

Current perspectives on endometrial cancer in Portugal: prevention, diagnosis, clinical management, challenges and opportunities

Perspetivas atuais sobre o cancro do endométrio em Portugal: prevenção, diagnóstico, gestão clínica, desafios e oportunidades

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Abstract

Endometrial cancer (EC) is one of the most common gynecological malignancies, with a rising global incidence driven by increasing obesity rates and aging populations. This growing burden highlights the need for enhanced prevention strategies, early detection, and equitable access to innovative treatments. This paper presents an expert-driven perspective on the current state of EC care in Portugal, addressing epidemiology, risk factors, diagnostic pathways, therapeutic innovations, and health policy challenges. Based on expert panel discussions and a structured questionnaire, key barriers were identified, including diagnostic delays, limited integration of molecular profiling, and unequal access to emerging therapies such as immunotherapy. Despite high adherence to National and European clinical guidelines, disparities in treatment access persist due to regulatory and financial constraints. Public health strategies targeting risk reduction, timely and enhanced diagnostic pathways, and expansion of treatment availability are needed. Experts emphasized the critical need for hospitals to adopt molecular classification, given its key role in guiding decisions on adjuvant treatment. In addition, the limited availability of certain emerging tests was noted as a challenge to the broader adoption of precision oncology. By bridging gaps in prevention, diagnosis, and treatment, this paper aims to support healthcare professionals, researchers, and policymakers in optimizing EC care and improving patient outcomes in Portugal.

Keywords: Endometrial cancer. Diagnosis. Treatment. Immunotherapy. Molecular profiling. Portugal. Public health. Personalized medicine.

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Introduction

Endometrial cancer (EC) was the second most common gynecological cancer in Portugal, with an age-standardized incidence of 8.9/100.000 and a mortality of 3 deaths/100.000 in 2022.^{1,2} The global increase in EC of over 130% in three decades is mirrored at the national level and is primarily driven by aging, obesity, and metabolic disorders.³⁻⁶

EC typically affects postmenopausal women, with peak incidence occurring between the ages of 65 and 75. It is often diagnosed at an early stage, leading to a favorable prognosis, with a 5-year survival rate exceeding 95%. However, up to 20% of endometrioid and 50% of non-endometrioid carcinomas ultimately experience recurrence.⁷ High-grade and serous subtypes are associated with a poorer prognosis, often presenting with aggressive behavior and a higher risk of recurrence.⁸⁻¹¹

Surgery remains the first-line treatment for early-stage EC. For advanced or recurrent cases, systemic chemotherapy, usually involving carboplatin and a taxane, has traditionally been the standard of care.¹² Management of advanced and recurrent EC is still a challenge, and several questions remain unanswered.⁷

In recent years, significant advances have been made in the diagnostic and therapeutic armamentarium for EC,⁷ including immunotherapy and targeted treatments guided by molecular profiling, which are increasingly integrated into clinical practice. In particular, the incorporation of molecular markers such as microsatellite instability (MSI), mismatch repair deficiency (dMMR), POLE mutations, and p53 expression into risk stratification has enabled more personalized treatment decisions, improving the precision of therapeutic approaches. Molecular profiling also plays a key role in guiding adjuvant treatment decisions, with significant implications for both survival outcomes and treatment-related toxicity.

Several guidelines for the management of EC, including the European Society of Gynaecological Oncology (ESGO)/European Society for Radiotherapy and Oncology (ESTRO)/European Society of Pathology/ (ESP), the European Society for Medical Oncology (ESMO), and the National Comprehensive Cancer Network (NCCN), have been developed and are constantly updated.^{8,10,13} In Portugal, the Portuguese Society of Gynecology has a national consensus for the clinical approach to gynecological cancers,¹⁴ Despite this, full adherence to recommendations is not always feasible across different resource settings and geographies,

resulting in variability in clinical practice and care delivery.^{11,15-17}

Portugal has kept pace with international advances in the treatment of EC, providing patients with access to new therapies and surgical techniques.¹⁸ The most recent Portuguese Gynecologic Oncology Consensus, which includes recommendations for EC, was published in 2020 by experts from national medical societies. An update is anticipated following the publication of the latest 2025 ESGO/ESTRO/ESP guidelines. However, despite these advances, there is still a lack of information on the current state of EC treatment in Portugal, particularly regarding access to innovative therapies, success rates, and the implementation of international guidelines. This makes it difficult to accurately assess the country's progress compared to other healthcare systems.

