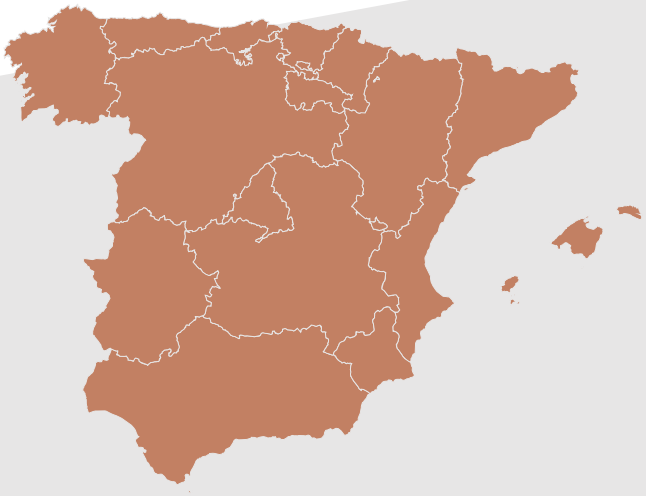
Endometrial Cancer – Improving Care and Driving Policy Change

A Case Study on Spain



BACKGROUND. Endometrial cancer is the most common gynecological cancer in high-income countries, with rising incidence and mortality attributed partly to demographic shifts and increasing rates of obesity (1). Unlike breast and cervical cancers, which benefit from global awareness and policy initiatives, endometrial cancer remains underrepresented in both international and national health agendas, including in Spain.

The Swedish Institute for Health Economics (IHE) published a comprehensive report titled ***Endometrial Cancer - Improving Care and Driving Policy Change*** in 2024 (1). Endorsed by the European Network of Gynaecological Cancer Advocacy Groups (ENGAGe) and the European Oncology Nursing Society (EONS), the report highlights unique challenges and opportunities for improving outcomes in this neglected cancer type. Building on the findings of the main report, this case study focuses on the situation in Spain. It provides an overview of the burden of endometrial cancer and identifies key areas for improvement in care and policy response.

1 WHAT IS ENDOMETRIAL CANCER?

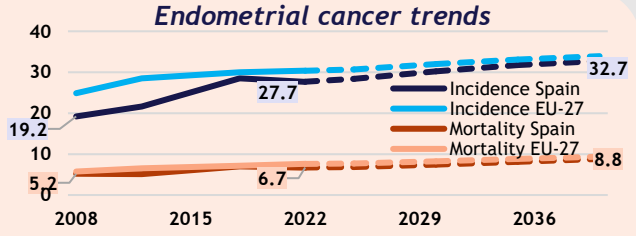
Endometrial cancer originates in the inner lining of the uterus (womb), called the endometrium, and accounts for around 90% of all cancers in the body of the uterus (also referred to as uterine cancer or corpus uteri cancer)* (1). Around 30-50% of all endometrial cancer cases are linked to excess body weight (2, 3). Abnormal vaginal bleeding (i.e., bleeding between menstrual periods or after menopause) is the most common symptom (1). In Spain, 90% of endometrial cancer cases are diagnosed in women over the age of 50, with a median age at diagnosis of 63 years. It is estimated that approximately 75%-80% of cases are diagnosed at stage I (4). However, information on the stage at diagnosis is limited, as cancer population registries in Spain do not systematically collect this data (5).

2 DISEASE BURDEN

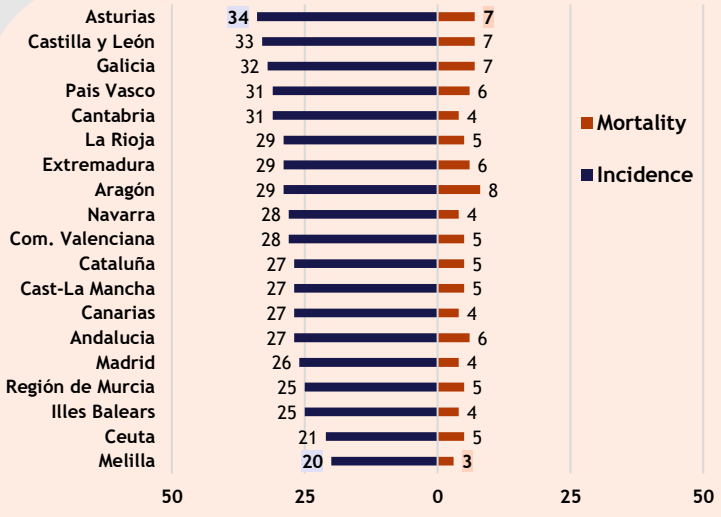
Spain is experiencing a rising number of endometrial cancer cases, driven by demographic shifts. By 2030, incidence and mortality among Catalonian women aged 65-74 are projected to rise by 8.4% and 21.5%, respectively, compared to 2020, driven by aging, obesity, and diabetes (6).

Endometrial cancer affects more women than cervical and ovarian cancer combined. Uterine cancer is the 4th most common cancer type among Spanish women. In Spain, the incidence rate of uterine cancer rose from 19.2 to 27.7 per 100,000 women between 2008 and 2022, approaching the EU average of 30.4, and is projected to reach 32.7 by 2040 (EU-27: 33.9) (7-10). Mortality rates increased from 5.2 to 6.7 per 100,000 women during the same period, projected to reach 8.8 by 2040 (EU-27: 9.4) (7-10). In 2024, approximately 7,305 new cases of uterine cancer are expected, more than the combined numbers of cervical and ovarian cancers (11). In 2022, uterine cancer caused 1,719 deaths, making it the 8th leading cause of cancer-related death among Spanish women (11).

Regional differences exist in the disease burden of endometrial cancer. In 2023, incidence rates per 100,000 women ranged from 20 in Melilla to 34 in Asturias, while mortality rates ranged from 3 in Melilla to 8 in Aragon (12).



Notes: Incidence and mortality crude rates per 100,000 women in Spain and the EU-27. ECIS: European Cancer Information System. EU-27: 27 European Union Member States.
Source: Ferlay et al, ECIS (7-10).



Endometrial cancer by Autonomous Region

Source: AECC *Asociación Española Contra el Cáncer). Dimensiones del cáncer (2023)* (12).

