nearby tissue. Stage 3 ("regionally spread") = tumor has grown larger and may have spread into nearby tissue or the lymph system. Stage 4 ("metastasized") = tumor has spread to other organs or parts of the body. Source: Office for National Statistics (106-108).

In addition to the potential health benefits from early diagnosis through screening, there are also economic implications to consider. The implementation and running of screening programs costs money and requires additional resources for testing and administration. However, the additional costs for screening might be partially offset by reduced costs for treatment. The figure below shows results from studies that determined the treatment costs of breast cancer and colorectal cancer by disease stage. Treatment costs of patients diagnosed with stage 1 are lowest, whereas treatment costs of patients diagnosed with stage 4 are highest and more than twice as high (>100%) as in stage 1. Screening thus can increase the proportion of "cheaper patients" and decrease the proportion of "more expensive patients".

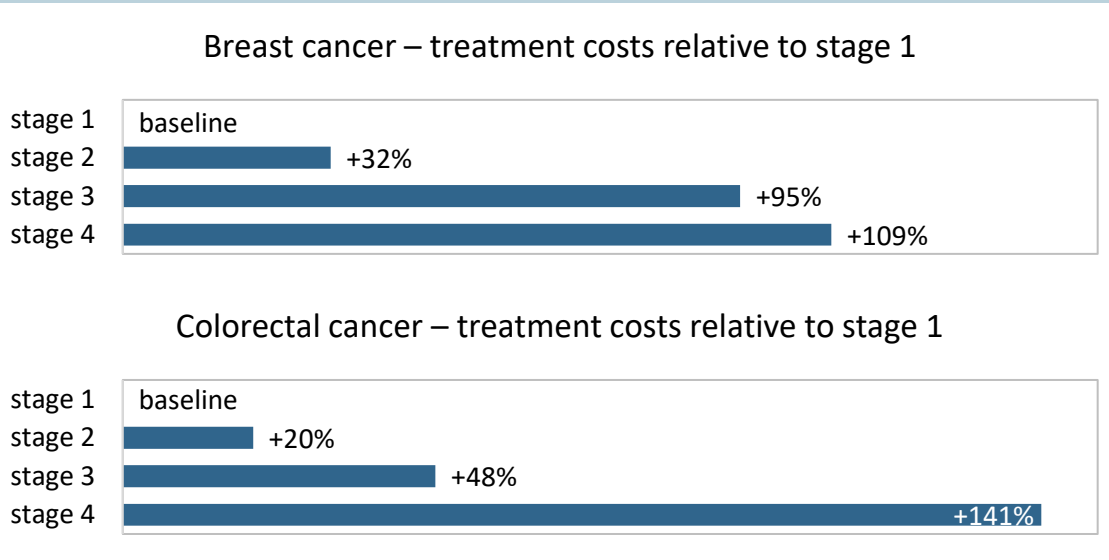


Figure 30: Treatment costs of selected cancer types by stage at diagnosis

Source: Systemic review of 20 international studies of treatment costs of breast cancer by Sun et al. (2018) (109), and analysis of medical costs of colorectal cancer in the United States by Mariotto et al. (2020) (110).

6.1 High-quality screening programs

Screening programs are an integral tool to take to tackle the growing disease burden of cancer. The WHO currently (as of 2022) recommends three cancer screening programs for breast, cervical, and colorectal cancer (105). These are also the same three programs that have been listed in all three Turkish NCCPs since 2009 (79-81), and that have been recommended since 2003 by the Council of the European Union (111).

Several factors determine the quality and success of a cancer screening program:

- **Type of organization**. Three types of organization can be distinguished (112):
    - Organized population-based programs: They address a healthy population segment eligible for screening and actively urge the whole target population to participate. The WHO emphasizes that only organized screening programs are likely to be fully successful in reaching a high proportion of the at-risk population (113). Türkiye has this type of organization for all three screening programs.
    - Non-organized programs: They define a healthy population segment eligible for screening which has a right to receive screening at the request of an individual.
    - Opportunistic programs: Screening is offered to an individual without symptoms of cancer when they present to health care for unrelated reasons.
- **Public information campaigns**. They are intended to raise awareness and to inform people about the availability and benefits of screening. Information campaigns have been shown to be a powerful tool to promote and increase the utilization of screening services by lowering peoples' reservations and concerns about it (114, 115). Involving NGOs such as patient organizations can increase the chances to reach a wide audience.
- **Target population**. The target population should be a population segment that has an increased risk of developing a certain cancer type. It should neither be defined too broadly or too narrowly. The WHO notes that screening of only a high-risk group is rarely justified, as identified risk groups usually represent only a small proportion of the cancer burden in a country (113). However, defining the target group too broadly will increase the number of people subject to false positive diagnosis and negatively impact on the cost-effectiveness of the screening program.
- **Test method**. The method has to be safe and effective. The effectiveness depends on the accuracy of the screening method. Accuracy is judged by having a high sensitivity (i.e., as

few people as possible with the disease get through undetected) and high specificity (i.e., as few people as possible without the disease are subject to further diagnostic tests) (113).

- **Screening interval**. If the interval between two screening sessions is too short, it will lead to high costs for screening with no additional patient benefits. If the interval is too long, screening will fail to detect many cancers at an early stage.
- **Follow-up actions**. Mechanisms for referral and treatment of abnormalities have to be put in place (113). There is little sense in spending money on screening if all patients with a diagnosis are not also offered appropriate treatment.
- **Coordination and quality assurance of activities across the entire pathway**. A quality control system to manage and monitor screening tests and clinical quality is essential (112). This requires an information system that can send out invitations for initial screening, recall individuals for repeated screening, follow those with a positive diagnosis, and monitor and evaluate the program.

In Türkiye, cancer screenings are executed by Cancer Early Diagnosis, Screening and Training Centers (KETEM, Kanser Erken Teşhis, Tarama ve Eğitim Merkezi). KETEMs operate three programs for breast, cervical, and colorectal cancer. The number of KETEMs has steadily increased from 11 in 2004 to 197 in 2013 (at least one in each of the 81 provinces) and to 336 in 2021 (80, 116). In the KETEMs, physicians, nurses, midwifes, x-ray technicians and medical technicians who take necessary training on protection and screening for cancer, are employed. Employees are also trained on communication and health education (80). KETEMs are supported by mobile teams, using trucks that tour more remote areas. These trucks may stop in villages for several weeks at a time and perform all kinds of screening using onboard facilities (117, 118).

For people in the target population of the three screening programs, there is no need to make an appointment at the KETEM. People can go there directly. People may also be referred to the KETEM by their family physician. At the KETEM, screenings are carried out free of charge for all people with an identification number (119). The Turkish Ministry of Health also regularly tries to raise awareness about screening in conjunction with Breast Cancer Awareness Month (October) and Colorectal Cancer Awareness Month (March) (120, 121).

6.2 Breast cancer screening

The WHO and the Council of the European Union recommend breast cancer screening (105, 111). The initial recommendation in Europe was to screen women aged 50–69 years with mammography. Guidelines from 2013 further specified that mammography should take place every 2 years (122). A

physical examination of the breast (clinical breast examination) by a health professional without a mammography is not recommended. In 2022, new recommendations extending the age group were issued by the European Commission (123). Mammography screening is nowadays "recommended" for women aged 45–74 and "strongly recommended" for women aged 50–69 (124). Also, the recommended screening interval is 2–3 years for women aged 45–49, 2 years for women aged 50–69, and 3 years for women aged 70–74 (124).

In Türkiye, an organized[14] breast cancer screening program is in place (121). Organized screening activities started in early 2004 (126). The current program targets women aged 40–69 to be screened with mammography every 2 years.[15] Women are invited (by mail or phone) for breast cancer screening via a call & recall system, and these invitations are done by family physicians and KETEMs (126), but opportunistic screening of women who visit health clinics or hospitals for unrelated reasons is also done (80). The aim of the NCCPs from 2009 and 2013 was to achieve a breast cancer screening rate of 70% in the target population, whereas the NCCP from 2021 no longer explicitly mentions the 70% benchmark (79-81).

Table 5 shows the key features of the Turkish screening program as well as of the three benchmark countries. Apart from the lower starting age in Türkiye, the program features in all countries are similar and also aligned with recommendations by the European Commission.Table 5: Screening programs for breast cancer

Table 5: Screening programs for breast cancer

	Year of launch	Type of organization	Target group (sex, age)	Interval	Test method
Recomm-endation	-	Organized	Women aged 45-49 Women aged 50-69 Women aged 70-74	2-3 years 2 years 3 years	Mammography Mammography Mammography
Türkiye	2004	Organized	Women aged 40-69	2 years	Mammography
Belgium (128**,** 129**)**	2001/02	Organized	Women aged 50-69	2 years	Mammography
France (130**)**	2004	Organized	Women aged 50-74	2 years	Mammography
Poland (131**)**	2007	Organized	Women aged 50-69	2 years	Mammography

The success of a breast cancer screening programs can be measured by its participation rate. Figure 31 shows the proportion of women aged 50–69 who were screened with mammography in the past 3 years. Türkiye achieved screening rates of 32% in 2014 and 40% in 2019, both well below the

[14] Some authors have pointed out that the current program is not strictly speaking an organized population-based program, as opportunistic screening occurs also (i.e., mammography is offered to women who visit health clinics for unrelated reasons) (125).

[15] Until 2013, the recommendation only applied to women aged 50–69 (125). The age was lowered to 40, because national data showed that breast cancer cases in women aged below 50 constituted 47% of all cases in Türkiye (127).

70%-aim specified in the Turkish NCCPs from 2009 and 2013. By contrast, the three benchmark countries all exceeded the 70%-mark in 2014 and also in 2019 (except Poland by a narrow margin), despite reductions in the screening rate between those years. The COVID-19 pandemic caused a drop in the screening rate in Türkiye; see Info Box 2 in section 2.3.

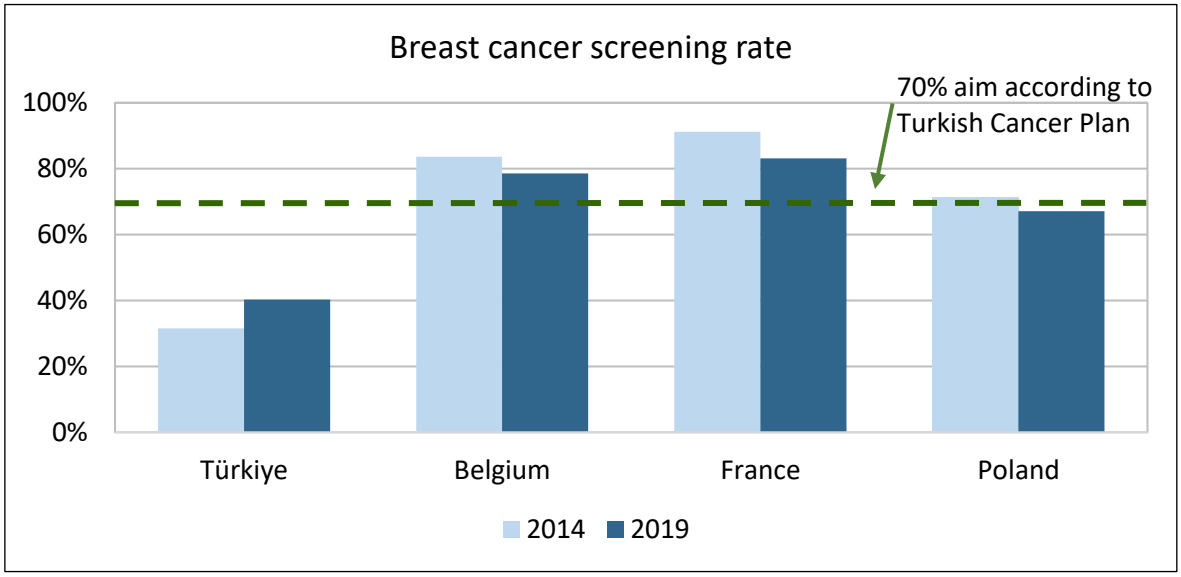


Figure 31: Breast cancer screening rate with mammography during the last 3 years among women aged 50–69 (self-reported)

Source: Eurostat (132).

Different studies have previously identified barriers to achieving high breast cancer screening rates in Türkiye. These barriers are:

- Low breast cancer awareness and awareness of screening (125, 127)
- Not knowing that breast cancer can be diagnosed early by mammography (133)
- Not knowing that breast cancer screening is for free (133)
- Geographical difficulties with accessing KETEMs due to limited means of transportation (126)
- Limited clinical staff to perform screening (126)

More detailed data for 2019 than those shown in Figure 31 revealed also large differences in the screening rate according to a women's formal level of education in Türkiye. Low-educated women (with at most lower secondary education) had a screening rate of 37%, mid-educated women (with at most a high school degree) had a screening rate of 51%, and high-educated women (with a university degree) had a screening rate of 58%. Awareness and willingness to participate in the screening program thus increases with the level of education in Türkiye.

6.3 Cervical cancer screening

The WHO and the Council of the European Union recommend cervical cancer screening (105, 111). The initial recommendation in Europe was to start screening women not before the age of 20 and not later than the age of 30 with a Papanicolaou (Pap) smear test (cytology testing). Guidelines from 2008 further specified that screening should continue at 3–5-year intervals until the age of 60 (134). In 2022, new recommendations changing the screening method from Pap smear testing to HPV testing were issued by the European Commission, motivated by the fact that almost all cervical cancers are caused by HPV infection (123). The recommendations also note that a negative HPV test is associated with a low risk of developing cervical cancer for 6 years (thus implying that the screening interval could be extended to at least 5 years), and that Pap smear testing can be reserved for women with persistent HPV infection. Furthermore, the roll-out of HPV vaccination programs among school children might in the future influence screening approaches and even end the need for screening.

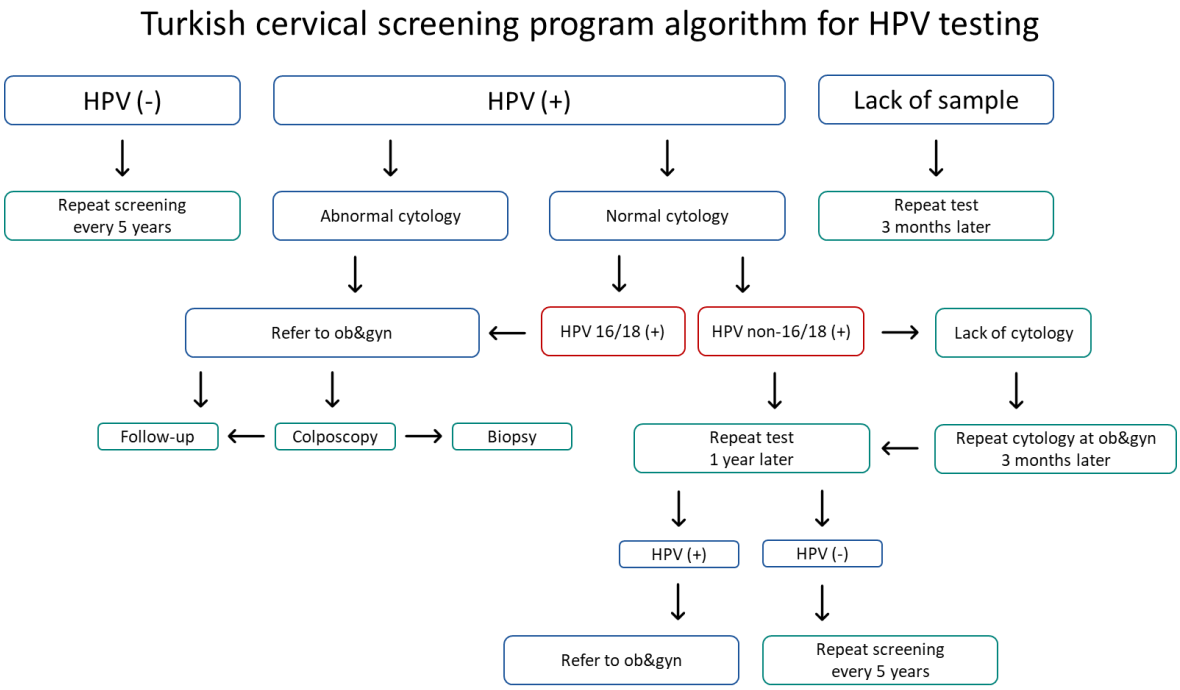


Figure 32: Algorithm of the Turkish cervical screening program with HPV testing
Notes: ob&gyn = obstetrics and gynecology specialist. Source: Ministry of Health (81).