Through an expert panel, we aimed to provide a comprehensive overview of the current EC landscape in Portugal, focusing on prevention, diagnosis, clinical management, and access to innovative therapies within the healthcare system. This collaborative effort also aimed to emphasize key challenges and opportunities for healthcare professionals, researchers, and policy-makers to implement effective strategies and improve patient outcomes.

Methodology

Expert panel

To gain in-depth insights into the EC landscape in Portugal, a panel of medical experts was organized by the Institute for Evidence-Based Health. This panel comprised six esteemed specialists in medical oncology selected by their extensive clinical and research experience in the management of EC, from Portuguese reference centers located in Lisbon, Coimbra, and Porto.

A first online expert meeting was held in September 2024 to gather expert opinions on the most relevant topics related to EC, including epidemiology trends, risk factors, prevention, screening, diagnosis, patient management, treatment, innovation, access, health policies, and myths. Following this, each expert independently and anonymously completed an electronic survey with 80 questions covering these topics during November 2024. The responses were analyzed and summarized. A second meeting was held in December 2024 to present the main results obtained from the survey and

obtain further information, promoting discussions between experts on less consensual topics.

Ethical considerations

Before the expert panel, all participants were informed of its nature and purpose. Ethical considerations were upheld throughout the entire process, ensuring that participants' contributions were voluntary.

Results

Epidemiology

The expert panel reached a consensus that EC incidence is rising in Portugal, primarily due to increasingly unhealthy lifestyles, including sedentary behavior and poor dietary habits, which contribute to obesity. An aging population was also identified as a driver, as EC primarily affects postmenopausal women. Although mortality is also perceived to be increasing, this trend is largely explained by the increasing number of diagnoses, which results in a greater absolute number of deaths. Despite this, survival rates have improved due to advancements in treatment, allowing a greater proportion of patients to live longer.

Risk factors

Regarding EC risk factors, specialists consistently identified metabolic factors, particularly obesity, as paramount. Excess adipose tissue elevates estrogen levels unopposed by progesterone, stimulating endometrial proliferation and increasing malignancy risk. They also noted that lower educational attainment and income levels are linked to a higher risk of obesity, further exacerbating this risk. Other risk factors include hormonal and reproductive factors such as early menarche, late menopause, nulliparity, delayed childbirth, and hormone replacement therapy with unopposed estrogen, as well as genetic predispositions, including Lynch syndrome, Cowden syndrome, and mutations in PTEN and p53.

Some experts noted that EC is increasingly being diagnosed in younger women, in line with global trends, likely reflecting earlier onset of obesity and metabolic syndrome, as well as changes in reproductive patterns. This trend raises concerns, as younger cases may be more likely to involve aggressive histological subtypes, such as serous and clear cell carcinomas, which are associated with poorer prognoses. In addition,

concerns were raised regarding the potential role of endocrine-disrupting chemicals, including bisphenol A, phthalates, and pesticides, which may mimic estrogenic activity. However, experts expressed differing views on the strength of the current evidence, emphasizing the need for further research in this area.

Other ongoing shifts in patient profile include increasing multimorbidity, a growing number of cases with prior breast cancer (often with tamoxifen exposure), and a higher number of patients presenting with advanced disease.

Looking ahead, specialists anticipate that EC incidence will keep rising, mainly due to obesity and population aging. Some expect an increase in early-stage diagnoses due to improved awareness and timelier diagnostic pathways.

Prevention

Overall, the panel observed that Portugal lacks public health campaigns specifically targeting EC risk factors, despite existing initiatives for other cancers and cardiovascular diseases that address some shared risks. In addition, there is uncertainty regarding their effectiveness, as these campaigns are often not sufficiently engaging, and their impact remains largely unmeasured. In their opinion, effective campaigns need to be transversal across all social media platforms, appealing, well-structured, and interactive, with support from associations of patients, healthcare professionals, health institutions, and medical influencers. Furthermore, campaigns should be implemented at schools and should be continuous over time rather than sporadic.

Screening

There was a consensus that routine screening for EC is not recommended for the general population, reflecting the absence of a cost-effective test for asymptomatic women.^{8,13,19} Screening should be targeted at high-risk individuals, particularly those with a family history of Lynch syndrome (the highest-risk group) or a previous diagnosis of Lynch-associated colorectal cancer. In hereditary syndromes, prophylactic surgery may be recommended to significantly lower the risk of developing EC. Nevertheless, some experts identify a gap in the systematic referral of these patients to genetic counseling. Addressing this gap could enhance early detection and prevention strategies for these high-risk populations.