*This case study focuses on endometrial cancer; however, where specific data is unavailable, statistics for uterine cancer (corpus uteri cancer) are used instead. Hence, uterine cancer and endometrial cancer are used interchangeably in this case study.

Progress in endometrial cancer care has stalled in the last two decades. Although five-year survival rates of endometrial cancer are relatively high (>70%) compared to other gynecological cancers, they remain lower than for breast cancer (1). In contrast to most other cancer types, survival rates have not improved in recent years. In Spain, five-year net survival for all stages of uterine cancer shows a slightly negative trend, declining from approximately 75% during the diagnosis period of 2002–2007 to 74% in 2008–2013 (11). When diagnosed at its earliest stage (stage I), where successful treatment is most likely, 5-year net survival rates are approximately 95% (4).

Lifestyle factors influence the disease burden. Obesity and overweight are well-established modifiable risk factors for developing endometrial cancer. Among the 20 most common malignancies, uterine cancer has the strongest association with obesity (13). It is estimated that approximately 30% to 50% of all endometrial cancer cases are attributable to excess body weight (2). In 2022, 40% of Spanish women over the age of 18 were expected to be overweight (14) and 15.5% were classified as obese in 2020 (15). Despite this high prevalence, the obesity rate among adults has remained relatively stable since 2006. Adding to the concern, sedentary lifestyles further exacerbate the risk of developing endometrial cancer (1). In the 2020 European Health Survey in Spain, 40.3% of women reported being sedentary during their leisure time (15).

Socio-economic inequalities in risk factors are linked to endometrial cancer. Surveys conducted in Spain have demonstrated a strong association between socioeconomic factors and the prevalence of unhealthy behaviors. Individuals with lower levels of education and income are more likely to engage in behaviors such as smoking and have higher rates of obesity (15, 16). Obesity is nearly twice as common among individuals with lower education compared to those with higher educational attainment (15). Sedentary behavior is another factor disproportionately affecting women from lower socioeconomic backgrounds. While 45.5% of individuals with basic or lower education report being sedentary, the percentage decreases to 24.6% among those with higher education (15). This disparity places women from lower socioeconomic groups at greater risk of health issues, including obesity-related conditions such as endometrial cancer.

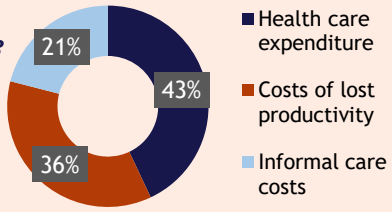
Financial challenges of having endometrial cancer. The impact of socioeconomic disparities extends beyond health behaviors to financial stability during illness. In 2022, only 6% of cancer patients from higher social classes (those with higher education and income) reported becoming financially dependent on family, relatives, or friends due to their illness (17). In contrast, nearly 25% of patients from middle or lower social classes faced this level of dependency (17). Endometrial cancer exclusively affects women, who are often more vulnerable to economic instability. Factors such as temporary employment, caregiving responsibilities, and lower salaries compared to men further compound the financial challenges faced by women (17).

3 ECONOMIC BURDEN

ECONOMIC BURDEN. In Spain, the overall economic burden of cancer amounted to €261 per capita in 2018 (18). Most of the burden was caused by healthcare expenditure (43%) and lost productivity among working-age patients (36%).

Composition of the economic burden of cancer in Spain in 2018

Source: Hofmarcher et al. (18)



The economic burden of cancer, excluding informal care costs, in Spain is estimated to have increased from €191 to €206 per capita from 2000 to 2018 (in 2018 years prices) (18). Healthcare spending on cancer increased by about 45% in 2018, corresponding to 4.9% of total health expenditure in 2018. At EU level the corresponding average was of 6.2% (18). Cancer health expenditures in Spain are expected to grow in the future (between 2023-2050), mainly driven by three factors: 1) the aging population leading to an increase in per capita health spending on cancer 2) efforts in improving cancer outcomes leading to more people surviving for longer and 3) higher treatment costs from new medicines and technologies that could increase costs further (19).

The economic burden of endometrial cancer in Spain is unknown. A 2017 literature review on the economic burden of cancer in Spain revealed a significant gap in the available research (20). The review also noted significant variability in reported costs due to a lack of methodological consensus on estimating the economic burden of cancer. Most studies underestimated total costs by focusing primarily on healthcare expenditure, neglecting indirect costs such as lost productivity. Among the limited cost-of-illness studies identified, seven focused on breast cancer and five on cervical cancer, but none specifically addressed endometrial or uterine cancer. This gap persists, as of the time of writing this case study, no comprehensive studies or reports have been conducted to evaluate the economic burden of endometrial/uterine cancer in Spain, either at a national or regional level. In addition, there is no publicly available data on healthcare system investments in the care of this cancer. In contrast, estimates from other high-income countries suggest that uterine cancer accounts for 1–3% of all cancer care expenditure (1).

4 EARLY DETECTION

EARLY DETECTION. Early detection of endometrial cancer increases the chances of successful treatment, improves survival rates, and reduces treatment costs (1). Unlike breast and cervical cancer, there is no established screening method for endometrial cancer. The condition is typically identified through symptoms — such as abnormal vaginal bleeding — noticed by the patient, making early detection heavily reliant on symptom awareness combined with easy access to healthcare services and prompt medical assessment by a gynecologist (1).

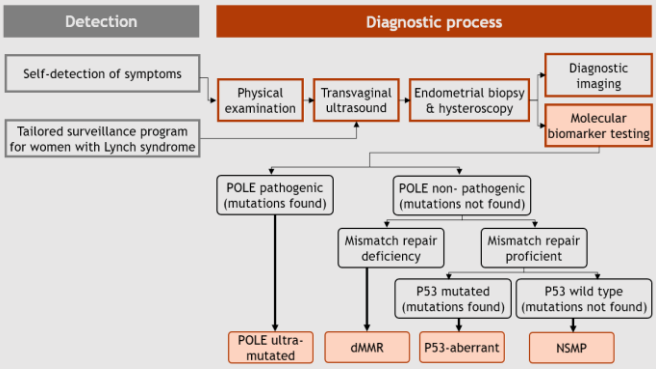
Role of awareness and health literacy in early detection. Symptom awareness of cancer is vital for timely intervention. In Spain, while 69% of the population consider cancer a very serious health issue, only half can identify symptoms signaling a potential diagnosis (21). Awareness is notably lower among older individuals, a concern given that endometrial cancer primarily affects postmenopausal women. Abnormal vaginal bleeding, the most common symptom of endometrial cancer, was among the better-known warning signs and often prompted individuals to seek medical attention more quickly (21). A 2023 study in a Spanish community found that women with inadequate or problematic health literacy (HL) were significantly less likely to attend gynecological visits for preventive check-ups compared to those with sufficient HL (48% vs. 19%) (22).