In Türkiye, an organized cervical cancer screening program is in place (121); see Figure 32. Screening activities with Pap smear testing have been done for four decades but the organized program only started in 2004 (80, 135, 136). The current program targets women aged 30–65 to be screened with an HPV test every 5 years. The switch from Pap smear testing to HPV testing followed a complete overhaul of the program in 2014. Since then, the call and recall system and a centralized

monitoring system have been revamped. A single nationwide centralized diagnostic laboratory for HPV tests has been put in place (135, 136). The aim of the NCCPs from 2009 and 2013 was to achieve a cervical cancer screening rate of 70% in the target population, whereas the NCCP from 2021 no longer explicitly mentions the 70% benchmark (79-81).

Table 6 shows the key features of the Turkish screening program as well as of the three benchmark countries. Türkiye has a higher starting age (30 years) than all other countries (25 years), and it is the only country that already has made the recommended switch from Pap smear testing to HPV testing as the primary screening method.

Table 6: Screening programs for cervical cancer

	Year of launch	Type of organization	Target group (sex, age)	Interval	Test method
Recomm-endation	-	Organized	Women aged 20/30-65	5 years	HPV test
Türkiye	2004	Organized	Women aged 30-65	5 years	HPV test (primarily)
Belgium (128, 129)	n/a	Opportunistic	Women aged 25-64	3 years	Pap smear
France (137)	2018	Organized	Women aged 25-65	3 years	Pap smear
Poland (138)	2006	Organized	Women aged 25-59	3 years	Pap smear

The success of a cervical cancer screening programs can be measured by its participation rate. Figure 33 shows the proportion of women aged 20–69 who were screened with a smear test[16] in the past 3 years. Türkiye achieved screening rates of 23% in 2014 and 31% in 2019, both well below the 70%-aim specified in the Turkish NCCPs from 2009 and 2013. By contrast, the three benchmark countries all exceeded the 70%-mark in 2014 and also in 2019 (except Belgium by a narrow margin), despite reductions in the screening rate between those years in Belgium and France. In Belgium, one explanation for the reduction is that reimbursement of Pap smear tests has been made more restrictive (only one test every three years as opposed to one test every year) due to over-consumption of tests by some women (129). The COVID-19 pandemic caused a drop in the screening rate in Türkiye; see Info Box 2 in section 2.3.

[16] Eurostat does not explicitly state whether this also includes HPV testing in addition to Pap smear testing. However, previous studies have also reported low cervical cancer screening rates in Türkiye (133).

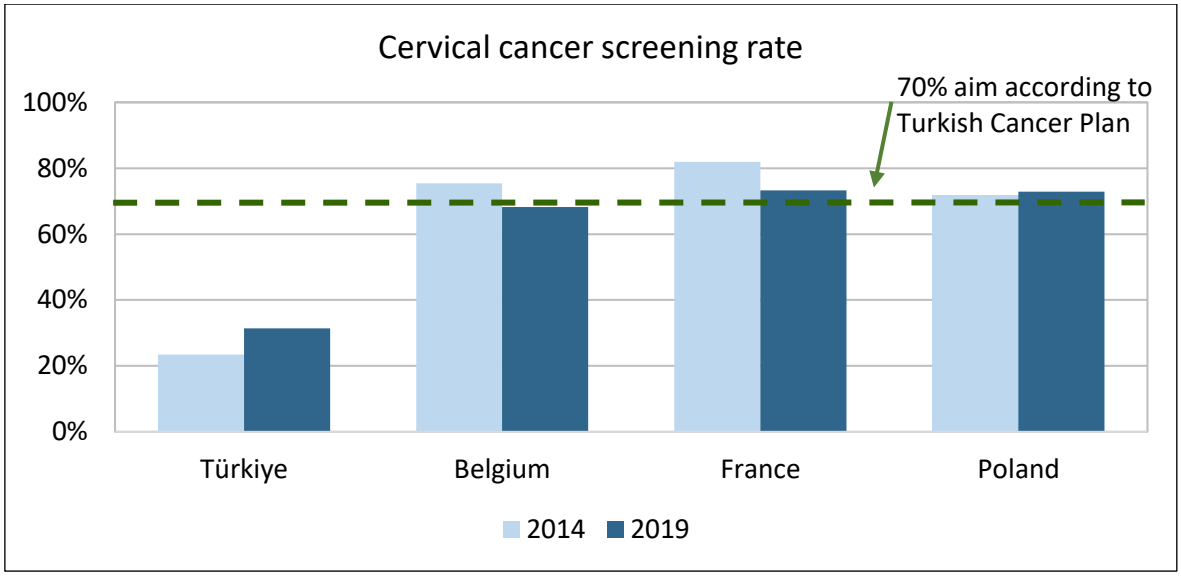


Figure 33: Cervical cancer screening rate with smear test during the last 3 years among women aged 20–69 (self-reported)

Source: Eurostat (139).

Different studies have previously identified barriers to achieving high cervical cancer screening rates in Türkiye. These barriers are:

- Low cervical cancer awareness and awareness of screening (140)
- Not knowing that cervical cancer can be diagnosed early (133)
- Not knowing that cervical cancer screening is for free (133)

More detailed data for 2019 than those shown in Figure 33 did not reveal any noteworthy differences in the screening rate according to a women's formal level of education in Türkiye. Low-educated, mid-educated, and high-educated women all had screening rates of between 30–34%. Awareness and willingness to participate in the screening program thus do not seem to be related to the level of education (as opposed to the results for breast cancer screening).

6.4 Colorectal cancer screening

The WHO and the Council of the European Union recommend colorectal cancer screening (105, 111). The initial recommendation in Europe was to screen men and women aged 50–74 years with fecal occult blood test (FOBT). Guidelines from 2010 added the fecal immunochemical test (FIT) as a recommended test method (141). They stated that the screening interval with FOBT should not exceed two years, and the screening interval for FIT should not exceed three years. They also noted that there is evidence showing that FIT is superior to FOBT with respect to detection rates and positive predictive value for adenomas and cancer. It was also noted that there exists some evidence

that FIT is a cost-effective alternative to FOBT (141). In 2022, new recommendations established FIT as the preferred triage test for referring individuals for follow-up colonoscopy (123). Colonoscopy-based screening is only recommended for people that tested positive with FIT and not as an upfront screening method.

In Türkiye, an organized colorectal cancer screening program is in place (121). Organized screening activities started in 2013 (121). The current program targets men and women aged 50–70 to be screened with FOBT every 2 years and colonoscopy every 10 years (even if all previous FOBT test were negative) (142). People get test kits for FOBT from the family physician or at the KETEM and then take test (stool sample) at home before returning the test kit. In case of a positive test result, the patient will be referred to a specialist physician for colonoscopy (142). The aim of the NCCPs from 2009 and 2013 was to achieve a colorectal cancer screening rate of 70% in the target population, whereas the NCCP from 2021 no longer explicitly mentions the 70% benchmark (79-81).

Table 7 shows the key features of the Turkish screening program as well as of the three benchmark countries. Türkiye has a lower stop age (70 years) than Belgium and France (75 years), and it uses FOBT instead the recommended FIT as in Belgium and France. Türkiye is also the only country that uses two primary screening methods (FOBT and colonoscopy). Poland uses only colonoscopy and offers only one screening per person in their life, as opposed to two colonoscopies in Türkiye.

Table 7: Screening programs for colorectal cancer

	Year of launch	Type of organization	Target group (sex, age)	Interval	Test method
Recomm-endation	-	Organized	Men and women aged 50-74	<3 years	FIT
Türkiye	2013	Organized	Men and women aged 50-70	2 years	FOBT
				10 years	Colonoscopy
Belgium (143, 144)	2009/2013	Organized	Men and women aged 50-74	2 years	FIT
France (145, 146)	2008	Organized	Men and women aged 50-74	2 years	FIT
Poland (147, 148)	2012	Organized	Men and women aged 55-64	10 years	Colonoscopy

The success of a colorectal cancer screening programs can be measured by its participation rate. Figure 34 shows the proportion of men and women aged 50–74 who were screened with a stool test (FOBT or FIT) in the past 3 years. Türkiye achieved screening rates of 24% in 2014 and 34% in 2019, both well below the 70%-aim specified in the Turkish NCCPs from 2009 and 2013. The three benchmark countries also all underperformed. Belgium managed to double the screening rate from

2014 to 2019,[17] whereas the rate decreased in France.[18] In Poland, screening rates remained at 10%, probably because stool tests were not the primary screening method, yet other data from Eurostat show that the use of colonoscopies was also very low. The COVID-19 pandemic caused a drop in the screening rate in Türkiye; see Info Box 2 in section 2.3.

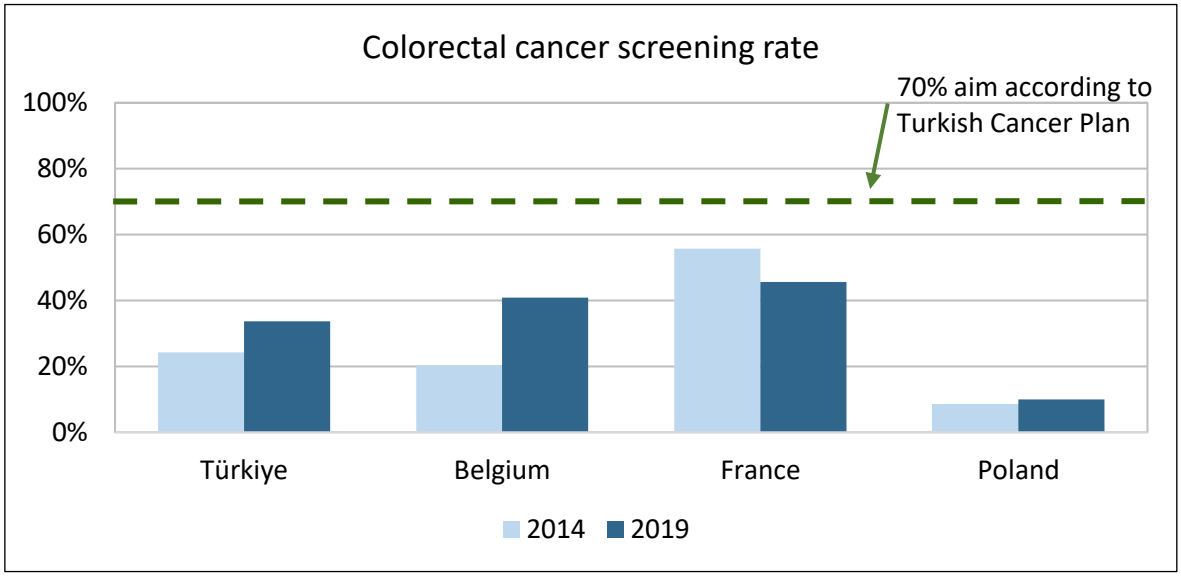


Figure 34: Colorectal cancer screening rate with stool test during the last 3 years among men and women aged 50–74 (self-reported)

Source: Eurostat (150).

Different studies have previously identified barriers to achieving high colorectal cancer screening rates in Türkiye. These barriers are:

- Low levels of knowledge, awareness, and advice compatible with colorectal screening guidelines among primary health care providers (family physicians and family health personnel) (151)
- Primary health care providers experiencing patients' inability to access definite medical information, deficiencies in the reminder system, and patients' lack of interest in colorectal cancer screening (151)

[17] One reasons for the sharp increase in Belgium is the gradual roll-out of the organized screening program in the Flanders region (57% of the Belgian population) between October 2013 and 2020 (144).

[18] Reasons for the decrease in France are not well established in the literature. However, low participation rates have previously been explained by multiple factors (149). Awareness among the public is lower compared to breast cancer screening, as colorectal cancer screening is less often publicly discussed in the media or among relatives or by patient associations. There is a lack of knowledge about the risk of getting and dying from colorectal cancer, as people think that it only affects older people and people at high risk with a family history of colorectal cancer. Disgust associated with the handling of the stool for the test and then of rectal examinations if the test is positive also plays a role.

- Lack of knowledge about colorectal cancer screening methods and lack of awareness of the risk to develop colorectal cancer (152, 153)

More detailed data for 2019 than those shown in Figure 34 revealed also some differences in the screening rate according to a people's formal level of education in Türkiye. Low-educated people had a screening rate of 33%, mid-educated people 35%, and high-educated people 40%. Awareness and willingness to participate in the screening program thus increases with the level of education. There were small differences in the participation between women (35%) and men (32%).

6.5 Other cancer screening programs

6.5.1 Lung cancer screening

Lung cancer screening with low-dose computed tomography (LDCT) has been trialed in the recent decade, but its use is still very limited worldwide. The WHO currently (May 2022) does not recommend its introduction (105). The cost-effectiveness of LDCT lung cancer screening is an important barrier to its implementation. Convincing evidence on the cost-effectiveness is still scarce, with some results indicating cost-effectiveness (at a rather high cost-effectiveness ratio) in European countries with high smoking prevalence (154), similar to findings for the United States (155), but unlike findings for Australia (156) and countries in the Middle East and North Africa (157).

In Europe, the European Commission did not recommend the introduction of organized lung cancer screening until recently. In 2022, new recommendations were issued to introduce lung cancer screening programs with LDCT for current and former smokers (123). Croatia is thus far the only country in Europe that has started to roll out a national lung cancer screening program in October 2020 (158). In France, the NCCP for 2021–2030 foresees the establishment of an organized lung cancer screening program once the data indicate a favorable benefit-risk balance (89). In the United States, LDCT lung cancer screening is recommended in people aged 50–80 years who have a 20 pack-year smoking history and currently smoke or who have quit smoking within the past 15 years (159).

In Türkiye, lung cancer screening was not part of the NCCPs from 2016 and 2021 (80, 81). LDCT lung cancer screening is not done in Türkiye, but calls have been made in the past to assess its cost-effectiveness in a Turkish context (160).

6.5.2 Prostate cancer screening

The most common method for prostate cancer screening is the prostate-specific antigen (PSA) test, a blood test. PSA testing had received regulatory approval as a screening tool in 1986 in the United States and has been widely used in many Western countries – mostly at an opportunistic basis – since the 1990s. The WHO currently (May 2022) does not recommend "*systematic prostate cancer screening of all men above a certain age using prostate-specific antigen (PSA)*" (105).

In Europe, the European Commission did not recommend the introduction of organized prostate cancer screening with PSA testing until recently. In 2022, new recommendations were issued to perform PSA testing in combination with additional magnetic resonance imaging (MRI) scanning as a follow-up test (123). Nonetheless, PSA testing remains controversial due to the high risk of a false positive diagnosis which increases the risk of overdiagnosis and overtreatment leading to side effects such as impotence and incontinence (161, 162).

In Türkiye, prostate cancer screening was not part of the NCCPs from 2016 and 2021 (80, 81). Nonetheless, PSA testing is done to some extent by men in Türkiye (163).

6.5.3 Stomach cancer screening

In Europe, the European Commission issued new recommendations in 2022 that recommend population-based screening and treatment programs for Helicobacter pylori, a bacterium causing stomach cancer, only in regions with intermediate to high stomach cancer incidence (123).

In Türkiye, screening for Helicobacter pylori was not part of the NCCPs from 2016 and 2021 (80, 81). Although the incidence of stomach cancer is comparatively high in Türkiye (see section 2.2.1), there is no screening program (164).

7. Diagnosis and treatment

This chapter describes the current state of diagnosis and treatment of cancer patients in Türkiye. Diagnosis and treatment are at the core of the care process. The diagnostic workup of solid tumors typically requires radiographic imaging, blood analysis, and a biopsy to obtain tumor tissue in order to make a pathological confirmation of the cancer and to perform biomarker testing. After a review of the diagnostic results, a treatment decision is made. The exact treatment modalities vary by cancer type, but include usually either surgery to remove the tumor, radiation therapy, medical therapy, or a combination thereof.

The chapter covers key elements of diagnosis and treatment; see Figure 35. This includes the organization of the patient pathway (section 7.1), medical staff (section 7.2), medical equipment for diagnosis (section 7.3), treatment facilities (section 7.4), medical equipment for radiation therapy (section 7.5), cancer medicines for medical therapy (section 7.6).

For the analysis of the different elements of diagnosis and treatment, a targeted literature search was performed to obtain publicly available data for key performance indicators.