Experts stressed the importance of vigilant assessment of postmenopausal bleeding, as it is a common early symptom of EC. Public awareness campaigns have been shown to enhance knowledge of symptoms and risk factors, leading to increased medical consultations and potentially earlier diagnoses. For optimal impact, these campaigns should be meticulously designed and culturally tailored, forming a multifaceted strategy that includes public education, guaranteed access to healthcare services (including imaging and biopsy when indicated), evidence-based screening, and active engagement of healthcare providers.²⁰⁻²²

Diagnosis

Limited awareness of postmenopausal bleeding as a warning sign and unequal access to healthcare, particularly in certain regions, were highlighted as barriers to early diagnosis. Several experts stressed that lower socioeconomic status increases the risk of late-stage diagnosis due to lower health literacy and reduced healthcare access.

According to experts, the Portuguese National Gynecology Cancer Consensus, along with ESGO, ESMO, and NCCN guidelines, are followed in the diagnosis of more than 90% of the cases.

Although gynecology is typically the first specialty to diagnose EC, patients' pathway often begins in the emergency room due to abnormal uterine bleeding, rather than through primary care. Time from the onset of initial symptoms to EC diagnosis may range between 1 and 4 months.

In advanced disease, experts point out that computed tomography or positron emission tomography scans are used to evaluate potential metastases. However, delays in scheduling imaging and receiving pathology results are frequently cited as bottlenecks in the diagnosis. These waiting periods, combined with the limited capacity of some primary care settings, contribute to the overall time gap between first suspicion and EC diagnosis.

Experts expressed being satisfied with the diagnostic quality, but highlighted the need for more timely access to diagnostic exams. A key suggestion is to develop "fast-track pathways" with enforced maximum waiting times and to centralize care in reference centers. Experts also underscore the uneven distribution of diagnostic tools between urban and rural areas, noting resource constraints that can delay hysteroscopic biopsy and imaging.

To improve outcomes, they stressed that raising public health literacy and encouraging earlier evaluation of postmenopausal bleeding are essential measures. Although transvaginal ultrasound, hysteroscopy, and endometrial biopsy remain standard, additional molecular profiling is a point of debate. Some clinicians support universal testing to guide personalized therapy, while others question its immediate benefits and feasibility.

Current treatment and access to medication

Clinical practice in Portugal closely follows national and European recommendations and also integrates the American NCCN guidelines. At the time of the panel, some experts noted that current protocols fall short in certain scenarios, specifically (a) when standard therapies have been exhausted or (b) in the management of advanced disease, including decisions around neoadjuvant systemic therapy, the integration of immunotherapy, and the use of locoregional treatments based on individual response.

In Portugal, the interval from diagnosis to treatment may span between 1 and 4 months, influenced by molecular testing, histopathology, accurate imaging staging, and operating room availability. Experts mentioned that 80-90% of cases undergo proper surgical staging and all are managed by multidisciplinary teams. The panel agreed that surgery is the first-line treatment for early-stage EC, with minimally invasive techniques such as laparoscopy, use of sentinel lymph node staging, or robotic surgery becoming more prevalent. Experts noted some variability in treatment approaches for advanced or recurrent EC. All practitioners adhere to consensus guidelines for chemotherapy and/or radiotherapy, and advocate for a broader therapeutic approach in selected cases, including the use of chemo-immunotherapy or target therapies.

Advanced or metastatic disease typically involves two or three therapy lines, with several experts observing increases in palliative hormonal therapy, chemo-immunotherapy combinations, or targeted agents such as anti-human epidermal growth factor receptor 2 (HER2). According to expert opinion, around 90% of patients with locally advanced disease and 10% with metastatic disease undergo locoregional therapy with curative intent. Approximately 20-30% of patients with advanced disease are eligible for targeted therapies upon confirmation of molecular alterations. However, many may remain untreated due to barriers such as reimbursement challenges, logistical constraints, and

socioeconomic factors. Financial and administrative hurdles hindered access to novel treatments, with some experts noting that Hospital Pharmacy and Therapeutics Committees could be overly restrictive, demanding that patients match trial inclusion criteria exactly to access new therapies.