Shortage of primary care physicians and regional disparities. Spain has a relatively high density of practicing physicians (of any specialty) with 449 per 100 000 inhabitants in 2021, surpassing the EU average of 394 physicians (23). General practitioners (GPs) play a key role in facilitating early diagnosis in primary care as they refer patients with signs and symptoms to the appropriate specialist. However, Spain faces a challenge in terms of general medical practitioners (GPs) working in primary care, with a density of 91 per 100 000 inhabitants in 2020, falling short of the EU average of 113 physicians (24). Spain also faces an imbalance in the distribution of healthcare professionals, including physicians and nurses, across different regions of the country (16). The number of practising physicians (of any speciality) in Spain varies significantly between regions. For example, in 2023, Catalonia had the highest physician ratio, with 397 physicians per 100,000 inhabitants, while Andalucía (258.4), the Balearic Islands (266.2), and Valencia (283.9) recorded the lowest ratios (25).

Socioeconomic disparities in early detection. In 2019, women with higher incomes were more likely to attend screening services compared to women with lower incomes (16). Additionally, cultural and linguistic barriers negatively impact ethnic minorities and migrant populations, hindering their ability to access preventive measures and healthcare services. This disparity exacerbates differences in health outcomes between these groups and the general population (17). Socioeconomic inequalities, cultural and linguistic barriers, and possible geographic disparities in access to healthcare services all play a role in delaying early cancer detection in women (26).

5 DIAGNOSTIC PROCESS

. Endometrial cancer diagnosis involves a multi-step process (visualized below), including physical exams, imaging, biopsies, and molecular biomarker testing, which collectively guide staging and treatment decisions (1). Historically, classification relied on histology, categorizing cases into Type I (estrogen-related, slower growth) and Type II (aggressive, poorer prognosis). Since 2021, a molecular classification has redefined endometrial cancer into four subtypes—(i) POLE-ultra mutated, (ii) dMMR, (iii) p53-aberrant, and (iv) no specific molecular subtype (NSMP) (1). This new classification, combined with staging insights and the introduction of novel medicines, enables more personalized treatment strategies tailored to each patient. Comprehensive biomarker testing is required to facilitate this personalized approach. Equitable access to diagnostic tools, biomarker testing, and specialized expertise is essential for integrating these advancements into clinical practice, especially as new medicines continue to emerge.



Source: Based on *ESGO/ESTRO/ESP and ESMO guidelines (27, 28).*
Notes: dMMR (deficient mismatch repair), NSMP (no specific molecular profile), POLE ultra-mutated (DNA polymerase epsilon ultra-mutated), and P53-aberrant (TP53-mutated tumors).

Availability of gynecologists. In 2023, the total ratio of obstetricians/gynaecologists, disregarding if publicly or privately employed, per 100 000 women was 28.1. By 2035, the availability of professionals in this specialty is projected to increase by 20%, reaching 34.2 per 100,000 women (25). This reflects a moderate increase compared to other specialties but highlights the need to consider factors such as regional distribution and the dynamics of future demand (25).

Regional disparities in waiting times for gynecological care. Publicly available data on waiting times for specialty care in Spain indicate waiting times in the public sector (SNS). Due to the lengthy delays in accessing public healthcare, the Spanish government established a task force in 2024 (Grupo de Trabajo de Listas de Espera) to standardize criteria and procedures for managing waiting times across the healthcare system (29). As of June 2024, the average waiting time when being referred for an outpatient appointment in any specialty, was 94 days. For gynecological appointments, the average waiting time was notably lower, at 58 days, making it one of the shortest waiting times for outpatient care ("consultas externas") at that time. However, significant regional disparities exist in waiting times for gynecological care. For instance, the average waiting time ranged from just 6 days in Melilla to 147 days in Extremadura. The share of patients waiting more than 60 days for a gynecological appointment in outpatient care was highest in Murcia with 78.5% and lowest in Ceuta with 2%, signaling the need of looking into reasons behind regional differences in waiting times and the respective regions healthcare performance (30).

Infrastructure and regional disparities in biomarker testing. Biomarker testing is part of the diagnostic process of cancer and an integral part of precision medicine. It identifies the molecular characteristics of the tumour and helps to select appropriate treatments (31). The availability of single biomarker testing in Spain is high in comparison with other EU countries, according to an international study from 2020 (32). However, multi-biomarker testing in Spain has been found to be comparatively low in two European studies from 2020 and 2021 (32, 33). In addition, significant regional variations in

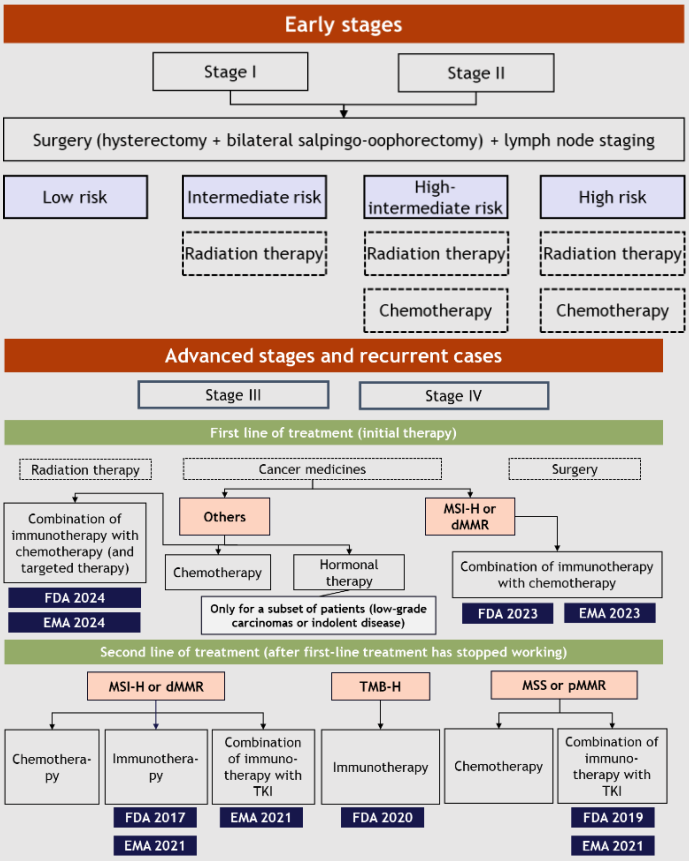
exist in Spain. This is due to a combination of limited infrastructure and variable public funding by regions. The existence of regional hospital budgets contributes to delays in reimbursement approval due to the need for sequential decision-making processes by national hospital stakeholders (32). In 2022, 40 million euros were allocated by the Spanish government for enhancing precision medicine (34). The common portfolio of genetic services was updated and officially presented by the Ministry of Health on January 23, 2024 (35). This update includes a 50-million-euro investment which focuses on developing infrastructure and capabilities essential for precision medicine and biomarker testing, targeting the noted regional disparities and infrastructure gaps.