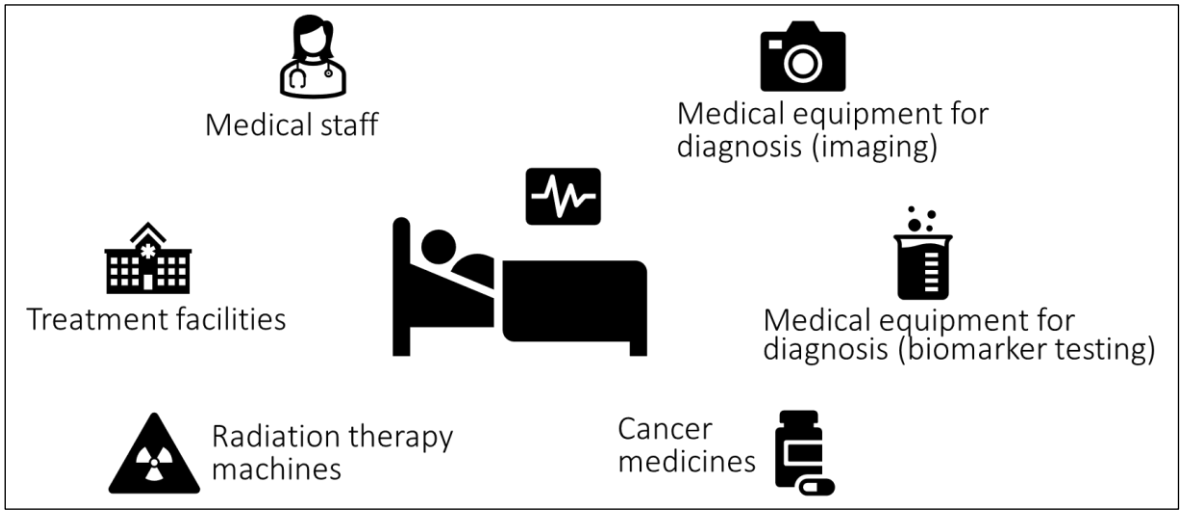


Figure 35: Key elements in the diagnosis and treatment of cancer patients

7.1 Organization of the patient pathway

Patients with cancer often face a long journey until they can receive treatment; see Figure 36 for a schematic illustration. Unless an asymptomatic cancer is detected through screening (see chapter 6), the patient journey starts with the patient experiencing symptoms, such as a lump in the breast, a persistent cough, blood in the stool, considerable weight loss or weight gain for no known reason,

swelling or lumps anywhere in the body. However, the symptoms are often vague and can also be caused by something other than cancer (165).

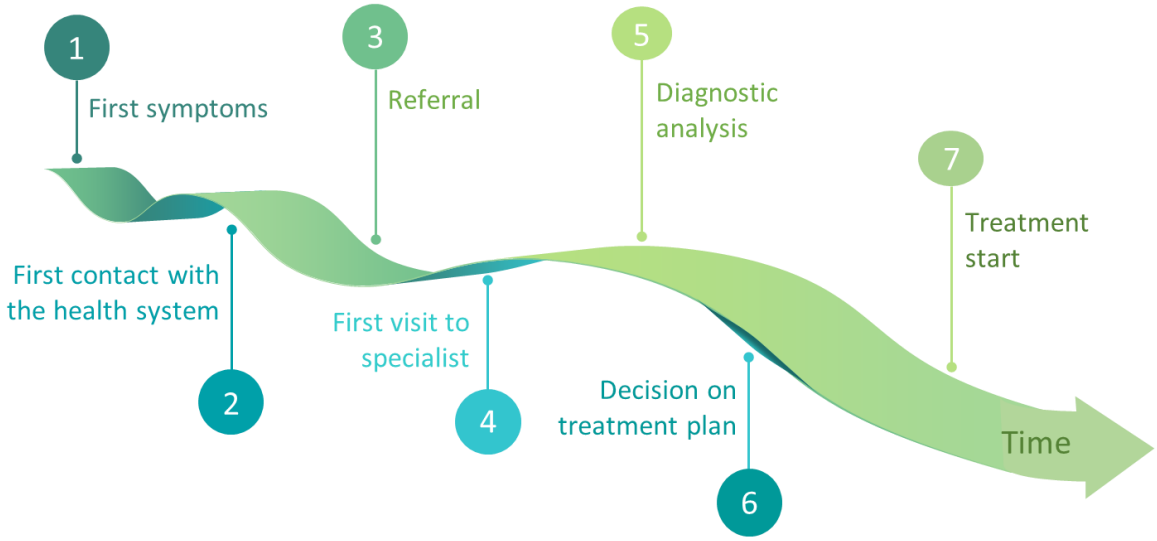


Figure 36: Steps in cancer care between first symptoms and start of treatment

Patients in Türkiye with cancer symptoms may have their first contact with the health system at their family physician in primary care or go directly to a specialist in secondary care or the hospital (see section 3.2). If the consulted physician suspects that the patient's symptoms are related to cancer, the patient is referred to a specialist for further consultation. The specialist runs diagnostic tests (e.g., X-ray, blood analysis) to confirm whether the symptoms are caused by cancer. If the suspicion is confirmed, further diagnostic tests and a biopsy are performed to assesses the spread and characteristics of the cancer to derive a comprehensive diagnosis. After the diagnosis, ideally a multidisciplinary team (also called tumor board) creates a treatment plan. Patients may be referred to a different hospital to perform treatment.

The steps from first symptoms until the start of treatment take time. During this time the tumor continues to grow and increasingly affects patients' daily functioning. A recent international systematic review of seven major cancer types demonstrated that already a four-week treatment delay is associated with increased mortality (166). Long delays until treatment can occur in Türkiye. For example, a study of lung cancer patients across several provinces showed that the average time from first symptoms until treatment start was 131 days (167). Keeping waiting times short between all steps is therefore essential to limit progression of the cancer and thereby to improve the odds of survival. This calls for a well-structured organization with clear and fast patient pathways (i.e., a well-functioning referral system) defining each step of the patient's journey and the services to be received along the way.

Several challenges in the organization of the patient pathway and delays in the diagnosis and treatment of cancer in Türkiye have been identified in previous literature:

- **Lack of patient awareness of cancer symptoms**: A study of 20,000 breast cancer patients in Türkiye has shown that there is still a significant portion of patients diagnosed at advanced stage due to lack of breast cancer awareness and despite the increasing number of KETEMs and free-of-charge mammography (127). Similarly, patients' disregard of their complaints was the main reason for delaying care seeking in almost 70% of lung cancer patients in various Turkish provinces according to a recent study (167).
- **Family physicians not encouraging early detection**: A study in Karabuk province showed that the proportion of family physicians who had not invited anyone in the last three months to screenings was 37.5% for cervical cancer screening, 26.8% for breast cancer screening, 19.0% for FOBT testing and 34.5% for the colonoscopy (168). In addition, only half of the family physicians provided health education regarding cancer prevention on a regular basis (168).
- **Lack of continuity and coordination of care**: A study in Karabuk province showed that there is insufficient coordination between the family physician and the specialists to whom patients are referred to. The lack of a clear referral system and transfer of patient data causes these problems (168). This can also lead to performing unnecessary diagnostic procedures and duplication of services/tests (167).
- **Slow diagnosis and time to treatment**: A study of lung cancer patients in various Turkish provinces showed that the main reasons for delays in receiving a pathological diagnosis were physician's opinion of another diagnosis, delays in pathologic examination, additional disease assessment, and delays in radiologic examination (167). In addition, this study showed that the main reasons for delays from the pathological diagnosis until treatment start were long waiting time for tests required for staging, patient refusal of the treatment, a large volume of patients, and additional disease assessment before treatment (167).
- **Geographic inaccessibility**: Cancer care services in Türkiye are more concentrated at hospitals in cities and bigger towns due to their specialized nature. A study of lung cancer patients in various Turkish provinces showed that patients living in villages experience longer referral delays between the first appointment with a non-pulmonary disease specialist physician until seeing a pulmonary disease specialist compared to patients living more urban areas (167).

7.2 Medical staff

Modern cancer care is highly specialized and requires competences from different medical fields. This includes pathologists and diagnostic radiologists for the diagnosis of cancer, and surgeons, radiologists, medical oncologists, and hematologists for the treatment. Nurses assist the medical doctors and are involved in all activities surrounding the care process.

Figure 37 compares the number of different types of physicians mainly involved in the diagnosis and treatment of cancer. The numbers are standardized per cancer patients rather than per inhabitants, because the number of cancer patients per capita differs considerably between Türkiye and the three benchmark countries; see section 2.2.1. According to this standardization, Türkiye has the highest number of pathologists and radiologists of all countries. The number of oncologists is similar as in France and the number of hematologists is similar to all three benchmark countries. Even though the distinction between different types of physicians may vary between countries and therefore complicate comparisons, the results in Figure 37 indicate no specific areas of undersupply of physicians. The comparatively high numbers of pathologists and radiologists might even point to potential inefficiencies. However, in Türkiye there might be differences in the availability of specialized physicians in the public sector (fewer physicians) and the private sector (more physicians).

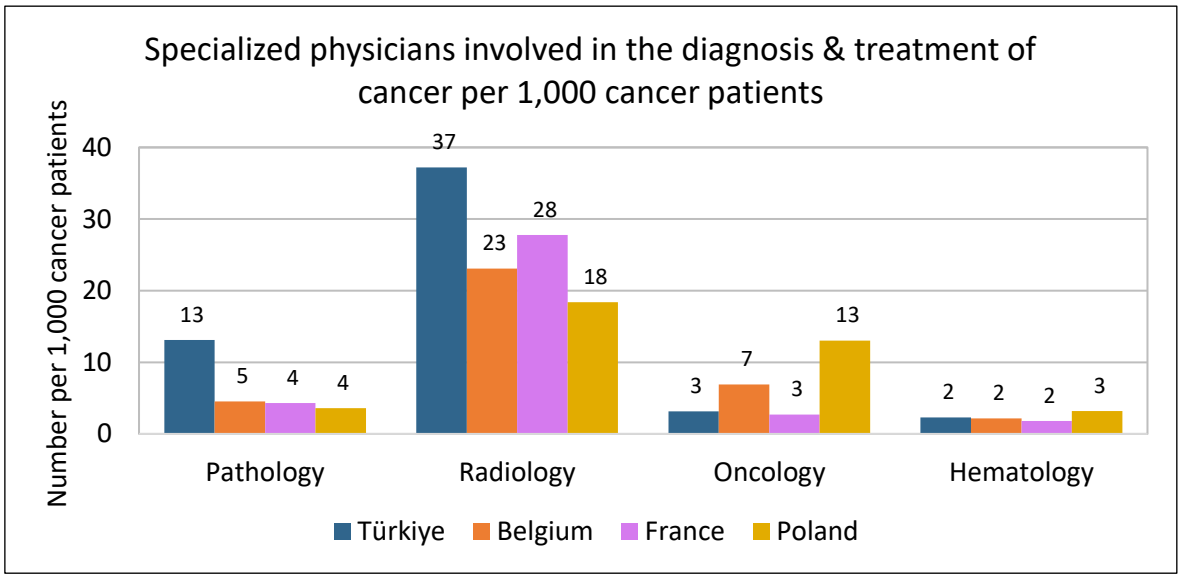


Figure 37: Number of specialized physicians per 1,000 cancer patients, 2016 (or latest available year)

Notes: No detailed data for different types of oncologists (e.g., surgical oncologist, medical oncologist, radiation oncologist) are available. National definitions might differ for the four categories of specialized physicians shown. Source: Eurostat (169).

An explanation for the comparatively high number of specialized physicians working with cancer in Türkiye might be found in the low number of nurses. Figure 38 compares the number of nurses caring

for all patients and not specifically only for cancer patients. It shows that Türkiye has only half the number of nurses as France and Belgium and also a slightly lower number than Poland. In the absence of enough nurses, physicians will have to spend a greater amount of time on activities that could be done by nurses. The predicted increase in cancer patient numbers in Türkiye (see section 2.3) will require the continuous training and recruitment of new medical staff. The training of new nurses requires less time than of specialized physicians and could thus be a way to future-proof the staffing requirements in cancer care.

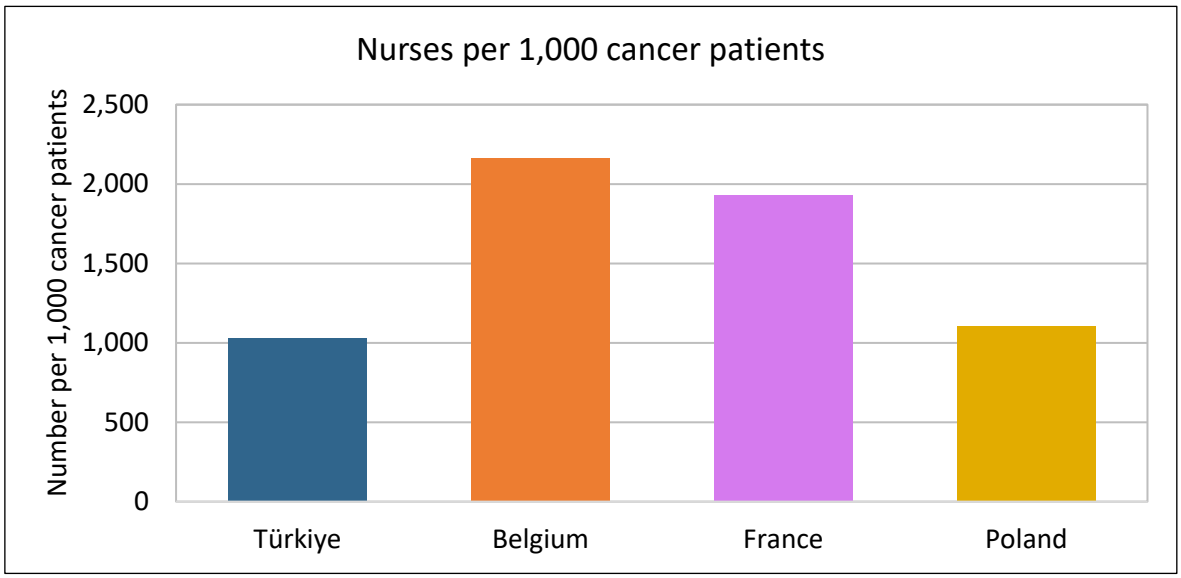


Figure 38: Number of professionally active nurses per 1,000 cancer patients, 2019 (or latest available year)

Notes: The data show numbers for all nurses and not just nurses involved in the diagnosis and treatment of cancer patients. Source: Eurostat (170).

7.3 Medical equipment for diagnosis

Medical equipment is needed to make an accurate cancer diagnosis. This includes imaging equipment and equipment for molecular diagnostic testing.

Imaging equipment is needed by diagnostic radiologists to locate the cancer and to determine its spread (e.g., locally contained cancer or metastatic cancer). X-ray units and later computerized tomography (CT) scanners and MRI scanners were originally used for diagnostic imaging. In the 2000s, the first PET scanners (later combined with CT or MRI) came into use in Europe and the United States. The initial investment costs for installing modern scanners are high. Their availability is thus naturally restricted by limited health care resources and by geography. Scanners are not only used during the diagnostic process, but also during treatment to assess the therapeutic response and to monitor disease progression.

Figure 39 summarizes information on the availability of modern imaging equipment. The numbers are standardized per cancer patients rather than per inhabitants, because the number of cancer patients per capita differs considerably between Türkiye and the three benchmark countries; see section 2.2.1. According to this standardization, Türkiye has markedly higher numbers of CT scanners, MRI scanners, and PET scanners per cancer patients than the three benchmark countries.[19] This higher number of scanners might have a connection to the high number of radiologists in Türkiye (see section 7.2). The availability of these units might also be worse in the public sector in Türkiye compared to the private sector. Benchmarks for the ideal number of diagnostic imaging equipment per inhabitant or per cancer patient do not exist (171). Nonetheless, the high numbers in Türkiye might point to an overuse and potential inefficiencies in the use of modern imaging equipment for cancer patients.