Some experts highlighted that distributing clinical trials more evenly across Portugal would reduce geographic disparities and speed patient enrolment in novel therapeutic options. The German model was referred to, where European Medicines Agency (EMA)-approved drugs were used. At the same time, reimbursement was finalized, while several underscored the uneven distribution of clinical research across the country. Despite the limited use of targeted therapies, significant benefits have been observed in terms of quality of life and overall survival. This gap between scientific evidence and access in real-life underscores the need for policy-level interventions to make these life-prolonging treatments more widely available.

The management of recurrent disease poses additional challenges, including the need to rely solely on chemotherapy in patients with microsatellite instability-high (MSI-H)/dMMR disease, despite strong evidence that this subgroup derives greater benefit from immunotherapy; limited access to clinical trials; and insufficient scientific evidence to guide treatment decisions after exhaustion of standard therapeutic options. Additional challenges include low health literacy regarding palliative care, difficulties in care coordination, and barriers to the early integration of palliative care following recurrence diagnosis. Experts also noted structural constraints, particularly limited consultation time, which hampers adequate support for patients and their caregivers.

From their experience, there is a growing trend in patients using complementary or alternative therapies.

Most experts confirmed some disparities in drug access across Portuguese centers, particularly for immunotherapy, due to heterogeneity in the treatment eligibility decisions by Ethics Committees or Hospital Pharmacy and Therapeutics Committees, prolonged national approval procedures, and fragmentation within the healthcare system, leading to inconsistent care pathways. Experts recommended centralized decision committees or expedited approval pathways to align with EMA decisions and broaden patient access more equitably.

Experts identified a lack of sharing best practices among healthcare centers treating EC patients.

Development and innovation

Regarding biomarkers, experts identified the most promising advances in the EC as the integration of molecular classification into clinical practice, including the assessment of POLE mutations, p53 status, and MMR/MSI deficiency in guiding adjuvant treatment decisions, allowing treatment de-intensification in patients with POLE-mutated tumors, which are associated with an excellent prognosis, while guiding more aggressive strategies in p53-aberrant tumors linked to poorer outcomes. The identification of dMMR/MSI-H also has significant predictive value, enabling the selection of patients most likely to benefit from immunotherapy. Additional biomarkers, such as HER2 overexpression in serous or high-grade carcinomas, alterations in the PI3K/AKT/mTOR pathway (e.g., PTEN and PIK3CA), and hormone receptor expression, further support a more targeted approach, particularly in advanced or recurrent disease. In parallel, the development of integrated genomic and molecular profiles has refined risk assessment, helping to avoid overtreatment in patients with favorable prognostic features while supporting closer surveillance and more intensive treatment in higher-risk subgroups. Finally, experts mentioned that minimally invasive biomarkers, including circulating microRNAs (blood), circulating tumor DNA, and biomarkers in urine samples, represent significant emerging tools, although they remain largely under investigation.

Another potential advancement in biomarker research is the ongoing investigation into homologous recombination deficiency (HRD) in EC, which aims to determine its prevalence, predictive value, and utility as a biomarker to guide treatment strategies.

Regarding advances in personalized medicine, experts mentioned (a) immunotherapy as a major step forward for advanced, metastatic, or recurrent disease, as it has shown significant improvements in progression-free survival, (b) the use of next-generation sequencing test, for heavily pretreated patients with no remaining therapeutic options, to identify genomic alterations predictive of treatment response (it is important to ensure access through referral to clinical trials or off-label treatment administration), (c) the use of clinical data combined with genomic data to predict treatment responses and patient outcomes, (d) the use of drugs targeting specific molecular pathways, such as PI3K inhibitors for treating specific subtypes of EC, (e) the use of immunotherapy with chemotherapy, and (f) the

identification of patients with HRD and HER2 in therapeutic decisions.

Notably, only one of the six represented centers is currently participating in clinical trials related to gynecological cancers. However, experts agreed that broader enrollment would be key to driving further innovation.

Health policies and health literacy

There was a consensus that significant policy reforms are essential to enhance prevention, early detection, treatment, and outcomes in Portugal. Experts believe that public health campaigns addressing both EC and its risk factors, such as obesity, are vital. They also emphasized the importance of supporting expert groups to develop and issue recommendations. Earlier access to innovative treatments and a strengthened network of centers for diagnosis and care should also be prioritized. Some experts emphasized that complex or high-risk cases should be managed in specialized centers by gynecologic oncology teams, citing evidence that high-volume centers achieved better outcomes. However, others argued that with proper training and networking, regional hospitals could provide adequate care without overburdening tertiary centers. In their opinion, treatment decisions should be made by multidisciplinary teams at highly experienced centers.