Low adoption of timely MSI/MMR biomarker testing. Microsatellite instability (MSI) and mismatch repair (MMR) testing are essential for tailoring treatment options in recurrent or advanced endometrial cancer. A retrospective study conducted across five European countries, including Spain, analyzed data from patients diagnosed between 2016 and 2019 (36). The study revealed that only 34.9% of these patients underwent MSI/MMR testing, indicating limited adoption of these crucial tests during that period (36). While more recent studies suggest that the uptake of MSI/MMR testing has improved in Spain, specific data on endometrial cancer remains limited. For instance, a multicenter observational study conducted between 2020 and 2021 across 14 Spanish tertiary hospitals found that 84% of patients with metastatic colorectal cancer underwent dMMR/MSI-H testing (37). However, only 81% of these patients had their test results available before initiating first-line treatment, highlighting areas for improvement in timely testing. Whether similar improvements have occurred for endometrial cancer patients remains unclear.

6 TREATMENT

The treatment of endometrial cancer depends on the stage at diagnosis, but typically comprises surgery, radiation therapy, and systemic therapies. Surgery involves the removal of the uterus (hysterectomy) and often also the removal of the fallopian tubes and ovaries. Radiation therapy is commonly used to target residual cancer cells after surgery or as a standalone option for non-surgical candidates (1). Chemotherapy has been the cornerstone systemic therapy for decades, usually administered after surgery or as a standalone option for non-surgical candidates.

Recent advancements, however, have introduced a wave of innovative therapies, particularly immunotherapies and targeted therapies, designed to leverage the cancer's molecular profile (1). These therapies transform the management of advanced and recurrent endometrial cancer cases. Treatment algorithms for early-stage and advanced/recurrent-stage endometrial cancer (based on ESMO and NCCN guidelines) are presented below (1, 28, 38). Comprehensive, timely and equitable access to innovative medicines, specialized expertise, and multidisciplinary care is essential for integrating these advancements into clinical practice.



Source: (1) *Based on ESMO and the NCCN guidelines (28, 38).*
Notes:EMA: European Medicines Agency, FDA: Food and Drug Administration, MSI-H (microsatellite instability-high), dMMR (deficient mismatch repair), TMB-H (tumor mutational burden-high), MSS (microsatellite stable), and pMMR (proficient mismatch repair), TKI (tyrosine kinase inhibitor). Latest updates on combination therapy for first-line treatment (39, 40).

Short-term workforce challenges for oncologists. It is projected that nearly 30% of oncologists (both medical and radiation oncologists) will retire within the next five years, as 27% of oncologists were aged 60 or older in 2023 (25). While long-term projections for oncology human resources appear optimistic, with the ratio of medical oncologists expected to grow from 4.4 to 6.8 per 100,000 inhabitants and radiation oncologists from 2.0 to 2.1 by 2035, these gains may be insufficient to address the immediate challenges (25). Nationwide surveys conducted by the Sociedad Española de Oncología Médica (SEOM) further highlight these concerns, revealing a need for a 2.5% annual growth in the oncology workforce, alongside increased job stability (41). The limited availability of permanent employment, with only 16.3% of young medical oncologists holding fixed positions, adds to the difficulty of attracting and retaining talent (41-43). Nearly 65% of the surveyed oncologists considered working in other areas outside clinical work (43).

Challenges in gynecologic oncology training. Gynecologic oncologists play a pivotal role in treatment outcomes, with evidence showing that these specialists are associated with higher overall survival rates (44). For instance, there has been evidence that surgeries performed by gynecologic oncologists are associated with better survival outcomes for high-risk patients, as compared to surgeries done by other types of surgeons (45). In Spain, the gynecologic oncologist is a sub-specialization in gynecology (46). A study focusing on the training of young gynecologic oncologists in Spain found that one of the major concerns is the limited training opportunities available to them. The study revealed that after completing their residency-training program, 30 out of 37 (81%) responders did

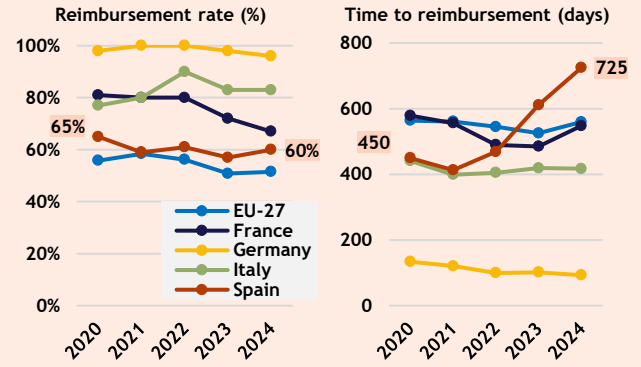
not feel qualified to work as gynecologic oncologists, mainly due to limitations in their surgical training (47). A comparison of national data with European results revealed significant differences in the confidence levels of gynecologic oncologists from Spain (ENYGO) and Europe (ESGO) in performing complex open surgeries and minimally invasive radical surgeries relevant to endometrial cancer. For instance, only 40.5% of ENYGO Spain gynecologic oncologists felt confident performing open radical hysterectomies, compared to 78% of their ESGO counterparts (47). Similarly, just 29.7% of ENYGO Spain oncologists expressed confidence in performing laparoscopic radical hysterectomies, compared to 42.2% in ESGO.