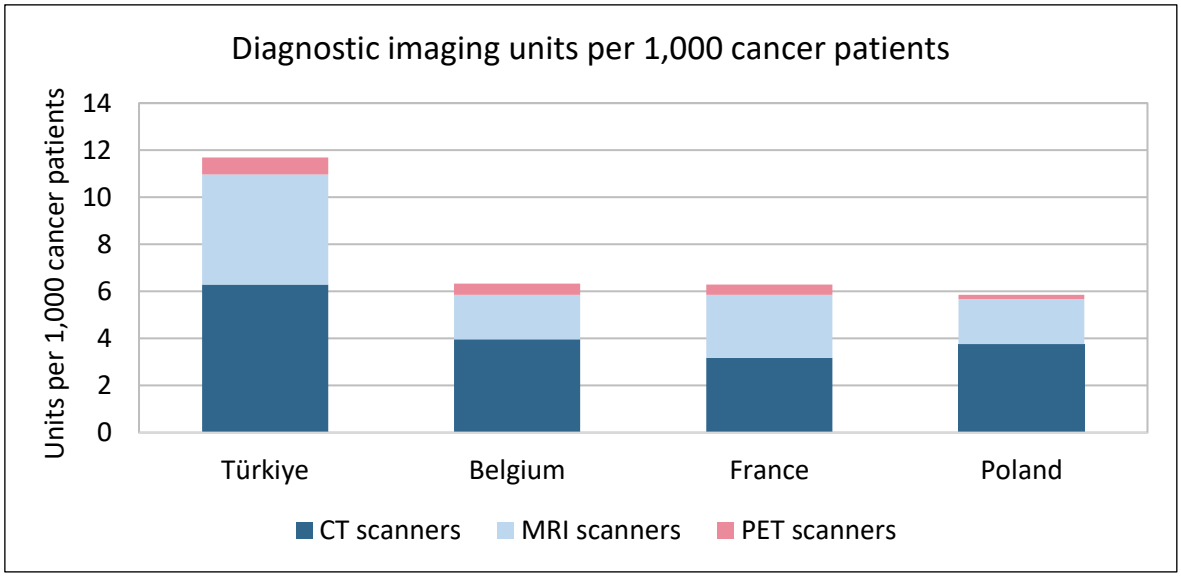


Figure 39: Diagnostic imaging units per 1,000 cancer patients, 2019

Notes: The data show numbers for all scanners and not just scanners used for cancer patients. Many non-cancer patients receive CT and MRI scans, whereas PET scans are predominantly used in cancer patients.
Source: Eurostat (172).

Molecular diagnostic testing, also called biomarker testing or molecular profiling, has become a prerequisite for administering modern cancer medicines (173). It provides a molecular characterization of the tumor, which is needed to decide which cancer medicines work best in a particular patient. Molecular diagnostic testing is at the heart of the ongoing shift towards personalized/precision medicine in cancer treatment. Usually, tumor issue that has been obtained through a biopsy is used for testing purposes. The testing is carried out in molecular diagnostic laboratories by pathologists and clinical laboratory scientists. When modern cancer medicines are reimbursed, it is important to not forget about the reimbursement of appropriate testing, as the lack

[19] It should be noted that CT and MRI scanners are widely used in non-cancer patients as well.

of cost coverage for testing would impede access for patients who cannot afford to pay out-of-pocket for the testing.

HER2 status in breast cancer was the first widely used biomarker to guide the administration of trastuzumab (approval in 1998 by the Food and Drug Administration (FDA) in the United States) (174). Many biomarkers in different cancer types have subsequently started to guide the administration of targeted therapies, most often using polymerase chain reaction (PCR) or fluorescent in situ hybridization (FISH) tests. PD-L1/PD-1 biomarker testing using immunohistochemistry (IHC) has guided the administration of immunotherapies since their launch in the 2010s (175). The increasing number of specific mutations that can be targeted by modern cancer medicines has made it tedious to test for these mutations individually and sequentially. In response, NGS testing has emerged as a tool to test for multiple mutations simultaneously, although this type of testing takes more time and is still considerably more expensive than PCR and FISH (176).

7.3.1 Case study: Molecular diagnostic testing in lung cancer

Scientific advances have increased the understanding of drivers of cancer growth in recent decades. The prime example non-small cell lung cancer (NSCLC) which accounts for around 85% of all lung cancer cases (177). Figure 40 shows known driver mutations in NSCLC. Since the discovery of the first targetable driver mutation called EGFR in 2004 (178), multiple additional driver mutations have been identified. Medicines that target some of these mutations have been developed and approved by regulatory authorities since then; see section 7.6.3. Similarly, many cases of NSCLC without known driver mutations overexpress the protein PD-L1, which is a target for immunotherapy medicines.

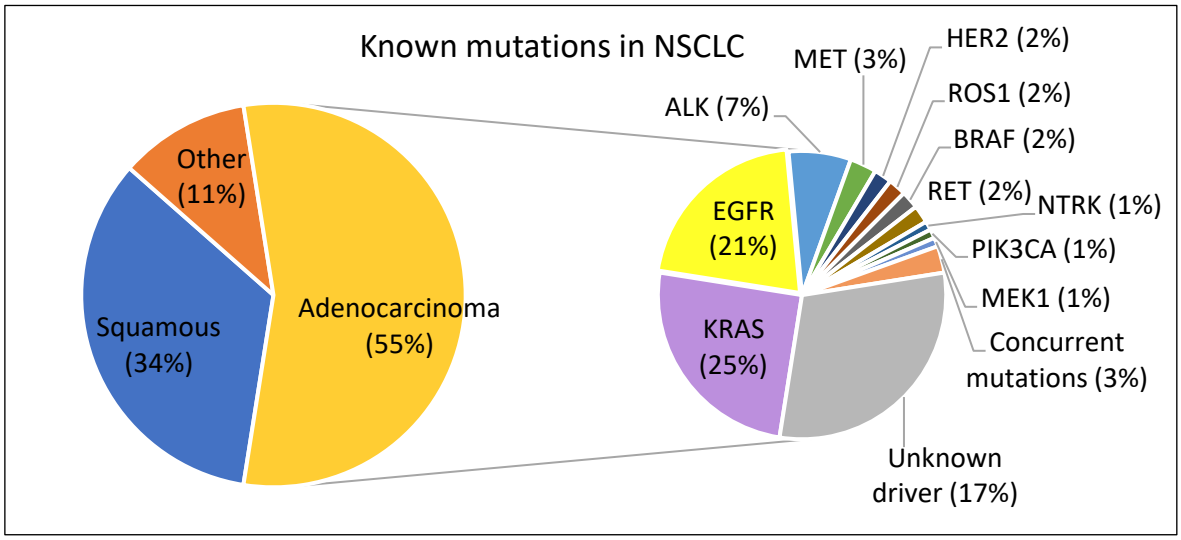


Figure 40: Genomic alterations in NSCLC

Source: Li et al. (2013) and Tsao et al. (2016) (179, 180).

Prior to the administration of a suitable targeted therapy or immunotherapy, NSCLC patients have to be tested in order to determine the driver mutations status and the PD-L1 status. The assessment of the PD-L1 status is done through IHC. IHC is a rapid and relatively inexpensive method that has been in use for several decades (181). Molecular testing for driver mutation status may be more expensive, especially if NGS testing is used instead of PCR or FISH testing, yet NGS testing is faster as it provides all results at once instead of after separate and sequential tests with PCR/FISH.

An overview of the current reimbursement status of different types of tests is provided in Table 8. In Türkiye, the need for PD-L1 testing is currently limited as only one immunotherapy medicine is reimbursed by the SSI as a second-line treatment; see section 7.6.3. PD-L1 testing in Türkiye is reimbursed with a fixed amount as part of IHC testing. In France, PD-L1 testing is standardly reimbursed, whereas pharmaceutical companies pay for testing in Belgium and partly also in Poland. Single biomarker testing for EGFR, ALK, ROS1 is reimbursed by the SSI in Türkiye, mirroring the targeted therapies currently reimbursed for these mutations (see section 7.6.3), whereas in France and Belgium additional biomarkers are reimbursed. NGS testing is not reimbursed in Türkiye and Poland, whereas in France and Belgium it is reimbursed. An additional challenge for molecular testing that Türkiye shares with Poland is the poor quality of the tumor tissue obtained during the biopsy (around 5–25% of cases in Türkiye), which requires re-biopsy (182, 183).

Table 8: Reimbursement status of diagnostic tests in advanced-stage NSCLC

	PD-L1 testing	Single biomarker testing	NGS testing
Recomm-endation by ESMO	Yes (184)	EGFR, ALK, ROS1, BRAF, NTRK (184)	Yes (185)
Türkiye	IHC is reimbursed by the SSI with a fixed reimbursement amount; IHC covers several tests including PD-L1 *	Reimbursement for sequential testing model for EGFR, ALK, ROS1*	Not reimbursed*
Belgium	Not reimbursed but paid by the pharmaceutical company (186)	Reimbursement for EGFR, ALK, BRAF, MET (186)	Reimbursed (187)
France	Reimbursed (186)	Reimbursement for EGFR, ALK, BRAF, NTRK, MET (186)	Reimbursed (186, 188)
Poland	Partly reimbursed, as the pharmaceutical company has to pay for negative tests (183, 186)	Reimbursement for EGFR and ALK (183, 189)	Not reimbursed (183)

Notes: * Information provided by MSD Türkiye. ESMO = European Society for Medical Oncology.

7.4 Treatment facilities

The diagnosis and treatment of cancer patients may take place in various facilities in Türkiye. This can include secondary care facilities at various specialists and tertiary care on an inpatient or outpatient basis at general hospitals or cancer clinics.

Cancer care has become more effective as new and improved treatment modalities have been introduced. In many cases, these improvements enable shorter hospital stays, entail fewer side effects, and result in quicker recovery and potentially fewer recurrences (190). Since the early 1990s, the introduction of antiemetic medicines meant that cancer patients experienced less vomiting and nausea due to treatment with chemotherapy (cytostatic agents). This enabled a shift of the treatment setting from inpatient to outpatient care for many cancer patients. Many modern targeted medicines are administered orally and not via intravenous injection like older chemotherapy, which reduces the need for inpatient stays.

Figure 41 shows the development of the number of bed days (i.e., overnight stays of hospitalized patients) and the number of day cases (i.e., patients who are formally admitted to the hospital but then discharged on the same day) between 2000 and 2019 in Türkiye and the three benchmark countries. Both the development for cancer patients (top graphs) and the general development for all patients (bottom graphs) are shown.[20] For cancer patients, there is a clear downward trend in the number of bed days (standardized by population size) and a simultaneous upward trend in day cases in the three benchmark countries. Although a similar pattern is observable in all patients (bottom graphs), the decreases in bed days and the increases in day cases were more pronounced in cancer patients.

In Türkiye, the number of bed days of cancer patients decreased between 2007 and 2016, even though the number of cancer patients increased; see section 2.2.1. This indicates shorter hospital stays of cancer patients. A reduction in the number of bed days does not automatically imply a decrease in the costs of inpatient care, since the cost per bed day may have increased over time. Nonetheless, fewer bed days of cancer patients free up hospital beds for other patients. No data are available for the number of days cases in Türkiye. It is therefore unclear if there was a shift of the treatment setting from inpatient care to outpatient care, which is typically cheaper than inpatient care.

[20] The latter development provides insights into whether the development observed for cancer simply reflects a general shift in the organization of health care (from inpatient care to outpatient care) in a country, or whether there is a disconnection between the overall trend and the specific trend in cancer patients. Note that comparable data for outpatient visits at health facilities that are not hospitals are not available.

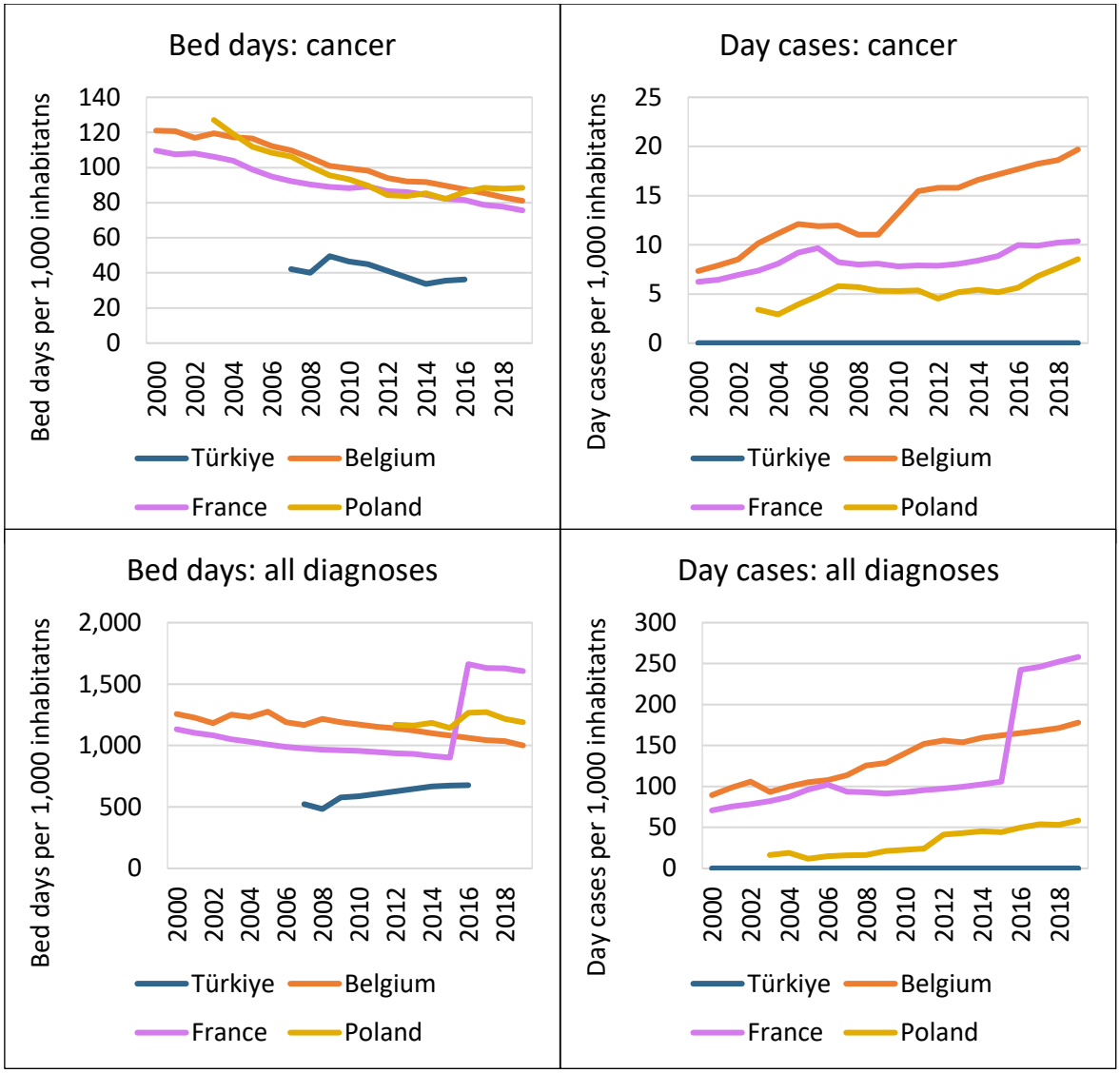


Figure 41: Bed days (left-side graphs) and day cases (right-side graphs) spent in hospitals per 1,000 inhabitants, 2000–2019

Notes: "All diagnoses" refers to and "cancer" refers to diagnosis with ICD-10 C00–D48 and "all diagnoses" to ICD-10 A00–Z99/V00–Y98. There are some breaks in the time series, notably in France from 2015 to 2016. Sources: Eurostat (191, 192).

The availability of cancer treatment facilities needs to be considered together with the availability of medical staff (section 7.2). Building additional hospitals and cancer clinics in view of the increasing future number of cancer patients (section 2.3) is motivated in Türkiye, but this needs to occur in tandem with an increase in the number of trained medical staff. Planning activities in this area need to take into account that proper training of medical staff takes time. The geographic location of new treatment facilities should also be aligned with the (future expected) patient population living in the catchment area and the availability of suitable means of transportation for patients.

The quality of cancer treatment facilities is important to achieve the best possible outcomes for patients. Treatment facilities that are designated Comprehensive Cancer Centers (CCCs) meet

rigorous quality standards in care delivery, provide access to clinical trials, and engage in research activities. The Europe's Beating Cancer Plan launched in 2021 aims to ensure that 90% of eligible cancer patients have access to such CCCs by 2030 across all EU member states (193). There is no universal definition of a CCC, and various national and international accreditation systems exist. Figure 42 shows the number of cancer centers with accreditations from the European Society for Medical Oncology (ESMO) and the Organisation of European Cancer Institutes (OECI). There are currently four cancer centers in Türkiye with either of these accreditations, while Belgium has 12, France has 24 and Poland has two.