They also recognized the need to balance the cost-benefit of innovative treatments and genetic testing in a context of limited resources, and they stated that prevention should remain a priority to reduce the number of patients requiring advanced therapies. They discussed the value of evaluating the entire patient journey, including the avoidance of unnecessary adjuvant therapies, and the potential long-term savings from referring families for genetic consultation when syndromes such as Lynch were identified. They added that any new approach for cost-effectiveness should include evidence-based prioritization, price negotiation, continuous monitoring of treatments, and equitable access without discrimination between public institutions.

Experts emphasized the crucial need to enhance awareness and health literacy about this disease, as misconceptions persist, particularly regarding postmenopausal bleeding, which is often mistakenly dismissed as benign. This unawareness and the mistaken belief that EC only affects women after menopause delay diagnosis and compromise clinical outcomes.

They also acknowledged other myths, such as the assumption that removing the uterus would eliminate

the need for further treatment or that endometriosis automatically constituted a direct risk factor for EC, and reiterated that these misunderstandings underscored the ongoing need for education, prevention, and research to support both patients and healthcare professionals alike.

Discussion

According to the Global Cancer Observatory, Portugal registered around 1400 new EC cases and 440 related deaths in 2022. Recent data confirmed the consistent rise in EC incidence worldwide, and Portugal is expected to follow this global trend. An aging population and escalating obesity rate appear to be drivers. Despite relatively high early-stage survival rates, advanced or recurrent cases still pose therapeutic challenges, especially given limited access to novel therapies.

By collecting the feedback and clinical experience of experts in EC, this panel allowed for a better understanding of the current EC landscape, challenges, and opportunities in Portugal. This panel is representative of the main centers treating EC in Portugal, acknowledging that while most cases are managed in these centers, peripheral units also provide treatment, albeit at lower volumes. It is foreseen that centers here represented treat at least 50% of the patients with EC in more advanced stages, which are treated by specialists in Portugal.

The Portuguese context reveals persistent challenges in early diagnosis, optimal disease management, and access to innovative treatments.

One of the key challenges is delayed diagnosis, with a typical interval of 1-4 months between symptom onset and histological confirmation. This gap is consistent with findings from other European countries contributing to poorer prognosis. Experiences from other countries show that public awareness campaigns and fast-track referral pathways can reduce the diagnostic interval.²² National strategies, including dedicated patient education and referral guidelines, could reduce the rate of late-stage disease and mortality. Furthermore, liquid biopsies may represent a promising minimally invasive tool for earlier detection in the future.

Public health interventions targeting obesity and sedentary lifestyles could have a major impact on primary prevention, given that an estimated 60% of EC cases in Europe are linked to overweight and obesity.⁵ Evidence suggests that weight loss interventions and hormonal contraceptives can significantly reduce EC risk.^{23,24} As with other gynecological cancers, an

effective approach should integrate education, widespread lifestyle modification programs, accessible screening for high-risk groups, and structured referral protocols. Currently, there is no comprehensive national strategy for EC in Portugal, unlike those in place for breast or cervical cancers, underscoring the urgent need for a dedicated plan to strengthen prevention, early detection, and equitable access to treatments.

According to the panel, approximately 80-90% of EC cases undergo appropriate surgical staging, and all EC patients are managed within multidisciplinary teams. While this reflects good adherence to recommended standards of care, ensuring consistent and comprehensive staging remains essential given its prognostic and therapeutic implications. Treatment pathways in Portugal largely follow European and national guidelines, complemented by the NCCN recommendations. Nevertheless, challenges arise in the management of advanced-stage disease and molecular subtypes with limited targeted therapies. In locally advanced disease, the high reliance on locoregional therapies, with curative intent in around 90% of patients, contrasts with the limited use of targeted therapies in metastatic settings. Research indicates that biomarkers such as POLE, MSI, and MMR status can refine prognosis and guide adjuvant therapy decisions,^{8,10} suggesting that biomarker-driven treatment strategies should be fully integrated into routine clinical practice.