Unequal distribution of radiation therapy equipment. In 2019, Spain had the second highest level of radiation therapy equipment units in hospitals and the ambulatory sector in the EU after Italy (16). However, the availability of the equipment is distributed unevenly across regions and creating distances to healthcare centers possessing them (16). The distance to a center becomes a challenge in accessing care, in addition to the costs (both direct and indirect costs) incurred by the patients when being diagnosed and later on when being in treatment (17).

Wait times to receive treatment. For elective surgery (any specialty) the average number of waiting days was 121 in June 2024, while the average waiting time for gynecological elective operation was slightly less than 100 days, being roughly the same average waiting time compared to June 2023. In June 2024, regional differences in average waiting times (days) for elective gynecological surgery were significant and ranged from 158 days in Melilla to 37 days in Pais Vasco. The largest population of patients waiting more than 6 months for an elective surgery in gynecology were found in Melilla (33.9%) and Andalucía (27.4%), while the region of Madrid hade the smallest with 0.2% of patients waiting more than 6 months for an operation (30).

Changing landscape of novel medicines. Recent advancements have significantly expanded treatment options for advanced and recurrent endometrial cancer, particularly through the introduction of immunotherapies and targeted therapies tailored to specific molecular characteristics (1). These therapies include options for patients with distinct tumor profiles, such as those exhibiting dMMR/MSI-H mutations or TMB-H. Importantly, some medicines now extend treatment options to patients regardless of their dMMR/MSI-H status, offering broader applicability. They have also moved from second-line to first-line treatment options (1). According to a European study into innovative medicines availability in Europe and the time to patient access, oncology products currently take the longest time to reimburse (48). In January 2024, 48 oncology products received central-marketing authorisation between 2019 and 2022 at EU level. The EU average rate of availability of these oncology products was, however, 52%, or 25 products. Spain's rate of availability, between the years of 2019-2022, was 60% or 29 oncology products as of January 2024 (48).

Low reimbursement rates and long wait times for novel cancer medicines. In Spain, the reimbursement rate for EMA-approved cancer medicines between 2019 and 2022 was 60% as of January 2024, down from 65% in 2019 and the lowest among major European countries (48-52). Additionally, Spain reports the longest time to reimbursement among these countries, averaging 725 days in 2024, a substantial increase from 450 days in 2020 (48-52). These negative trends suggest persistent barriers to timely access to innovative treatments, limiting patient benefit from advancements in cancer care.



Reimbursement rate (%) and time to reimbursement (days) of novel cancer medicines

Notes: EU-27: 27 European Union Member States, WAIT: Waiting to Access Innovative Therapies. Source: EFPIA WAIT Indicator Survey, 2024 (48-52).

Balancing national regulation with regional inequalities in healthcare access. The approval process for new medicines in Spain is complex, involving decisions at both the national and regional levels (53). The national authority, Agencia Española de Medicamentos y Productos Sanitarios (AEMPS), must approve the effective commercialization of any medicine, including regulating its pricing and public reimbursement, in addition to decisions made by the EMA. Once commercialization is approved, pharmaceutical companies can apply for public reimbursement. This decision is made by the Comisión Interministerial de Precios de los Medicamentos y Productos Sanitarios, a body under the Ministry of Health, based on specific criteria (53). However, medicine expenses are covered by the budgets of Spain's autonomous regions. In summary, while the national level sets drug pricing and reimbursement policies and incorporates approved pharmaceuticals into the portfolio of common services for the National Health System, the financial burden falls on the autonomous regions (16). Recent developments in oncology, such as precision medicine and advanced therapies, have introduced significant innovations but also financial challenges. The rising expenditure for new cancer treatments, alongside the development of existing drugs, put pressure on healthcare budgets, making sustainable integration into the system a key challenge (53).

The adoption of treatment advances in clinical practice. The SEOM has developed clinical practice guidelines for cancer care since 2010. However, a 2023 assessment identified weaknesses in these guidelines, especially in terms of: 1) clinical applicability, 2) inclusion of patients perspectives, and 3) methods for updating recommendations (54). A cross-sectional study revealed significant differences between national/international guidelines and actual clinical practices among Spanish gynecologic oncologists. These gaps are particularly evident in the management of mid-risk endometrial cancer cases and follow-up care, suggesting a need for better alignment between guidelines and day-to-day clinical decision-making (55). Non-adherence to clinical guidelines by

oncologists can lead to inconsistencies in patient care, delays in adopting effective therapies, and compromised patient outcomes, ultimately hindering patient access to advancements in endometrial cancer treatment.

Regional disparities in cancer care delivery and patient outcomes. Since 2000, Spain's autonomous regions have successfully reduced hospital stays for cancer patients, although the pace of reduction has varied across regions, reflecting differences in healthcare quality and infrastructure. For uterine cancer, the average length of stay in Spain was 5.7 days in 2021, lower than the EU average of 6.3 days (56). While specific regional data for uterine cancer is unavailable, notable variations are evident in other cancers. For example, the average length of stay for breast cancer was 6 days in Catalonia compared to just 3 days in Valencia (16). These disparities highlight regional differences in healthcare delivery and efficiency.

Limited access to palliative care. In 2018, treatment at the end of life or palliative care was performed by 206 specialized palliative care centers across Spain, corresponding to 0.6 centers per 100 000 inhabitants, and was below the EU average of 1.1 centers (16). In 2017, this scarce service resulted in that a total of only 40% of people who died with complex needs and in necessity of palliative care, did receive this service (16).

7 POLICY INITIATIVES

Endometrial cancer has traditionally received limited attention in global and national health policies compared to other women's cancers like breast and cervical cancer (1). While initiatives such as the WHO's Global Breast Cancer Initiative and the Cervical Cancer Elimination Initiative demonstrate the potential for ambitious, coordinated action (57, 58), no similar large-scale strategies exist for endometrial cancer. International efforts, such as the Uterine Cancer Awareness Month (June) and World Gynecologic Oncology Day (September 20), have recently begun to address this gap, focusing on raising awareness and improving care. However, significant disparities remain in prioritization, funding, and research, underscoring the need for dedicated initiatives to reduce incidence, improve survival, and enhance the quality of care for endometrial cancer patients. Despite being the 4th most common cancer form in women in Spain, it remains being a quite unknown cancer type in the Spanish society compared to other women cancers such as breast cancer or cervical cancer where screening programs and awareness has been worked on by the healthcare system (59).