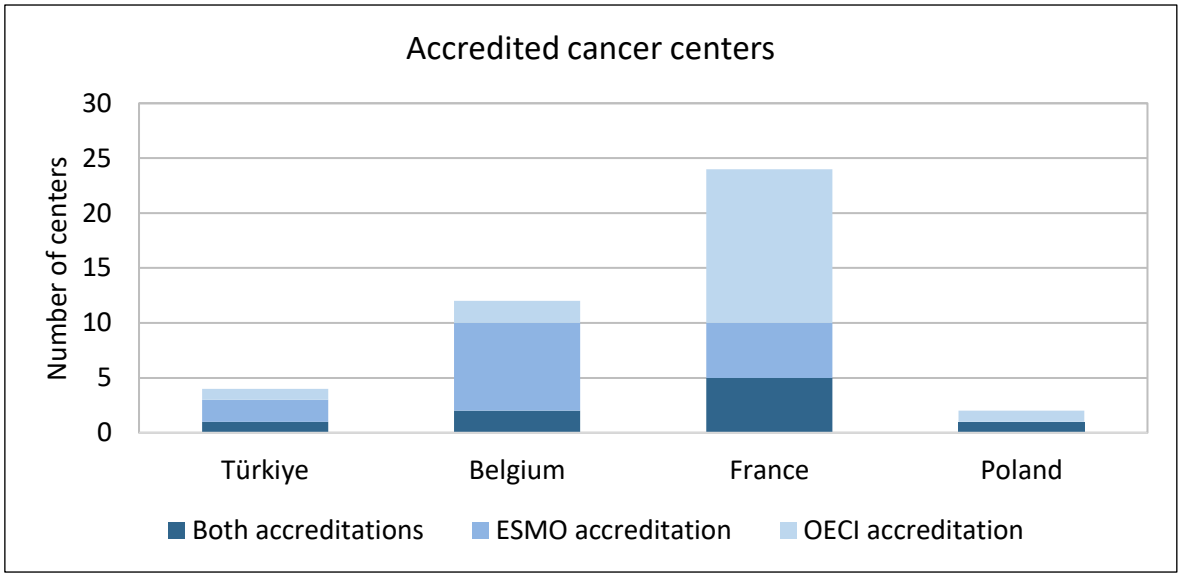


Figure 42: Number of accredited cancer centers, 2022

Notes: ESMO = European Society for Medical Oncology; OECI = Organisation of European Cancer Institutes (OECI). The numbers show the accreditation status as of June 2022. In Türkiye, the Anadolu Medical Center in Kocaeli province has both accreditations, the Hacettepe Oncology Hospital in Ankara province and the Baskent University Dr. Turgut Noyan Application and Research Center in Adana province have an ESMO accreditation, and the Dokuz Eylül University Institute of Oncology in Izmir province has an OECI accreditation. Source: (194, 195).

7.5 Radiation therapy

The treatment of cancer depends on the site and grade of the tumor and the stage of the disease as well as patients' general health status. Radiation therapy is a cornerstone of cancer treatment besides surgery and medical therapy (196). Solid cancer types are usually initially treated with surgery or radiation therapy if there is a curative treatment intent. Radiation therapy is also extensively used if there is a palliative treatment intent in solid cancer types and might also be used for hematologic cancers. Around 50% of all cancer patients have an indication for radiation therapy at least once during the course of their disease (196, 197).

The most commonly used machines for radiation therapy are medical linear accelerators (linacs). Linacs provide external beam radiation therapy in the megavoltage (MV) range. They have replaced cobalt-60 machines. Brachytherapy is another common type of radiation therapy where the radiation source is placed inside the body and close to the tumor (198).

An international analysis of the availability of radiation therapy machines in relation to patient need from 2012 indicated two challenges for patients in Türkiye (197). The first challenge was the use of old technology. Of the 201 MV machines in Türkiye in 2012, 29% (58 machines) were cobalt-60 machines and the other machines were newer linacs. The three benchmark countries had a much lower proportion of old cobalt-60 machines still in use – Belgium 4%, France 2%, Poland 6%. The second challenge was the low number of MV machines in relation to patient need. The number of needed MV machines was 44% lower than the actual number of available MV machines in Türkiye.[21] Poland had a similar shortage (-45%), whereas the shortage in France was limited (-8%) and Belgium had an excess number of machines (+16%).

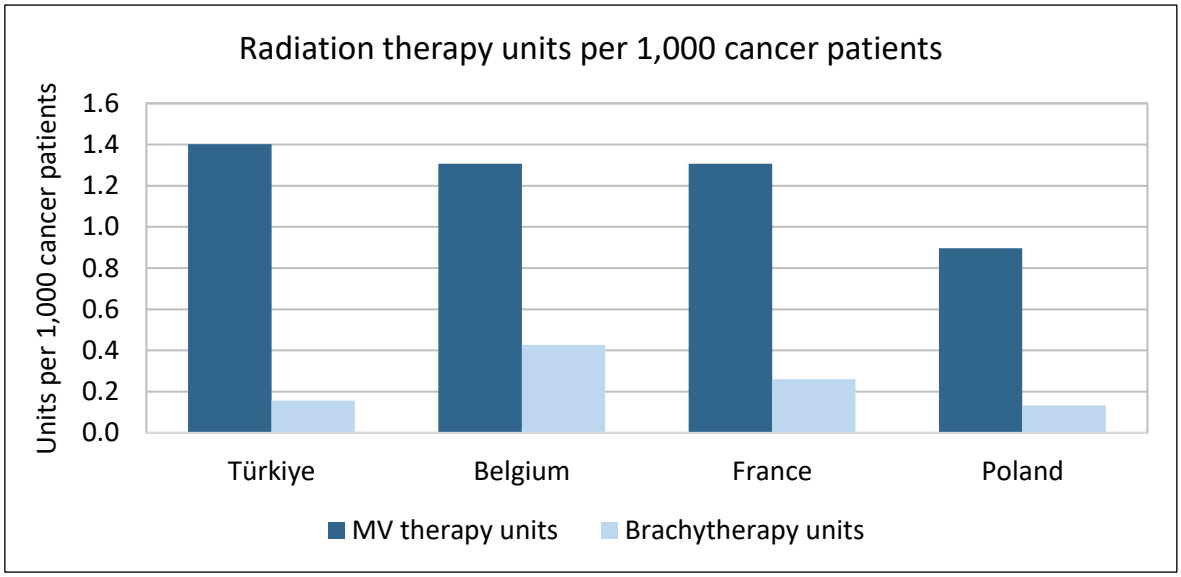


Figure 43: Radiation therapy units per 1,000 cancer patients, 2022 (or latest available year)

Notes: MV therapy includes medical linear accelerators (linacs) and cobalt-60 machines. The number of cancer patients refers to the latest year with available data on incidence; see section 2.2.1. Source: IAEA DIRAC database (199).

The current availability of different types of radiation therapy machines is shown in Figure 43. There were 138 radiation therapy centers in Türkiye in 2022 (no distinction is available for public vs.

[21] The unmet need calculated for Türkiye might have been overestimated, because the study estimated the number of cancer patients from incidence numbers in neighboring countries, resulting in over 257,000 new patients per year (197). This is distinctly higher than the numbers estimated by the Turkish Ministry of Health; see section 2.2.1.

private centers). These centers were equipped with 277 MV machines (no split between linacs and cobalt-60 machines is available) and 31 brachytherapy units. These numbers translate into around 1.4 MV machines and 0.16 brachytherapy units per 1,000 cancer patients in Türkiye. This puts Türkiye slightly ahead of Belgium and France which have around 1.3 MV machines and Poland with 0.9 MV machines per 1,000 cancer patients. The number of brachytherapy units is lower in Türkiye than in Belgium and France but higher than in Poland.

In relation to meeting patient needs, the International Atomic Energy Agency (IAEA) and the European Society for Radiotherapy and Oncology (ESTRO) have previously published recommendations of one linac per 450 newly diagnosed cancer patients per year (200). However, recent advances in hypofractionation in major cancer types (e.g., breast cancer and prostate cancer) are changing this recommendation.

Hypofractionation offers the benefits of shortening treatment time without impeding health outcomes. Major clinical trials have demonstrated that the number of radiation therapy sessions (called fractions) in adjuvant breast cancer treatment could be reduced from a 3-week (15 fractions, 5 days per week) to a 1-week (5 fractions, 5 days per week) schedule (201, 202). Similarly, the number of fractions in prostate cancer could be reduced from an 8-week (39 fractions, 5 days per week) to a 2.5-week (7 fractions, 3 days per week) schedule (203, 204). Hypofractionation offers a more cost-effective use of available health care resources and frees up resources that can be used in other areas of cancer care. It also reduces non-medical costs for patients and their families, such as travel costs and the time spent by informal caregivers going back and forth to the hospital every day.

To infer the quality of care, a consideration of the mere number of radiation therapy units is not enough. The availability of trained professionals to operate the machines (radiation oncologists and medical physicists; see section 7.2) would also need to be taken into account. A analysis from 2019 concluded that progress has been made in the availability of trained professionals in the recent decade in Türkiye (205).

The geography of the country, with poor access to radiation therapy centers in rural areas, can also be a challenge and affect compliance with the treatment. This remains a challenge in Türkiye where, for instance, rural patients in Sakarya, Kutahya, and Iskenderun need to travel on average 120 km every day to receive radiation therapy (206). Changing the treatment to hypofractionation when medically feasible could be a great relief to rural patients.

7.6 Cancer medicines

Cancer medicines are an indispensable part of modern cancer care and are essential for improving patient outcomes (207-209). Several different types of cancer medicines can be distinguished:

- Chemotherapy was first introduced in the 1940s and still today constitutes a standard-of-care treatment modality in the treatment course of many cancer types (210). Chemotherapy can cause toxic side effects, as it may damage healthy cells alongside malignant cells in the body (211).
- Hormone therapy was first discovered in the 1940s for prostate cancer and in the 1970s for breast cancer (210). It is still the standard-of-care treatment modality in most patient subgroups of these cancer types to reduce testosterone and estrogen levels, respectively (5).
- Targeted therapy was introduced toward the end of the 1990s (210). It uses a different mode of action than chemotherapy by acting on specific molecules involved in the growth and survival of cancer cells (5).
- Immunotherapy in the form of checkpoint inhibitors and more recently CAR-T cell therapies was introduced during the 2010s (210). Immunotherapy medicines help the body's own immune system to recognize and attack cancer cells (4).

Targeted therapy and immunotherapy are nowadays the main treatment option for many cancer types, mostly replacing chemotherapy. In some cases, these newer therapies are also added to chemotherapy. Targeted therapy and immunotherapy have initially been used in the metastatic treatment setting. In recent years, the indications of some effective medicines have been expanded to the curative treatment setting, where they are used as adjuvant therapy (i.e., given after surgery) or even neo-adjuvant therapy (i.e., given before surgery).

The continuous launch of new and more effective cancer medicines is essential for improving patient outcomes. However, before new cancer medicines can reach all eligible patients in a country, three key hurdles need to be overcome; see Figure 44. These are regulatory approval by the national regulatory body, reimbursement by the public health care payer, and uptake in clinical practice. The following sub-sections provide an analysis of the three hurdles in Türkiye.

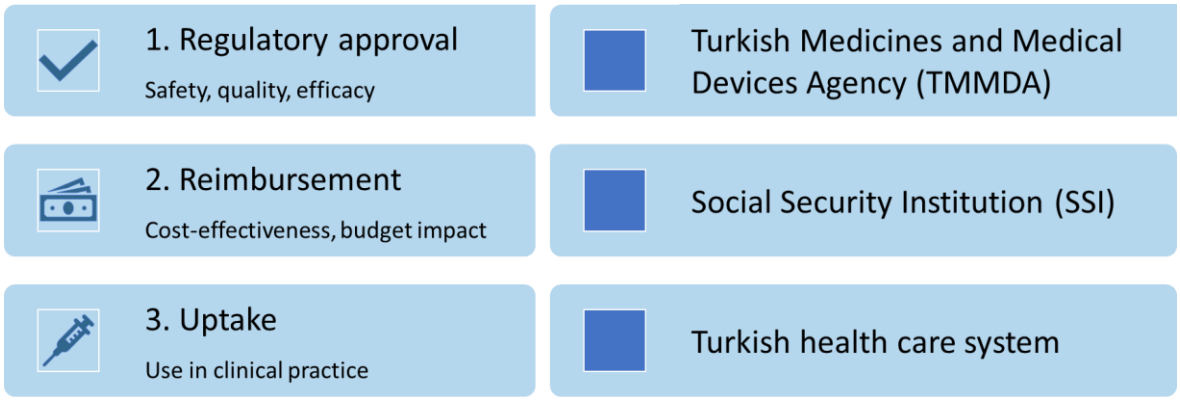


Figure 44: General key hurdles for patient access to new medicines and responsible institutions in Türkiye

7.6.1 Regulatory approval of cancer medicines

The first hurdle for patient access to new cancer medicines in Türkiye is marketing authorization by the regulatory body, the Turkish Medicines and Medical Devices Agency (TMMDA), which is affiliated with the Ministry of Health. The TMMDA evaluates safety, quality, and efficacy of new medicines before granting marketing authorization (212). Before the review of efficacy, medicines have to go through the good manufacturing practices (GMP) accreditation process. This process involves a physical inspection by the TMMDA of manufacturing sites worldwide and may delay the review of efficacy by 12 to 18 months (212).

Evidence of regulatory approval in another country, such as by the European Medicines Agency (EMA) in the EU or the FDA in the United States, is required for marketing authorization by the TMMDA (212). Regulations by the TMMDA stipulate an overall approval target timeline of 210 calendar days for standard applications, but actual approval timelines tend to be longer in practice (212, 213). The EMA which is responsible for the three benchmark countries (Belgium, France, Poland) also works with pre-defined timelines. The assessment of a standard application to the EMA for a new medicine takes up to 210 “active” days (214). This active evaluation time is the time spent by EMA staff to evaluate the evidence. The evaluation is interrupted by one or two “clock-stops” during which the applicant answers questions raised by the EMA (214).

The TMMDA also requires information on pricing as part of the evaluation process, whereas the EMA does not include this element in its evaluation process. However, pricing information is not required by the TMMDA at the time of submission of the application, and regulatory approval can be obtained prior to pricing approval. Upon TMMDA approval, the Ministry of Health publishes a list price based on external reference pricing, drawing on a basket of five countries (France, Greece, Italy, Portugal, Spain) (212, 213). The Turkish reference price is set according to the lowest price

among the basket countries and defined in euros (€) at a fixed exchange rate (213). After regulatory approval and publication of a list price, a new medicine can be sold in the private sector but must be paid for out-of-pocket by patients. Few, wealthy patients can afford to pay for modern cancer medicines out-of-pocket in reality, just like in the three benchmark countries.

The regulatory approval of new cancer medicines has accelerated considerably in recent years. This can be seen in Figure 45, which shows all 151 new cancer medicines with centralized marketing authorization by the EMA between 1995 and 2021. Three distinct periods are noticeable. Between 1995 and 2000, on average one new medicine was approved per year. Between 2001 and 2011, the average annual number was close to four. Around ten new medicines were approved per year between 2012 and 2020. 2021 has been an exceptional year with 17 approvals. The TMMDA is generally lagging behind the EMA in approvals as shown in section 7.6.3 based on the example of lung cancer.