The introduction of immunotherapy has shown significant efficacy in clinical trials and is becoming the standard of care. In Portugal, immunotherapy is currently used; however, its access remains a challenge. In October 2024, the Portuguese National Authority of Medicines and Health Products authorized the use of dostarlimab in the treatment of patients with recurrent or advanced EC exhibiting dMMR, who have progressed following prior platinum-containing chemotherapy. There are currently three early access programs ongoing in Portugal for advanced or recurrent EC, including dostarlimab, pembrolizumab, and durvalumab. However, access to innovation in Portugal often lags due to slower drug approval processes and potential funding constraints, which delay timely patient access to these therapies.

Overall, while Portugal adheres to evidence-based practices in EC management, there remains a pressing need to reduce diagnostic delays, expand access to innovative treatments, and raise public awareness of EC risk factors. Integrating molecular profiling into standard care and ensuring equitable access to novel

therapies should be prioritized to optimize patients' outcomes.

Table 1 summarizes the strengths of EC healthcare in Portugal, and table 2 describes challenges and opportunities in this area.

Implementing effective measures fast will help Portugal stay aligned with evolving international standards and more effectively address the needs of patients with EC.

Therefore, several recommendations can significantly reduce the future EC burden, including:

- Early detection and diagnosis
 - Implement targeted screening strategies for high-risk individuals, particularly those with Lynch syndrome
 - Analyze molecular profiles to identify genetic predispositions to hereditary syndromes, thereby enabling the detection of at-risk family members and guiding the implementation of prophylactic surgeries to reduce the risk of EC development
 - Reduce diagnostic delays by streamlining referral pathways from primary to specialized care.
- Treatment and therapeutic innovation
 - Increase access to molecular profiling to support personalized treatment decisions
 - Expand the availability of immunotherapy and targeted treatments through centralized drug approval pathways
 - Enhance multidisciplinary collaboration to standardize treatment across healthcare centers.
- Public health interventions
 - Develop and implement national awareness campaigns on EC risk factors and early symptoms
 - Promote lifestyle interventions aimed at obesity reduction and metabolic health improvement
 - Encourage gynecological health literacy to improve early medical consultations for abnormal uterine bleeding.
- Healthcare policy and system improvements
 - Establish reference centers for EC treatment to ensure standardized, high-quality care
 - Advocate for fast-track approval processes for innovative treatments
 - Strengthen research investment in EC to improve evidence-based guidelines implementation and optimal treatment.

Table 1. Strengths of EC healthcare in Portugal

Area	Strengths
Diagnosis and disease management	High adherence to national and European guidelines: implementation in 90-100% of patients.
	Use of imaging for staging: CT or PET scans are used to evaluate potential metastases in advanced disease.
	Effective multidisciplinary approach: 80-90% undergo proper surgical staging, and 100% are managed by multidisciplinary teams.
Treatment	Advanced surgical techniques: minimally invasive techniques such as laparoscopy surgery are widely used.
	Consensus guidelines are widely followed.
	High curative intent for locally advanced disease: 90% of patients with locally advanced disease receive locoregional therapy with curative intent.
Technological strengths	Integration of molecular profiling: molecular classification (POLE, p53, MMR) in guiding personalized therapy.
	Immunotherapy as a major advancement: immunotherapy has significantly improved progression-free survival in advanced cases.

MMR: mismatch repair, CT: computed tomography; PET: positron emission tomography; EC: endometrial cancer.

Table 2. Challenges and opportunities for EC healthcare in Portugal

Area	Challenges
Epidemiology and preventions	Rising EC incidence due to lifestyle and aging: incidence of EC is increasing in Portugal due to widespread obesity, metabolic syndrome, and changes in reproductive patterns. In addition, an aging population contributes to a higher burden of disease.
	Increasing mortality due to late-stage diagnosis: late-stage diagnosis remains a major issue, driven by a lack of awareness regarding early symptoms, particularly postmenopausal bleeding, and unequal access to healthcare. Socioeconomic disparities further exacerbate this problem.
	Increasing incidence in younger women: there is a growing trend of EC diagnoses in younger women, which is likely linked to the earlier onset of obesity and metabolic syndrome. This shift is concerning because younger patients often present with more aggressive disease subtypes.
	Endocrine-disrupting chemicals EDCs as a potential risk factor: the potential role of EDCs (such as BPA and phthalates) in increasing EC risk remains uncertain, highlighting the need for further research to understand their impact.
	Socioeconomic disparities in EC prevention: lower education and income levels reduce access to preventive care and early diagnosis, increasing the likelihood of late-stage presentation and poorer outcomes.
	Lack of public health campaigns: few public health initiatives specifically target EC risk factors, resulting in a missed opportunity to raise awareness and encourage preventive behaviors.
	Lack of systematic referral for genetic counseling: there is an absence of systematic referrals for genetic counseling, particularly for hereditary cancer syndromes such as Lynch syndrome, which could improve prophylactic and preventive care.
Diagnosis	Diagnostic delays: long waiting times for imaging and pathology results cause significant delays in EC diagnosis, prolonging the time from first suspicion to histological confirmation.
	Uneven access to diagnostic tools. Healthcare resource disparities between urban and rural areas result in unequal access to essential diagnostic procedures, causing delays in biopsy and imaging.
	Limited capacity in primary care settings: The shortage of resources in primary care settings leads to longer diagnostic intervals, affecting early detection and timely treatment.
Treatment	Limited access to innovative therapies: financial and administrative barriers currently prevent many patients from accessing EMA-approved novel treatments, restricting treatment options.
	Delays from diagnosis to treatment: the time from diagnosis to treatment initiation is prolonged due to delays in molecular testing, imaging, and surgical scheduling.