Fragmented cancer data. Spain lacks a centralized registry for tracking cancer cases, treatments, and outcomes. The network of Spanish cancer registries (Redecan) covered in 2022 around 27% of the Spanish population (16). Redecan is considered being one of the main sources of cancer information systems in the country and under continuous progress by the initiatives of the participating regions (60). The population based regional cancer registries collect relevant data for their respective regions, that is later used for monitoring cancer care by the regional healthcare system. The distribution of regional registries and information systems across the country is nevertheless unequal, leading to uncertainty in the evaluation of policy efficiency and knowledge gap regarding disease development (16).

No policy initiatives targeting gynecologic cancers. The first version of the National Cancer Strategy of the National Health System (SNS) was approved in 2006, resulting from a collaborative effort involving the scientific community, patient associations, cancer care professionals, and representatives from all autonomous regions (16). In 2021, the SNS Cancer Strategy was updated to align with the Europe's Beating Cancer Plan (EBCP) (16, 61). The current strategy focuses on five key areas; health promotion and cancer prevention, health care, health care for children and adolescents, cancer data and information and research (61). It does not include specific initiatives targeting endometrial cancer or gynecological cancers in general, with the exception of cervical cancer through the screening initiative.

Lack of patient/advocacy groups for endometrial cancer. Despite being the 4th most common cancer form in Spain among women, patients with endometrial cancer are in general not having an equal strong representation as other patients with female cancers such as breast cancer and ovarian cancer. For ovarian cancer, the association ASACO (Asociación de afectados por cancer de Ovario) supports women across the country who suffered by this cancer and their relatives (62). Patients with breast cancer or hereditary genetic predisposition find representation in Asociación de Mama y Ovario Hereditario (AMOH), where a focus is in supporting research in cancer (63). The association Grupo Español de Pacientes con Cáncer (GEPAC), consisting of 132 member associations across Spain, and its division División de Cáncer de Mama y Ginecológico de Madrid (ASCAMA) is covering both breast cancer and gynecological cancers including endometrial cancer (64, 65), although its focus seems to be mostly on breast cancer. This study has not found patient or advocacy groups focusing solely on gynecological cancers covering endometrial cancer/uterine cancer.

Research investments in endometrial cancer. The Administración General del Estado (AGE) develops three-year plans to implement the Estrategia Española de Ciencia, Tecnología e Innovación (EECTI), a national strategy aimed at advancing science, technology, and innovation. These plans involve coordinated efforts across several ministries and public authorities to allocate funding and prioritize key areas. The current plan for 2024-2027 includes strategic focus areas such as personalized medicine—covering advanced therapies, immunotherapies, and genomics—and non-communicable diseases, including oncological diseases (66). However, no specific cancer type is mentioned as a priority (66). In September 2024, the Minister of Health announced that the government had allocated €839.2 million to cancer research and innovation since 2018, describing the investment as unprecedented (67). Despite this, public funding specifically for research on uterine cancer between 2007 and 2017 amounted to only €6 million, a mere 0.8% of the total public financing for cancer research (68). This stark disparity is evident when considering that uterine cancer represents 4% of total cancer cases and 2% of cancer-related deaths but receives disproportionately low funding compared to more prevalent cancers such as lung, breast, and colorectal cancer. In general, gynecological cancers overall, receive limited research funding and

attention relative to their disease burden. This lack of investment is further evident in the limited number of clinical trials, with uterine cancer accounting for only 1% of the total, and research publications, where it represents 3%(68). Without targeted prioritization in national strategies, resources are likely to remain focused on more well-known or prevalent cancers, further perpetuating the research and funding gaps.

HIGH-LEVEL RECOMMENDATIONS

Integrate endometrial cancer into national and regional health strategies. Develop specific goals, initiatives, and funding mechanisms to address its growing disease burden. Ensuring alignment with national cancer plans while considering regional disparities in care delivery and access.

Enhance early detection and diagnostics. Raise awareness of symptoms and risk factors, and ensure equitable access to advanced diagnostic tools, including comprehensive biomarker testing to support timely and accurate diagnoses across all regions.

Ensure equitable and optimal care delivery. Improve gynecologic oncology training programs and reduce wait times for diagnostics and treatments. Introduce separate metrics to monitor wait times for cancer treatment, enabling better evaluation of cancer care efficiency. Address regional disparities in specialist availability and ensure the establishment of multidisciplinary teams and collaborative practices that prioritize patient-centered care.

Support advocacy and patient voices. Establish a national advocacy group for endometrial cancer – to raise awareness, shape research priorities, and ensure patient involvement in guiding care policies.

Expand research funding and collaboration. Allocate proportional research funding to endometrial cancer that reflects its disease burden. Foster collaboration across regions to drive innovation in prevention, diagnostics, and treatment.