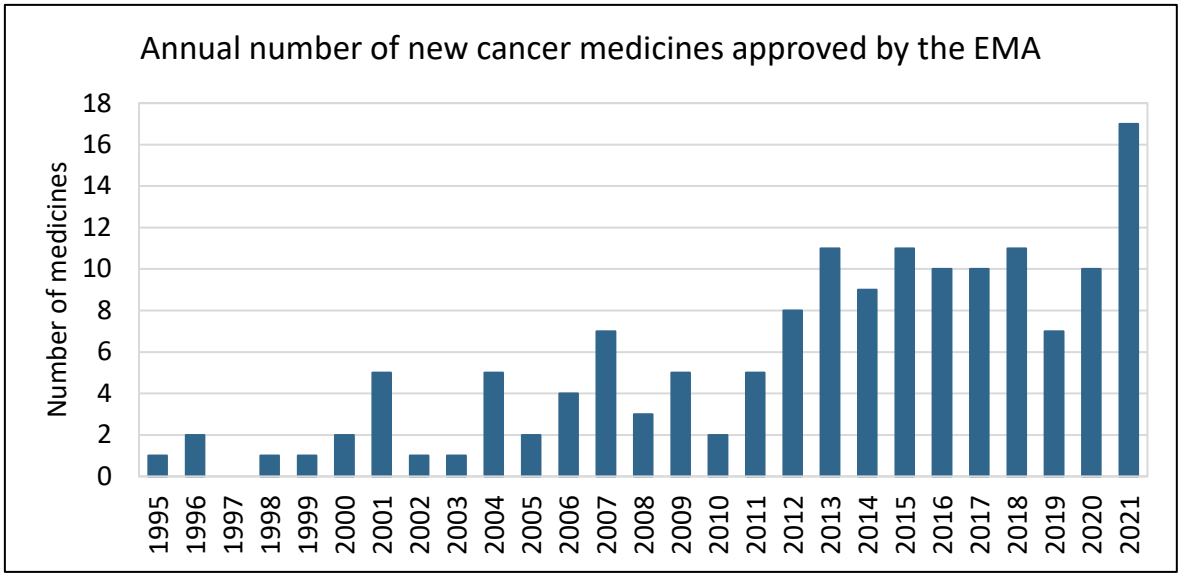


Figure 45: Annual number of new cancer medicines approved by the EMA, 1995–2021
Source: Own calculations based on information from the EMA (215). Medicines (new chemical entities) used to treat cancer patients in the groups L01, L02, and L04 in the Anatomical Therapeutic Chemical (ATC) classification system are included.

7.6.2 Reimbursement of cancer medicines

The second hurdle for patient access to new cancer medicines in Türkiye is reimbursement by the SSI (213). The use of health technology assessment (HTA) as a tool to assess "value-for-money" of new medicines and to guide reimbursement decisions is limited in Türkiye (216, 217). Cost-effectiveness of a new medicine is a necessary but not a sufficient criterion for a positive reimbursement decision. The main emphasis is on price negotiations and limiting the budgetary impact (67, 213). Reimbursement decisions are made by the Reimbursement Commission, composed of representatives from the SSI, the Ministry of Health, the Ministry of Finance, and the Department

of Strategy and Budget (213). The list price of a new medicine determined via external reference pricing (see section 7.6.1) serves as the starting point for negotiations on discounts with the applicant. Since the list price is defined in euros, the depreciation of the Turkish lira in the recent decade (1 EUR = 2.31 TRY in 2012, and 1 EUR = 10.51 TRY in 2021, (218)) results in low prices from the perspective of international pharmaceutical companies, which acts as a disincentive to apply for reimbursement. Upon agreement on a net price, the medicine is included in the positive list of the SSI. This gives almost the entire Turkish population (see section 3.1) access to the new medicine.

The three benchmark countries also use external reference pricing for new medicines to set a list price; see Table 9. As in Türkiye, this price serves as the basis for negotiations on a discounted net price. By contrast, the use of HTA by dedicated bodies is well-established in all three benchmark countries (Belgium since 2001 (219), France since 2005 (220), Poland since 2005 (221)) and a more comprehensive assessment is carried out to inform the reimbursement decision than in Türkiye. Compared to Türkiye, these countries place less emphasis on the price and the budget impact, and more emphasis on the value in the form of added therapeutic value and cost-effectiveness.

Table 9: Pricing and reimbursement of new medicines

	Main principles for pricing	Main criteria for reimbursement
Türkiye	External reference pricing (France, Greece, Italy, Portugal, Spain) (212)	Price, budget impact (67, 213)
Belgium	External reference pricing (EU countries) (222)	Added therapeutic value, price, unmet clinical need, budget impact, cost-effectiveness (67, 223)
France	External reference pricing (Germany, Spain, Italy, United Kingdom) (222)	Added therapeutic value (mainly); also cost-effectiveness and budget impact if high budget impact is anticipated (222, 224)
Poland	External reference pricing (EU and EFTA countries) (222)	Added therapeutic value, cost-effectiveness, budget impact (221)

The reimbursement status of new cancer medicines in Europe is regularly assessed by IQVIA and EFPIA (European Federation of Pharmaceutical Industries and Associations) through surveys administered to the local pharmaceutical industry associations (77). The reimbursement status of 41 new cancer medicines[22] approved by the EMA in 2017–2020 at the beginning of 2022 is shown in Figure 46. Only 15% (6 of 41) of new cancer medicines had received full reimbursement in Türkiye, which is similar to Poland with 12%, but far less than Belgium and France with 66%. When both full

[22] Figure 45 shows 38 new cancer medicines for 2017–2020, because four medicines included by IQVIA only contain chemical substances already used in the treatment of cancer before their approval (chlormethine (Ledaga), treosulfan (Trecondi), daunorubicin / cytarabine (Vyxeos liposomal), pertuzumab / trastuzumab (Phesgo)), whereas IQVIA did not include dinutuximab beta (Qarziba).

and limited reimbursement[23] by the public payer is considered, Türkiye ranks last with 20% compared to Poland's 31%, Belgium's 66%, and France's 81%.

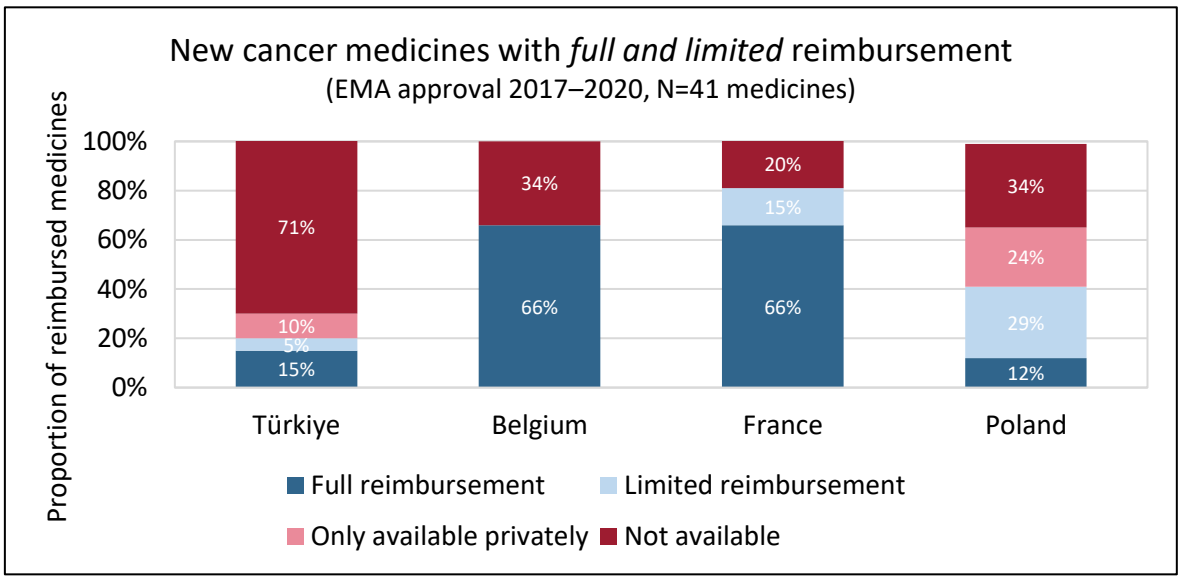


Figure 46: Reimbursement status of new cancer medicines approved by the EMA in 2017–2020 on January 1st, 2022

Notes: Percentages may not total 100% due to rounding. Reimbursement is defined as a medicine being on the public reimbursement list; in Türkiye this is the list of the SSI. The reimbursement status refers to a medicine's initially EMA-approved indications(s). Source: EFPIA (225).

This analysis suggests that patient access to newer cancer medicines is fairly limited in Türkiye. The strong emphasis on containing pharmaceutical expenditure (i.e., budget impact) (67), rather than on cost-effectiveness might be an important reason for this. Finding an adequate balance between access to new, more effective treatments whilst operating with constrained budgetary resources is a challenge shared by all countries. The use of HTA to systematically assess medicines, coupled with clear and transparent thresholds of what constitutes "value-for-money" (cost-effectiveness), might be a path that Türkiye could follow.

7.6.3 Case study: Medical treatment of advanced lung cancer

Lung cancer is the leading cause of cancer death in men and the second leading cause in women in Türkiye; see section 2.2.2. There is a high unmet need in lung cancer patients, with 5-year survival rates of around 15% in Türkiye and the three benchmark countries; see section 2.2.3. One explanation for the low survival rates are difficulties faced by lung cancer patients in accessing care (183, 226). The pathway from first symptoms until diagnosis may take a long time, because most of the common

[23] Limited reimbursement to specific subpopulations of the approved indication, limited reimbursement on a named patient basis (individual patient basis), limited reimbursement while decision is pending (where system permits), availability through a special program (e.g., managed entry agreements).

symptoms of lung cancer are more likely to be caused by something other than lung cancer. In addition, symptoms of lung cancer are usually mild in early stages and may remain unnoticed. Therefore, around 70% of lung cancer patients may be diagnosed at an advanced stage (177).

The recommended treatment option for advanced-stage lung cancer is therapy with cancer medicines if patient's health status is still good enough to tolerate medical therapy according to ESMO (184, 227). The medical therapy of lung cancer has recently undergone major changes. Lung cancer was the solid tumor type with the highest number of new medicines approved by the EMA in 2010–2020 (183). Almost all of these medicines were approved for use in advanced-stage NSCLC. This has changed the medical therapy landscape in advanced-stage NSCLC profoundly between 2015 and 2020, with altered standard-of-care treatment in all lines of treatment and histological and molecular subtypes; see Figure 47. The most notable change was the introduction of immunotherapy. Initially, immunotherapy was introduced as a second-line treatment in 2015, but as of 2017 it started to be used as a first-line treatment. By 2020, first-line immunotherapy had replaced the sole use of chemotherapy in advanced-stage NSCLC in all cases without druggable targets for targeted therapy according to recommendations by ESMO (184). This eliminated the use of immunotherapy as a second-line treatment, because a patient receiving immunotherapy as first-line treatment should not receive it again as second-line treatment (184). It should also be noted that only around 40% of patients who have received and progressed on first-line treatment are still alive and in good enough health to receive second-line treatment (183). The administration of immunotherapy in first line increases long-term survival more than in second line (228-231).

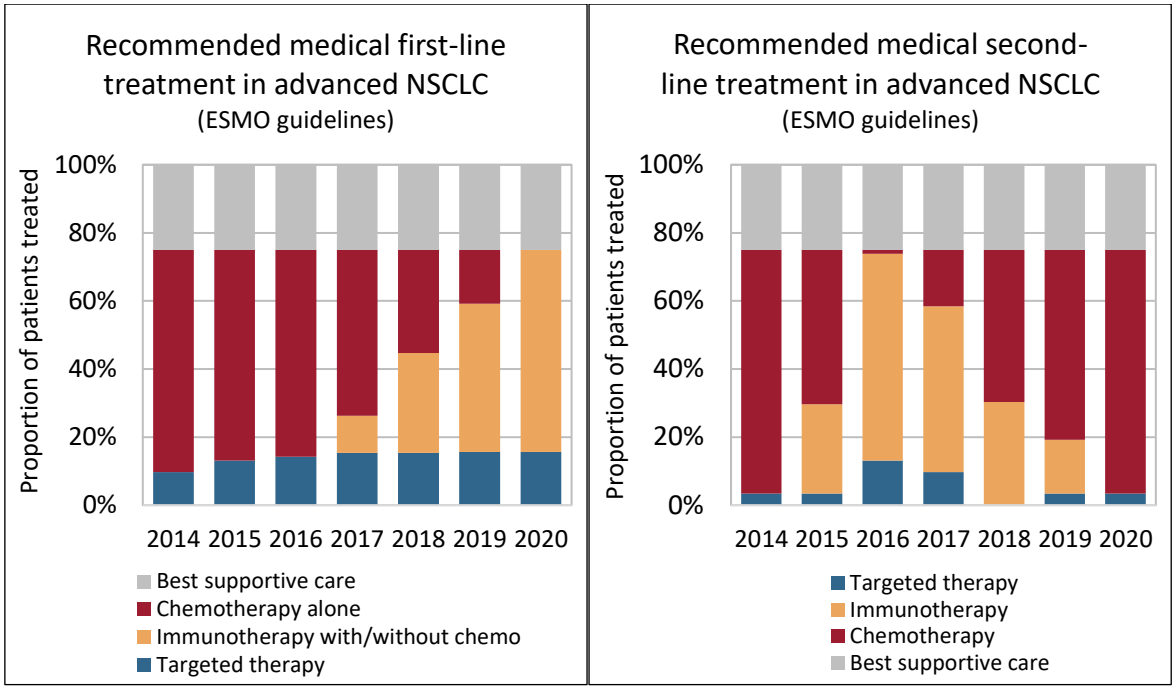


Figure 47: Recommended medical first-line and second-line treatment of advanced NSCLC based on ESMO guidelines, 2014–2020

Notes: Best supportive care = no treatment with cancer medicines. Chemotherapy alone = platinum-based chemotherapy, Immunotherapy with/without chemo = immunotherapy as monotherapy or in combination with platinum-based chemotherapy. 25% of newly diagnosed patients were assumed to have ECOG PS 3–4 and receive best supportive care. 55% of newly diagnosed patients were assumed to have ECOG PS 0–1 and 20% ECOG PS 2, and these patients were assumed to receive systemic therapy. The same ECOG PS proportions were assumed also for second-line treatment. Cancer histology was assumed to be 65% non-squamous disease (including all druggable mutations) and 35% squamous disease; the same histological proportions in first and second line were assumed. The proportion of druggable mutations was assumed to be EGFR 13%, ALK 4.5%, ROS1 1.5%, BRAF V600E 1.5%, NTRK 0.3%, and the proportion of patients with PD-L1 ≥ 1% and PD-L1 ≥ 50% expression was assumed to be 54% and 25%, respectively, in both non-squamous disease (excluding all druggable mutations) and squamous disease, with the same proportions assumed in first and second line. Source for assumptions: Hofmarcher et al. (2022) (183), and ESMO guidelines in its versions from 2014, 2016, 2018, 2019, and 2020 (184, 232, 233) combined with EMA approval dates.

The current availability of lung cancer medicines used as first-line treatments for advanced-stage disease is shown in Table 10. In Türkiye, none of the four immunotherapies with their nine EMA-approved indications was reimbursed by the SSI at the beginning of 2022. Four of the nine indications also lacked regulatory approval by the TMMDA, although three of those indications had a non-substantial clinical benefit (ESMO-MCBS score of 3) which means that they are not a priority for reimbursement according to ESMO's assessment (234). The only reimbursed immunotherapy by the SSI at the beginning of 2022 was nivolumab for the second-line treatment of advanced NSCLC.[24] This means that the access of patients in Türkiye to recommended treatment options in 2022 looked similar to the ESMO-recommended treatment pattern in 2016 in Figure 47. In the three benchmark

[24] Information provided by MSD Türkiye.

countries, all patients with SCLC and with NSCLC without druggable targets for targeted therapy could receive immunotherapy as a first-line treatment with at least one reimbursed medicine.

Access to targeted therapies for lung cancer in Türkiye was comparatively good; see bottom half of Table 10. All medicines/indications with a substantial clinical benefit (ESMO-MCBS score of 4) according to ESMO's assessment were reimbursed by the SSI at the beginning of 2022, whereas most indications with a non-substantial clinical benefit (ESMO-MCBS score of 1-3) were not reimbursed by the SSI or not even approved by the TMMDA. The reimbursed indications in Türkiye covered three mutations, EGFR, ALK, and ROS1. This was the same coverage as in Poland, whereas in Belgium and France also medicines targeting BRAF and NTRK were reimbursed.

The lack of reimbursement of immunotherapy in Türkiye prevents the vast majority of lung cancer patients from accessing modern and recommended treatment. This makes it impossible to address the high unmet need in these patients and improve survival. Providing access could generate significant health benefits for patients and also have a positive impact on family members and society at large as indirect costs might decrease if survival increases see section 2.4. A recent impact projection study of the broad introduction of immunotherapy in Türkiye for lung cancer and five additional cancer types showed that over 100,000 patients could benefit (235). This would lead to over 23,000 additional life years and the prevention of almost 15,000 adverse events at additional costs of €1.9 billion over a five-year period, representing 1.67% of the expected total healthcare expenditure (235).