(Continues)

Table 2. Challenges and opportunities for EC healthcare in Portugal (*continued*)

	Unequal access to palliative care: there are significant gaps in palliative care services, including inadequate inpatient and outpatient capacity, which affects the management of advanced disease.
Innovation	Lack of routine biomarker testing, which may limit the ability to tailor treatments based on genetic profiles.
Health policy	Regional disparities in healthcare resources: differences in healthcare infrastructure result in uneven access to diagnostic and treatment services, particularly between urban and rural areas.
	Need for stronger networks of diagnosis and treatment centers: high-risk cases would benefit from specialized centers, but current networks remain inadequate to ensure optimal care.
Prevention	Improved awareness and literacy: public awareness campaigns should be implemented to educate the population about risk factors, early symptoms, and the importance of timely medical evaluation, particularly for high-risk groups.
Screening	High-risk group screening potential: targeted screening strategies for high-risk groups, such as Lynch syndrome carriers, to improve early detection and reduce mortality rates.
Diagnosis	Fast-track pathways: implementing fast-track pathways with enforced waiting time limits could reduce diagnostic delays and improve patient outcomes.
Treatment	Expansion of clinical trial participation: increasing participation in clinical trials across Portugal could provide more patients with access to cutting-edge therapies and reduce regional disparities.
Innovation	Molecular profiling and genomics: advances in molecular profiling and genomic medicine offer opportunities for personalized treatments that improve patient outcomes.
Health policy	Centralized approval pathways for new treatments: streamlining approval processes and aligning with EMA recommendations could facilitate broader and faster access to new treatments.
Health literacy	Education campaigns to enhance awareness: well-designed public awareness campaigns could encourage early medical consultations and improve EC outcomes.

EC: endometrial cancer; EMA: European medicines agency; BPA: bisphenol A; EDC: endocrine-disrupting chemicals.

Conclusion

The incidence and mortality of EC are increasing in Portugal, in line with global trends. Although national and European guidelines are in place, significant challenges remain, particularly in early diagnosis, equitable access to treatment, and public awareness. There is an urgent need for robust public health initiatives, streamlined diagnostic pathways, increased participation in clinical trials, and expanded access to innovative therapies. Addressing these gaps through well-structured policies and reforms in clinical practice is essential to improving patient outcomes and reducing the overall burden of the disease in Portugal.

Authors' contributions

All authors provided substantial contributions to the conceptualization, design, and methodology of the study. J. Pedro-Aguiar and Catarina Pestana-Silva were involved in collecting and analyzing information from questionnaires. All authors substantially contributed to critically reviewing the manuscript for important intellectual content. All authors read and approved the

final version of the manuscript. All authors agreed to be accountable for the work in ensuring that questions related to the integrity of any part of the work are appropriately investigated and resolved.

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Conflicts of interest

J. Rodrigues has participated in advisory boards or acted as a consultant for GSK. A.R. Lopes, D. Pessoa, M. Magalhães, and R. Teixeira de Sousa established a financial contract with GlaxoSmithKline Portugal to participate in the project. J.P. Aguiar, C. Pestana-Silva, and A. Vaz-Carneiro are employees of ISBE, which established a financial contract with GlaxoSmithKline Portugal.

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Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

Data availability

Data are not publicly available due to the confidentiality agreement with experts.

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