REFERENCES

1. Manzano A, Hofmarcher T. Endometrial Cancer - Improving Care and Driving Policy Change. Lund, Sweden: IHE, 2024.
2. Arnold M, Pandeya N, Byrnes G, Renehan PAG, Stevens GA, Ezzati PM, et al. Global burden of cancer attributable to high body-mass index in 2012: a population-based study. Lancet Oncol. 2015;16(1):36-46.
3. Pearson-Stuttard J, Zhou B, Kontis V, Bentham J, Gunter MJ, Ezzati M. Worldwide burden of cancer attributable to diabetes and high body-mass index: a comparative risk assessment. Lancet Diabetes Endocrinol. 2018;6(6):e6-e15.
4. Sanchez Lorenzo L. Cáncer de endometrio-útero Sociedad Española de Oncología Médica 2023 [Nov 26, 2024]. Available from: https://seom.org/171-Informaci%C3%B3n%20al%20P%C3%BAblico%20-%20Patolog%C3%ADas/cancer-de-endometrio-utero.
5. Amenguala J, Montaño J, Franch P, Ramos M. Supervivencia por estadio del cáncer de cuello uterino en Mallorca y factores asociados recogidos por el Registro de Cáncer. Gac Sanit. 2020;34(6):589-94.
6. Frias-Gomez J, Peremiquel-Trillas P, Aleman L, Ameijide A, Marcos-Gragera R, Ponce J, et al. Predicting the rising incidence and mortality of endometrial cancers among women aged 65-74 years in Catalonia. Maturitas. 2021;Feb:144:11-15.
7. Ferlay J, Colombet M, Soerjomataram I, Dyba T, Randi G, Bettio M, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. Eur J Cancer. 2018;103:356-87.
8. Ferlay J, Parkin DM, Steliarova-Foucher E. Estimates of cancer incidence and mortality in Europe in 2008. Eur J Cancer. 2010;46(4):765-81.
9. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JW, Comber H, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer. 2013;49(6):1374-403.
10. European Cancer Information System (ECIS). Long-term incidence and mortality estimates up to 2040. [Accessed: Dec 5, 2024]. Available from: https://ecis.jrc.ec.europa.eu/en.
11. Sociedad Española de Oncología Médica (SEOM). Las cifras del cáncer en España 2024. 2024 [15 December, 2024]. Available from: https://seom.org/prensa/el-cancer-en-cifras.
12. Asociacion Española Contra el Cáncer (AECC). Dimensiones del cáncer. 2024 [Dec 10, 2024]. Available from: https://observatorio.contraelcancer.es/explora/dimensiones-del-cancer.
13. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008;371(9612):569-78.
14. World Health Organization. Prevalence of overweight among adults, BMI >= 25 (age-standardized estimate) (%). 2024 [Dec 13, 2024]. Available from: https://www.who.int/data/gho/data/indicators.
15. Ministerio de Sanidad. Informe Anual del Sistema Nacional de Salud 2023. 2023.
16. OECD. Country Cancer Profile 2023 Spain. 2023.
17. Fernández Marcos A, De Haro Gázquez D, Fernández Sánchez B, Diez Muñiz E, Puyol Escolar M, Yélamos Agua C, et al. Impacto del cáncer en España; Una aproximación a la inequidad y los determinantes sociales. Asociacion española contra el cáncer (AECC), 2022.
18. Hofmarcher T LP, Wilking N, Jonsson B. The cost of cancer in Europe 2018. . Eur J Cancer 2020;129:41-9.
19. OECD. Tackling the impact of cancer on health, the economy and society – Country notes: Spain. 2024 [28 November, 2024]. Available from: https://www.oecd.org/en/publications/tackling-the-impact-of-cancer-on-health-the-economy-and-society_40335421-en/spain_d1e3398d-en.html.
20. Andrade P, Sacristan JA, Dilla T. The Economic Burden of Cancer in Spain: A Literature Review. Health Econ Outcome Res Open Access. 2017;3(1).
21. Asociación española contra el cáncer (AECC). Oncobarómetro. 2021.
22. Tamayo-Fonseca N, Pereyra-Zamora P, Barona C, Mas R, Irles M, Nolasco A. Health literacy: association with socioeconomic determinants and the use of health services in Spain. Front Public Health. 2023;11:1226420.
23. Eurostat. Health personnel. [Dec 10, 2024]. Available from: https://ec.europa.eu/eurostat/databrowser/product/view/hlth_rs_prs2
24. Eurostat. Physicians by medical speciality historical data (1985-2016). [7 December, 2024]. Available from: https://ec.europa.eu/eurostat/databrowser/view/hlth_rs_spec/default/table?lang=en.
25. Ministerio de Sanidad GdE. Actualización: Informe de necesidad de médicos especialistas en España 2023-2035. 2024.
26. Sanz-Barbero B, Regidor E, Galindo S. Impact of geographic origin on gynecological cancer screening in Spain. Rev Saude Publica. 2011;45(6):1019-26.
27. Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marnitz S, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. Int J Gynecol Cancer. 2021;31(1):12-39.
28. Oaknin A, Bosse TJ, Creutzberg CL, Giornelli G, Harter P, Joly F, et al. Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2022;33(9):860-77.
29. Ministerio de Sanidad GdE. Las listas de espera quirúrgicas mejoran respecto a diciembre de 2023, pero siguen al alza en comparación con el año pasado. 2024.
30. Ministerio de Sanidad. Sistema de información sobre listas de espera en el sistema nacional de salud SISLE-SNS, Situación a 30 de Junio de 2024, Indicadores resumen. 2024.
31. Malone ER, Oliva M, Sabatini PJB, Stockley TL, Siu LL. Molecular profiling for precision cancer therapies. Genome Med. 2020;12(1):8.
32. IQN Path & European Cancer Patient Coalition (ECPC) & European Federation of Pharmaceutical Industries and Associations (EFPIA). Unlocking the potential of precision medicine in Europe. 2021.
33. Bayle A, Bonastre J, Chaltiel D, Latino N, Rouleau E, Peters S, et al. ESMO study on the availability and accessibility of biomolecular technologies in oncology in Europe. Ann Oncol. 2023;34(10):934-45.
34. Ministerio de Sanidad. El Gobierno distribuye a las comunidades autónomas 40 millones de euros para consolidar la medicina personalizada de precisión. 2022 [cited 13 March, 2025]. Available from: https://www.sanidad.gob.es/gabinete/notasPrensa.do?id=5926.
35. La Moncloa. Sanidad pone en marcha el catálogo común de pruebas genéticas. 2024.
36. Zhang J, Kelkar SS, Prabhu VS, Qiao Y, Grall V, Miles N, et al. Real-world treatment patterns and clinical outcomes from a retrospective chart review study of patients with recurrent or advanced endometrial cancer who progressed following prior systemic therapy in Europe. BMJ Open. 2024;14(4):e079447.
37. Garcia-Carbonero R, Gonzalez Astorga B, Vidal Tocino R, Contreras Toledo D, Pericay C, Fernandez Montes A, et al. Real-world study on microsatellite instability and mismatch repair deficiency testing patterns among patients with metastatic colorectal cancer in Spain. Clin Transl Oncol. 2024;26(4):864-71.
38. NCCN. Uterine Neoplasms (Version 2.2024, March 6, 2024). NCCN, 2024.
39. ESMO. EMA Recommends Additional Extensions of Indications for Pembrolizumab. 2024 [3 March, 2025]. Available from: https://www.esmo.org/oncology-news/ema-recommends-additional-extensions-of-indications-for-pembrolizumab.
40. ESMO. EMA Recommends Extension of Therapeutic Indications for Durvalumab to Patients with Primary Advanced or Recurrent Endometrial Cancer. 2024 [March 13, 2025]. Available from: https://www.esmo.org/oncology-news/ema-recommends-extension-of-therapeutic-indications-for-durvalumab-to-patients-with-primary-advanced-or-recurrent-endometrial-cancer.
41. Rivera F, Andres R, Felip E, Garcia-Campelo R, Lianes P, Llombart A, et al. Medical oncology future plan of the Spanish Society of Medical Oncology: challenges and future needs of the Spanish oncologists. Clin Transl Oncol. 2017;19(4):508-18.
42. Martinez D, Quilez-Cutillas A, Jimenez-Labaig P, Sesma A, Tarazona N, Pacheco-Barcia V, et al. Current professional standing of young medical oncologists in Spain: a nationwide survey by the Spanish Society of Medical Oncology + MIR section. Clin Transl Oncol. 2023;25(3):796-802.
43. Sociedad Española de Oncología Médica (SEOM). Informe: Situación laboral de los oncólogos médicos jóvenes en España, Octubre de 2022. SEOM: 2022.
44. Minig L, Padilla-Iserte P, Zorrero C. The Relevance of Gynecologic Oncologists to Provide High-Quality of Care to Women with Gynecological Cancer. Front Oncol. 2016;5:308.
45. Chan JK, Sherman AE, Kapp DS, Zhang R, Osann KE, Maxwell L, et al. Influence of gynecologic oncologists on the survival of patients with endometrial cancer. J Clin Oncol. 2011;29(7):832-8.
46. Consejo Nacional de Especialidades en Ciencias de la Salud. Boletín Oficial del Estado, Núm. 129, 8882; Orden SAS/1350/2009, de 6 de mayo, por la que se aprueba y publica el programa formativo de la especialidad de Obstetricia y Ginecología. 2009.
47. Padilla-Iserte P, Minig L, Zapardiel I, Chiva L, Laky R, de Santiago J. Current situation in gynecological oncology training in Spain: where we are and where we want to go. Clin Transl Oncol. 2018;20(4):517-23.
48. European Federation of Pharmaceutical Industries and Associations (EFPIA). EFPIA Patients W.A.I.T. Indicator 2023 Survey. 2024.
49. European Federation of Pharmaceutical Industries and Associations (EFPIA). EFPIA Patients W.A.I.T. Indicator 2019 Survey. 2020.
50. European Federation of Pharmaceutical Industries and Associations (EFPIA). EFPIA Patients W.A.I.T. Indicator 2020 Survey. 2021.
51. European Federation of Pharmaceutical Industries and Associations (EFPIA). EFPIA Patients W.A.I.T. Indicator 2021 Survey. 2022.
52. European Federation of Pharmaceutical Industries and Associations (EFPIA). EFPIA Patients W.A.I.T. Indicator 2022 Survey. 2023.
53. Bernal-Delgado E, Angulo-Pueyo E, Ridao-López M, Urbanos-Garrido RM, Oliva-Moreno J, García-Abiétar D, et al. Spain: health system review 2024. 2024.
54. Santero M, de Mas J, Rifa B, Clavero I, Rexach I, Bonfill Cosp X. Assessing the methodological strengths and limitations of the Spanish Society of Medical Oncology (SEOM) guidelines: a critical appraisal using AGREE II and AGREE-REX tool. Clin Transl Oncol. 2024;26(1):85-97.
55. Zapardiel I, Blancafort C, Cibula D, Jaunarena I, Gorostidi M, Gil-Moreno A, et al. Utility and Actual Use of European and Spanish Guidelines on the Management of Endometrial Cancer Among Gynecologic Oncologists in Spain. Int J Gynecol Cancer. 2017;27(6):1293-7.
56. Eurostat. In-patient average length of stay (days) [Dec 18, 2024]. Available from: https://ec.europa.eu/eurostat/databrowser/view/hlth_co_inpst__custom_14748335/default/table?lang=en.