Table 10: Regulatory approval and reimbursement status of EMA-approved indications in first-line advanced lung cancer on January 1st, 2022

Medicine	Indication	Year of EMA approval	ESMO-MCBS	Regulatory approval and reimbursement status			
				Türkiye	Belgium	France	Poland
				Immunotherapies			
Pembrolizumab	NSCLC, mono, metastatic, PD-L1≥50%	2017	5	not reimbursed	reimbursed	reimbursed	reimbursed
Durvalumab	NSCLC, mono, stage III, PD-L1≥1%	2018	4	not reimbursed	reimbursed	reimbursed	not reimbursed
Nivolumab	NSCLC, with ipilimumab & Pt-chemo, metastatic	2020	4	not approved	reimbursed	not reimbursed	not reimbursed
Pembrolizumab	NSCLC, with Pt-chemo & pemetrexed, metastatic NSQ	2018	4	not reimbursed	reimbursed	reimbursed	reimbursed
Pembrolizumab	NSCLC, with carboplatin & (nab)paclitaxel, metastatic SQ	2019	4	not reimbursed	reimbursed	reimbursed	reimbursed
Atezolizumab	NSCLC, with carboplatin, paclitaxel & bevacizumab, metastatic NSQ	2019	3	not approved	reimbursed	reimbursed	not reimbursed
Atezolizumab	NSCLC, with carboplatin & nab-paclitaxel, metastatic NSQ	2019	3	not approved	reimbursed	not reimbursed	not reimbursed
Atezolizumab	SCLC, with carboplatin & etoposide, extensive stage	2019	3	not reimbursed	reimbursed	reimbursed	reimbursed
Durvalumab	SCLC, with carbo-/cisplatin & etoposide, extensive stage	2020	3	not approved	reimbursed	reimbursed	not reimbursed
				Targeted therapies			
Afatinib	NSCLC, mono, EGFR+, advanced	2013	4	reimbursed	reimbursed	reimbursed	reimbursed
Alectinib	NSCLC, mono, ALK+, advanced	2017	4	reimbursed	reimbursed	reimbursed	reimbursed
Ceritinib	NSCLC, mono, ALK+, advanced	2017	4	reimbursed	not reimbursed	reimbursed	reimbursed
Crizotinib	NSCLC, mono, ALK+, advanced	2015	4	reimbursed	not reimbursed	reimbursed	reimbursed
Erlotinib	NSCLC, mono, EGFR+, advanced	2011	4	reimbursed	reimbursed	reimbursed	reimbursed
Gefitinib	NSCLC, mono, EGFR+, advanced	2009	4	reimbursed	reimbursed	reimbursed	reimbursed
Osimertinib	NSCLC, mono, EGFR T790M+, advanced	2016	4	reimbursed	reimbursed	reimbursed	reimbursed
Osimertinib	NSCLC, mono, EGFR+, advanced	2018	4	reimbursed	reimbursed	reimbursed	not reimbursed
Bevacizumab	NSCLC, with erlotinib, EGFR+, advanced NSQ	2016	3	not approved	not reimbursed	not reimbursed	not reimbursed
Brigatinib	NSCLC, mono, ALK+, advanced	2020	3	reimbursed	not reimbursed	reimbursed	not reimbursed
Crizotinib	NSCLC, mono, ROS1+, advanced	2016	3	reimbursed	reimbursed	reimbursed	reimbursed
Dacomitinib	NSCLC, mono, EGFR+, advanced	2019	3	not reimbursed	not reimbursed	reimbursed	reimbursed
Entrectinib	NSCLC, mono, NTRK+, advanced	2020	3	not approved	not reimbursed	not reimbursed	not reimbursed
Entrectinib	NSCLC, mono, ROS1+, advanced	2020	3	not approved	not reimbursed	not reimbursed	not reimbursed
Larotrectinib	NSCLC, mono, NTRK+, advanced	2019	3	not approved	reimbursed	reimbursed	not reimbursed
Ramucirumab	NSCLC, with erlotinib, EGFR+, metastatic	2020	3	not approved	reimbursed	reimbursed	not reimbursed
Dabrafenib/Trametinib	NSCLC, mono, BRAF V600+, advanced	2017	2	not approved	reimbursed	reimbursed	not reimbursed
Necitumumab	NSCLC, with gemcitabine & cisplatin, EGFR+, advanced SQ	2016	1	not approved	not reimbursed	not reimbursed	not reimbursed

Notes: Inclusion criteria were (1) first-line indication in advanced lung cancer, (2) EMA approval in 2009–2020, (3) immunotherapies and targeted therapies. The medicines/indications are ranked according to ESMO-MCBS score (5=highest, 1=lowest) and alphabetical order. NSCLC = non-small cell lung cancer, SCLC = small cell lung cancer, mono = monotherapy, NSQ = non-squamous, SQ = squamous, Pt-chemo = platinum-based chemotherapy. Source for indications: EMA (215). Source for approval and reimbursement status: Information provided by MSD.

7.6.4 Uptake of cancer medicines

The third hurdle for patient access to new cancer medicines in Türkiye is uptake, i.e., patients being treated with newly reimbursed medicines by the SSI. Despite reimbursement, new medicines may take time – months or years – until they are used on a broad scale in clinical practice throughout the entire country, as shown in a recent study on lung cancer medicines in Europe (183). General factors that can delay broad uptake in oncology are the following:

- Change/update of clinical routines and clinical guidelines. An example is melanoma stage II for which the current standard-of-care after complete surgical resection is observation (no adjuvant therapy), but where adjuvant immunotherapy might soon become a new standard-of-care (236), requiring new clinical routines.
- Training requirements for medical staff to ensure the safe use of new medicines. An example is the new class of CAR-T cell therapies, which have a unique toxicity profile and require a tailored management of side effects (237).
- Few comprehensive cancer centers. University hospitals or leading cancer treatment centers (see section 7.4) may often be earlier adopters of new technologies, whereas other hospitals, often located in rural areas with fewer specialists, are typically slower.
- Low capacity of the diagnostic testing infrastructure. The administration of many modern cancer medicines requires prior biomarker testing (see section 7.3). This necessitates an adequate number of molecular diagnostic laboratories with appropriate staffing.
- No reimbursement of diagnostic testing. The reimbursement of medicines requiring biomarker testing without reimbursement of the testing means that patients have to pay out-of-pocket or alternative payers, such as pharmaceutical companies, patient organizations, or physician organizations (see section 7.3), have to cover some or all of the expenses for certain patients.
- Limited budget for reimbursed medicines of the public payer. This might find an expression in volume caps, which restrict the total number doses of a medicine allowed to be sold per year.
- High patient co-payments on reimbursed medicines. This will restrict the number of patients with limited financial means to access new medicines. In Türkiye, this is not a problem, because there are no co-payments for cancer medicines reimbursed by the SSI.

Full uptake (full patient access) is achieved when every patient that may benefit receives the appropriate medicine (238). Studying patient access is difficult without the availability of nationwide individual patient records. In this report, uptake in a country was inferred from national sales data of cancer medicines. Data on sales were obtained from reports by the Pharmaceuticals Manufacturers Association of Türkiye which based their analysis on data from IQVIA, a global provider of pharmaceutical sales data (239, 240). For the three benchmark countries, data were obtained from a previous report that also relied on IQVIA data (4). Total sales data for all cancer medicines were used. It is important to note that IQVIA sales data are based on list prices, which often do not represent actual final sales prices, because medicines are granted confidential discounts to payers; see section 7.6.2. The size of the discounts may also vary over time and between countries. Consequently, the use of sales data based on list prices overestimates the expenditure on cancer medicines presented here.

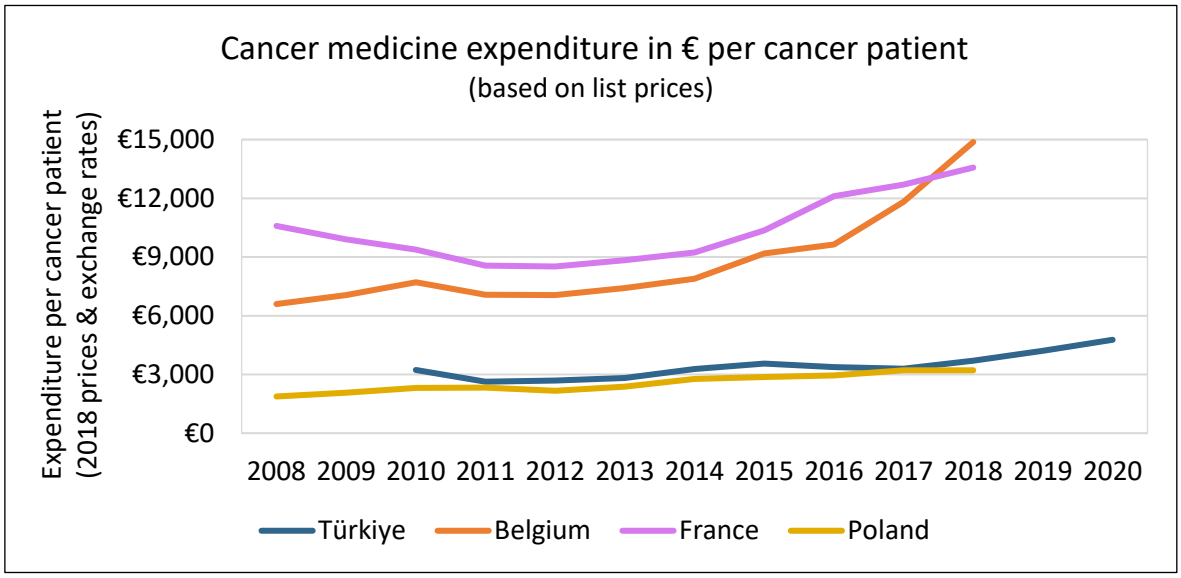


Figure 48: Total expenditure on cancer medicines per cancer patient in € (at list prices, inflation-adjusted to 2018 price levels and constant exchange rates with base year 2018), 2008–2020

Notes: No data are available for Türkiye in 2008–2009 and the three benchmark countries in 2019–2020. The number of cancer patients refers to incidence and uses extrapolations for missing years; see section 2.2.1. List prices do not contain confidential rebates. Source: Own calculations based on IEIS (2021), IEIS (2019), and Hofmarcher et al. (2019) (4, 239, 240).

Figure 48 shows total cancer medicine sales per cancer patient in Türkiye and three benchmark countries (at 2018 price levels and exchange rates). In Türkiye, the expenditure per patient remained relatively stable at around €2,700–€3,700 between 2010 and 2018. Afterwards, there was a gradual increase to €4,800 per patient until 2020. Throughout the period 2010–2018, spending in Türkiye was slightly above the increasing spending level in Poland. The spending levels in Belgium and France were 2–3 times higher than in Türkiye in the first half of the 2010s, but then increased considerably and were close to 4 times higher in 2018 at around €14,900 and €13,600, respectively.

Even though list prices of medicines might be higher in Belgium and France than in Türkiye, the big difference in the spending levels indicates a likely gap in the broad use of modern, higher-priced medicines in clinical practice in Türkiye.

The increase in cancer medicine sales in the recent decade in Türkiye and the three benchmark countries is a product of various factors relating to prices and volume:

- Higher (list) prices of newly introduced medicines (241), i.e., higher costs per treatment
- Increasing number of approved cancer medicines and indications (see Figure 45)
- Increasing number of lines of therapy (e.g., two lines of therapy in lung cancer whereas in the past most patients had died after the first line)
- Increasing use of combination therapies (i.e., more than one medicine administered at the same time – either of several new medicines or of a new medicine added to the existing standard-of-care medicine(s))
- Introduction of cancer medicines for previously untreated patient groups (e.g., metastatic castration-resistant prostate cancer)
- Increasing use of cancer medicines in the neoadjuvant and adjuvant setting instead of just in the metastatic setting

Efforts to improve access to cancer medicines in the benchmark countries

A key question for Türkiye is how to improve access to new and effective medicines and ensuring broad uptake while operating with constrained budgetary resources. Some learnings from the three benchmark countries are provided below. They demonstrate that all countries use their NCCPs to improve the access environment. In addition, France and Poland created dedicated funding systems to finance innovative cancer medicines along with innovative medicines from other disease areas.

- **Belgium – NCCP:** One of the aims of the Belgian NCCP 2008–2010 was to make effective cancer medicines quickly available and accessible (83). This included faster assessment of reimbursement applications and an investigation of differences in the speed of assessments, prices, and reimbursement conditions of cancer medicines between Belgium and neighboring countries. The NCCP also specified a handful of medicines that were not reimbursed yet, but that have been defined as priorities by physicians. In addition, the NCCP pointed to the fact that new medicines are very expensive but that they often represent real added value in response to a medical unmet need and/or in terms of effectiveness and tolerance. It called for an assessment of the willingness of society to pay for medical advances.

- **France – NCCP & funding system:**[25] The first NCCP (2003–2007) marked a turning point for the financing of cancer medicines (87). Until 2003, all public hospitals had to finance cancer medicines from their yearly budget, which was disconnected from the need for newer, more expensive medicines and the number of cancer patients. As part of the NCCP, the government decided to remove new innovative cancer medicines from the general budget of hospitals in 2004 and finance them instead out of the general AMO budget by covering the hospital expenses for cancer medicines for each euro spent. This improved patient access and resulted in a tripling of expenditure for innovative cancer medicines from €335 million in 2003 to €1,038 million in 2009 (87).
- **France – NCCP:** The roadmap of the first half (2021–2025) of the current NCCP contains several actions to improve access to new cancer medicines (89). These actions put a heavy focus on developing a more comprehensive evaluation model of new medicines taking into account long-term health effects, improving early access while imposing requirements for real-world follow-up, a fast-track evaluation procedure for faster reimbursement, a new funding system for high-priced medicines.
- **France – funding system:** In June 2021, the French president introduced the "Health care Innovation 2030" strategy aimed to make France "the leading European nation in innovation and sovereignty in health care" by 2030 (243). As part of this strategy, the government started to accelerate access to new high-priced medicines (both for oncology and non-oncology) in a 2-year pilot project since January 2022 (244). The project gives patients access to medicines directly after the evaluation of the added therapeutic value (ASMR) by the National Authority for Health (HAS), i.e., without having to wait for a price to be negotiated, if the medicine has an ASMR of IV (minor improvement). Previously this was only possible for medicines with an ASMR of I to III (major improvement to moderate improvement). Medicines with an ASMR I to IV are placed on the "liste en sus", which is a funding system within AMO for innovative medicines that are usually too expensive to be included within the ordinary hospital financing system.
- **Poland – funding system:** Public expenditure on medicines by the NFZ are capped at 17% of total public health expenditure (245), which is maintained through mechanisms such as payback obligations and risk-sharing instruments (221). In order to support the access to

[25] Already in 1994, France implemented an early access program for new medicines (both oncology and non-oncology products) called ATU (Autorisation temporaire d'utilisation), which granted access to patients to promising new therapies before national reimbursement or even before EMA approval (242). However, the number of cancer patients benefiting from this program (16,000 patients between 2007 and 2019, compared to the annual number of new cancer cases of 380,000) is vanishingly small (242).

modern high-priced medicines, the Ministry of Health established special drug programs in 2011. Most modern cancer medicines are covered by these drug programs. The programs define clear criteria for patient enrolment. Around half of the budget for these programs goes to cancer medicines, and the overall budget has been extended by 45% from USD 635 million in 2015 to USD 921 million in in 2018 in order to support the increasing launch of modern medicines (221).

- **Poland – NCCP:** The current NCCP for 2020–2030 contains actions to shorten the patient's access time to innovative medicines through legislative changes (95). It also contains the aim to gradually expand the list of reimbursed medicines until 2030 to achieve an access level of at least 90% of available cancer medicines among all reimbursed medicines in the EU (95).

Creating budget headroom for new cancer medicines

A general sticking point in the reimbursement and uptake of new cancer medicines is the need for additional budget. Even if a new cancer medicine is considered to be cost-effective, its use in clinical practice will most often require an additional budget compared to the current standard-of-care. In Türkiye, there are several areas of opportunity to create budget headroom for new cancer medicines.

Opportunity 1 – Prioritization of cancer medicines with high clinical benefit. Even though over 100 new cancer medicines have been launched over the last decade alone (see Figure 45), not all medicines offer the same level of benefit. Constrained health care budgets could be aided by an increased focus on cancer medicines that provide the greatest benefit to patients. In France this is done through the assessment of the ASMR scale by the HAS. However, international value frameworks that are less susceptible to the influence by the pharmaceutical industry or governments have also been put forward. The prime example is the ESMO-MCBS scoring system that classifies cancer medicines in order to identify those with a "substantial clinical benefit" (i.e., ESMO-MCBS score of 4 and 5 or B and A), as they should be priorities for rapid reimbursement by national bodies from a clinical perspective (234). Medicines with a limited clinical benefit (i.e., small gains in overall survival compared to current standard-of-care) or not clearly established relative clinical benefit because of a lack of a good comparator (e.g., single-arm trials) would be deprioritized. The example of lung cancer and immunotherapies (see section 7.6.3) shows that Türkiye is currently not clearly prioritizing cancer medicines with high clinical benefit according to ESMO-MCBS.

Opportunity 2 – Encourage the use of generics and biosimilars. Türkiye has a large local production of generics, whereas the local production of biosimilars is still limited to only a handful of products (240). A well-functioning and competitive local production could ensure low prices after patent expiry, which frees up resources for newer medicines. Stimulating competition among existing

biosimilars through establishing local production of high-volume cancer medicines such as bevacizumab, rituximab, trastuzumab could probably reduce prices. A recent analysis showed that countries in the Asia-Pacific region could save between 3–20% of their total cancer medicine expenditure through greater competition among generics and biosimilars (47).

Opportunity 3 – Facilitate the implementation of clinical trials for medicines. In recent years, the TMMDA has implemented initiatives to improve the clinical trials ecosystem and align it with international standards (246). Through the participation in clinical trials, some patients can receive the newest medical treatments without the need by the SSI to pay for them. However, Türkiye cannot fall too far behind the current global standard-of-care (such as in lung cancer; see section 7.6.3) to remain a relevant and attractive location, in particular for phase III trials.

Opportunity 4 – Re-allocate budget to medicines through realizing savings opportunities in other areas of cancer care. Innovations in cancer care do not always have to come at a higher price. A prime example is the recent discovery of hypofractionation in radiation therapy (see section 7.5). By bringing down the number of radiation therapy sessions while maintaining treatment outcomes, the need for radiation therapy equipment and medical staff decreases. Recent estimates indicate that the cost of breast cancer treatment with hypofractionation is around 30% lower than with conventional radiation therapy (247).

8. Policy recommendations

Cancer is a growing challenge for the Turkish health system and the Turkish society. Making the fight against cancer a top priority can be facilitated by political leadership. Shining examples are the Nixon administration's "War on Cancer" in 1971 in the United States (248), the Delors Commission's first "Europe Against Cancer" program in 1987 in the EU (249), and the von der Leyen Commission's "Europe's Beating Cancer Plan" in 2021 in the EU (193). Policy makers in Türkiye could draw inspiration from these examples of high-level political commitment to prioritize effective and comprehensive cancer control efforts to address the many current and future challenges.

There are three key steps to improve cancer care. Step one is to measure and understand the magnitude and the development of the burden of cancer. This report brings together available statistics on the burden in Türkiye showing that (1) cancer is already the second-leading cause of death, (2) economic costs of cancer amount to €2.48 billion or €30 per capita, and (3) current cancer numbers (around 200,000 new cases per year) could almost double until 2040. Step two is to plan, coordinate, and implement – financial and legislative – actions to address shortcomings in all areas of cancer care, ideally through an NCCP. This report examines three of those areas – governance, early detection (with a focus on screening), and diagnosis and treatment – and provides recommendations on how to improve the status quo below. Step three is to monitor and evaluate the effectiveness of all actions taken. This necessitates good local cancer registration. All three steps need to involve and build on cooperation between relevant stakeholders, including the ministries of health and finance, the SSI, physician organizations, patient organizations, industry, and academia.

Despite the demographic changes in Türkiye being the driving force behind the increase in cancer numbers, these changes cut both ways. While the proportion of people aged ≥65 years will increase considerably in the coming decades, the proportion of the working-age population (15–64 years) will remain stable. The latter trend is favorable for continuing to build a strong economy ("the demographic window of opportunity") through the social insurance contributions of the workforce, especially if the female labor participation rates could be increased. This creates additional public budget to invest in health care and cancer care. The health returns from additional spending can reinforce the economy because healthy people can contribute more than sick people. Indeed, previous research has not just shown a positive association between the level of spending on cancer care and survival rates, but also that increasing survival rates were paralleled by decreases in indirect costs (productivity loss) for the economies in Europe over the past decades (4).

Organization and financing of health care

The introduction of universal health coverage in the years after 2003 in Türkiye was an important step to provide more equal care to the whole population across the country. However, several challenges remain to be addressed. These general challenges of the health care system also affect cancer care.

- The health care system has been characterized by comparatively low spending levels for the last two decades. In 2019, the public part of the total health expenditure amounted to 3.4% of GDP, falling short of the informal WHO spending target of 4–5% of GDP. Additional public spending to bring the country closer to the benchmark would be needed.
- The allocation of an adequate budget towards health care might be hampered by the current joint public budget for health care and pensions. There is a risk that shortfalls in either of those two areas have to be covered up through cross-financing. Earmarking social insurance premiums into two separate budgets could prevent this.
- The quality and the range of modern health services provided through public health insurance by the SSI needs to be improved. A sign of the current unmet health need of patients despite the public coverage is the growing number of people purchasing complementary private health insurance to cover some costs of treatment in private hospitals.
- Despite the enhanced role of primary care with family physicians, they do not act as gatekeepers to secondary and tertiary care. Establishing family physicians as gatekeepers could unburden the rest of the health care system. Monetary incentives, such as differentiated patient fees in primary care and secondary care, could be used to encourage patients to seek help in the primary care for minor complaints.
- The responsibilities of primary care and family physicians in cancer care need to be defined more clearly. This applies to the provision of health education/advice (prevention of cancer), the formal invitation to the three screening programs, as well as encouragement to go to screening at unrelated visits.

Governance of cancer care

The governance of cancer care in Türkiye has been shaped by three NCCPs issued by the Ministry of Health since 2009, with the current NCCP covering the period 2021–2023.

- The NCCPs are characterized by a waning level of comprehensiveness and ambition. Only the first NCCP included actions to address the whole continuum of cancer care, including prevention, early detection/screening, diagnosis and treatment, survivorship. The current NCCP includes merely five actions and none of these actions are related to “diagnosis and treatment” and “survivorship”. A new NCCP with a comprehensive set of actions across the whole continuum of cancer care should be established. This can prevent arbitrariness of actions and improve the coordination between different actors involved.
- Even though the actions defined in the three NCCPs included “indicators of progress”, there is no annual monitoring of the implementation progress. Annual evaluations of the implementation status of all planned actions should be done and published publicly.
- All three NCCPs lacked funding plans. Most of the planned actions in the first two NCCPs required major investments in infrastructure, human resources, training, equipment, medicines. A crude funding plan should be included in a future NCCP and discussed with the Ministry of Finance in order to check if all planned actions are financially viable.

Cancer registration & performance assessment

Türkiye has a good track record in cancer registration since the establishment of the first cancer registry in the Izmir province in 1992. Over the years, more and more cancer registries in all parts of the country have been established and cover all 81 provinces since 2013.

- The functionality and the quality of the data in many provinces is still inadequate. Only around 50% of the population lives in areas with cancer registries used for official statistics by the Ministry of Health. It is important that the current NCCP succeeds in its aim to improve cancer registration.
- Underreporting of the number of cancer patients needs to be addressed. This is mainly a result of the cancer registries not collecting data on non-nationals.
- The comprehensiveness and relevance of current data needs to be improved. The annual reports by the Ministry of Health only provide statistics on incidence. Information on mortality (which is already collected by TurkStat) should be added. The estimation of survival should also be prioritized by linking individual-level information on mortality to the registries.
- Official cancer statistics should be more up to date. Information on the latest incidence data is published with considerable delay (currently 4.5 years) by the Ministry of Health.
- Performance assessment in cancer care using cancer registries should be explored. The cancer registries could be developed further so that they can be used to analyze treatment patterns, outcomes of patients (survival), and efficient use of resources in all provinces of the country.

Screening

Türkiye was an early adopter of three organized, population-based cancer screening programs for breast, cervical, and colorectal cancer in line with WHO recommendations. The aim of the first two NCCPs was to achieve screening rates of 70% in the respective target populations, whereas the NCCP from 2021 no longer explicitly mentions the 70% benchmark.

- Screening rates need to be improved further. Between 2014 and 2019, the screening rates have improved in all three programs, reaching around 30–40% of the target population. These rates are still far below the previous national aim of 70%.
- Geographic inaccessibility to KETEMs has been a limiting factor in the past. The number of KETEMs has improved greatly and mobile teams using trucks have in recent years tried to reach remote areas. Having enough KETEMs with clinical staff in all provinces needs to be ensured.
- The lack of awareness in the population needs to be addressed concerning (1) the risks to develop cancer, (2) the benefits of early detection through screening, and (3) how screening and KETEMs work. Many people are also not aware that screening services are free of charge and that no appointment is required. This points to a potential ineffectiveness of current campaigns by the Ministry of Health in conjunction with Breast Cancer Awareness Month (October) and Colorectal Cancer Awareness Month (March). The fact that there is a socio-economic gradient in screening rates for breast and colorectal cancer, with higher participation rates among high-educated people than among low-educated people underlines the importance of campaigns to reach the latter group.
- Instead of inviting people in the target population by mail/phone for cervical and colorectal cancer screening, all people could automatically receive an invitation together

with the delivery of home test kits by mail. This removes the barrier of having to go to KETEMs to get the testing kit.

- The starting age for the cervical cancer screening program could be lowered from 30 years to 25 years to bring it more in line with international recommendations (starting age of 20–30 years). This is especially important in the absence of an HPV vaccination program.
- The screening method in the colorectal cancer screening program could be changed from the current combination of FOBT and colonoscopy to FIT as the only method in line with international recommendations. The stop age could be increased from 70 years to 75 years to bring it more in line with international recommendations.
- The feasibility and cost-effectiveness of additional screening programs could be evaluated. This concerns a lung cancer screening program for current and former smokers, a prostate cancer screening program for men, and a screening program for Helicobacter pylori either in the whole country or provinces with a high incidence of stomach cancer.

Diagnosis and treatment (excl. cancer medicines)

The patient pathway from first symptoms until treatment start can be lengthy in Türkiye due to a lack of continuity and coordination of care.

- Structured and standardized patient pathways defining each step of the patient journey, the services to be received along the journey, and the maximum time between each step could be gradually introduced for all cancer types.
- The coordination between family physicians and specialists to whom patients are referred to needs to be improved. This requires a better referral system with electronic transfer of patient data. This could prevent unnecessary diagnostic procedures and duplication of services/tests.

The availability of medical staff involved in the diagnosis and treatment of cancer is mixed in Türkiye. The number of oncologists, radiologists, and other specialists appears to be good in relation to the number of cancer patients, whereas the number of nurses appears to be low.

- Training of additional medical staff is required in anticipation of future increase in the number of cancer patients. More emphasis could be placed on the training of nurses specialized in oncology to unburden specialized physicians. This could be a cost-effective way to future-proof the staffing requirements in cancer care.

The availability of diagnostic imaging equipment (scanners) is high in relation to the number of cancer patients in Türkiye, which might even point to an overuse and potential inefficiencies. Basic biomarker testing is reimbursed and tied to the availability of appropriate reimbursed cancer medicines.

- Multigene testing through NGS could be evaluated for reimbursement in selected cancer types, such as lung cancer, due to the growing number of druggable targets. This would also require a modernization of molecular diagnostic laboratories and training of pathologists and clinical laboratory scientists.
- Measures to ensure appropriate handling of tumor tissue obtained through biopsies need to be taken to avoid the necessity of re-biopsy due to poor quality of the tissue sample.

There is an ongoing shift in the treatment setting of cancer patients from inpatient care to outpatient care in Europe. Türkiye has also witnessed a decline in the number of inpatient days by cancer patients in the past decade.

- The planning of new treatment facilities for cancer patients needs to consider the changing treatment setting away from inpatient care. A stronger focus on treatment in an outpatient setting might also be an opportunity for future savings without comprising patient health.
- The geographic location of new treatment facilities needs to be aligned with the (future expected) patient population living in the catchment area and the availability of suitable means of transportation for patients.
- A national quality assurance system of cancer treatment facilities could be considered. Alternatively, more treatment facilities could be encouraged to apply for international quality accreditations, such as by ESMO and OECI.

The number of radiation therapy machines and trained professionals to operate the machines have improved in the recent decade in Türkiye. In relation to the number of cancer patients, radiation therapy machines are nowadays available at a good ratio, even though the number of brachytherapy units might still be somewhat low.

- The adoption of hypofractionation should be prioritized in all cancer types with clinical evidence on non-inferior patient outcomes. This would shorten treatment times and prevent the need for additional radiation therapy machines. It would also free up health care resources that can be used in other areas of cancer care. Travel costs for patients and time required from informal caregivers driving them would also be reduced.
- Despite the increased number of radiation therapy machines, the geographic distribution is still a challenge with poor access and long travelling distances in some rural areas. Changing the treatment to hypofractionation when medically feasible could be a great relief to patients living in rural areas.

Cancer medicines

The regulatory approval process for new cancer medicines by the TMMDA is comparatively long. The overall approval target timeline of 210 calendar days for standard applications is often exceeded in practice.

- The GMP process, currently taking 12–18 months, could be greatly expedited by accepting GMP inspection outcomes and certificates of manufacturing sites from other well-established regulatory bodies, such as the EMA or the FDA.
- The TMMDA could consider skipping the pricing assessment as part of the evaluation process (as done by the EMA), because already now the regulatory approval can be obtained prior to pricing approval. The pricing assessment could instead follow directly after regulatory approval or start shortly beforehand when approval is imminent.

The reimbursement of newer cancer medicines by the SSI is comparatively limited in a European context. In the case of lung cancer, the access of patients to treatment options in Türkiye in 2022 corresponded to the treatment options recommended by European clinical guidelines in 2016, indicating a delay of at least six years to new cancer medicines. The main sticking point in the reimbursement decisions is the anticipated budget impact of high-priced medicines.

- Limited health care budgets call for an assessment of the costs and benefits of new medicines. However, the main emphasis in the evaluations of the Reimbursement Commission is currently on limiting the budget impact. Switching to “value-for-money” (cost-effectiveness) as the main criterion for the reimbursement decision could be considered. Clear and transparent cost-effectiveness thresholds would need to be established. As part of a full HTA, the budget impact could still serve as an important but not the main criterion.

- The next version of the NCCP could be used to systemically address weaknesses in the access environment to new cancer medicines. A comparison of the global standard-of-care treatment options with the locally accessible options could identify areas with the greatest potential to improve patient outcomes.
- Opportunities to create budget headroom for new cancer medicines could be explored more actively.
    - A dedicated fund for new, high-priced cancer medicines (and potentially also medicines from other disease areas) could be created and financed from the general public budget. This fund could be linked to conditions such as volume caps, free doses, or pay-for-performance payment models.
    - The reimbursement could prioritize more strongly cancer medicines with high clinical benefit and deprioritize those with limited benefit, using the ESMO-MCBS scoring system or a system such as the HAS in France.
    - The use of generics and biosimilars could be prioritized. A strong focus could be placed on the expansion of the local production of biosimilars, in anticipation of a great number of biologics in oncology coming off patent in the coming years. This would ensure more competitive prices after patent expiry of the originator medicine.
    - The implementation of clinical trials for medicines could be facilitated. Recent initiatives by the TMMDA have already improved the prerequisites to do this. To remain a relevant and attractive location, in particular for phase III trials, the reimbursement of newer medicines cannot fall too far behind the current global standard-of-care.
    - A broader, societal perspective in the evaluation of medicines could be considered instead of the sole focus on costs within the health care system. Potential reductions in indirect costs of patients' productivity loss and informal care costs from improved treatment outcomes could be counted against increases in medicine costs.

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Appendix

Table A1: Exchange rates and PPP factor in 2019 used in the calculation of direct and indirect costs

Country	Exchange rate (Local currency per €)	PPP conversion factor (PPP-€ per €)
Türkiye	6.36	2.29
Belgium	1.00	0.91
France	1.00	0.94
Poland	4.30	1.67

Notes: PPP = purchasing power parity. Source: Eurostat (39).

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