57. World Health Organization. Call for Innovation in women's cancers. [Nov 27, 2024]. Available from: https://www.who.int/news/item/15-06-2021-call-for-innovation-in-women-s-cancers.
58. World Health Organization. Global strategy to accelerate the elimination of cervical cancer as a public health problem. 2020. Available from: https://www.who.int/publications/i/item/9789240014107.
59. Corisco M. Endometrio, un cáncer cada vez más común del que apenas se habla. 2024 [17 December, 2024]. Available from: https://elpais.com/sociedad/transformar-hoy-el-manana/2024-09-17/endometrio-un-cancer-cada-vez-mas-comun-del-que-apenas-se-habla.html.
60. Red Española de Registros de Cáncer (REDECAN). ¿Cómo funcionamos? REDECAN2024 [9 December, 2024]. Available from: https://redecan.org/es/como-funcionamos.
61. Ministry of Health. Cancer Strategy of the National Health System (SNS). 2021.
62. Asociacion de Afectados por Cáncer de Ovario (ASACO). La asociación. 2024 [16 December, 2024]. Available from: https://www.asociacionasaco.es/asociacion/carta-de-la-presidenta/.
63. Asociacion Mama Ovario Hereditario (AMOH). Por qué AMOH. 2024 [16 December, 2024]. Available from: https://amohasociacion.org/quienes-somos/.
64. Grupo Español de Pacientes con Cáncer (GEPAC). Somos GEPAC. 2024 [09 December, 2024]. Available from: https://www.gepac.es/nuestras-asociaciones/.
65. Division de Cancer de Mama y Ginecologico de Madrid (ASCAMA). ¿Qué es ASCAMA? [9 December, 2024]. Available from: http://ascama.org/.
66. Ministerio de Ciencia IyU. PEICTI; Plan Estatal de Investigación Científica, Técnica y de Innovación 2024-2027. Ministerio de Ciencia, Innovación y Universidades (MICIU): 2024.
67. MInisterio de Ciencia IyU. Morant: "El Gobierno ha destinado en los últimos 6 años cerca de 840 millones de euros a proyectos de investigación contra el cáncer, la gran esperanza contra esta enfermedad". https://www.ciencia.gob.es/Noticias/2024/Septiembre/investigacion-contra-cancer.html2024-09-24.
68. Asociacion española contra el cancer (AECC), Asociación Española de Investigación sobre el Cáncer (ASEICA). Comprometidos con la investigación en cáncer, primer informe sobre la investigación e innovación en cáncer en España, 2018. 2018.