Endo Compass

Research roadmap for better hormone health

The EndoCompass Research Roadmap

Policy priorities for better hormone health in Europe

Addressing the endocrine causes and consequences of cancer

Why this matters for Europe:

- Hormones matter at every stage of life, from early development to older age.
- Some of Europe's most costly health challenges are linked to endocrine disruption, such as diabetes, obesity, thyroid disease, cancer, osteoporosis and infertility, and more than 440 rare endocrine diseases.
- Most Europeans will be affected by an endocrine-related condition in their lifetime, weakening our capacity to live, work and age well.
- Endocrine science is an investment in Europe's future.

ESPE European Society for Paediatric Endocrinology

European Society of Endocrinology

This document is an excerpt from *The EndoCompass Research Roadmap – Policy Priorities for Better Hormone Health in Europe*. For more information, please contact the European Society of Endocrinology at info@ese-hormones.org or the European Society for Paediatric Endocrinology at secretariat@eurospe.org

Addressing the endocrine causes and consequences of cancer

Why this matters

Cancer is one of Europe's most urgent health challenges. Each year, more than 3.7 million people are diagnosed with cancer and almost 2 million die from the disease, making it the second leading cause of death and morbidity in the region.[16] Beyond the personal cost, cancer places a heavy and growing burden on health systems and economies. Total societal costs are estimated at almost €228 billion annually.[17]

Significant EU investment through initiatives such as Europe's Beating Cancer Plan and the EU Cancer Mission have led to important progress in prevention, diagnosis and treatment. But cancer's prevalence and impact continue to grow. There is more work to be done to understand and address its biological drivers and long-term consequences.

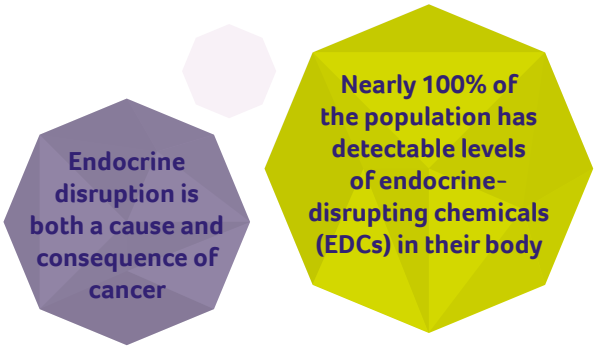
Endocrine disruption is both a cause and consequence of cancer. The EndoCompass Research Roadmap shows how targeted research into the cancer-endocrine relationship can help improve prevention and treatment in both fields, reducing the burden on individuals and society.

This relationship can be understood in five ways:

1. Endocrine cancers
Some cancers occur directly in hormone-producing glands, such as the thyroid, adrenal and pituitary glands. Thyroid cancer is one of the most common endocrine cancers, with nearly 80,000 new cases diagnosed in Europe each year.[6] It is a common secondary cancer following childhood cancer treatment.

2. Hormone-dependent cancers
The two most common cancers in Europe are hormone-dependent cancers, meaning their growth is regulated by hormones. These are: oestrogen receptor (ER)-positive breast cancer, which accounts for around 75% of all breast cancer cases, and prostate cancer, the most common cancer in men.[18] Pharmacological treatments are designed to target the hormonal drivers of these cancers.

3. Endocrine effects of cancer treatment
The endocrine system is highly sensitive to many anti-cancer treatments. Damage to hormone-producing glands can result in long-term hormone deficiencies, affecting adrenal, thyroid, growth and other endocrine functions (see ESE's and ESPE's guidelines on the adverse effects of immune checkpoint inhibitors,[19,31]



for example). As cancer survival improves, more people are living with lasting endocrine complications such as infertility, metabolic disease, bone loss and increased risk of cardiovascular disease. Childhood cancer survivors, now numbering more than 500,000 in Europe, are at particularly high risk, with an average of 4.7 severe complications per survivor at age 50.[20]

4. Obesity as a gateway endocrine disease and cancer risk
Obesity, a disease with significant endocrine-related causes and consequences, is a major risk factor for cancer. Between 25% and 40% of all cancers are attributed to overweight and obesity.[21] As obesity rates increase, especially among young people, Europe can expect the cancer burden to grow.

5. Environmental factors that affect hormones and cancer
Nearly 100% of the population has detectable levels of endocrine-disrupting chemicals (EDCs) in their body.[22] Exposure to these environmental factors can disrupt hormone systems and is associated with many types of cancers, particularly breast, kidney, prostate, ovarian, uterine and testicular cancers. Substances such as per- and polyfluoroalkyl substances (PFAS), often referred to as "forever chemicals", are widely used in everyday consumer products and accumulate in the body over time. Effects can be seen across multiple generations, so urgent action is essential.

The two most common cancers in Europe are hormone-dependent cancers[18]

What research is needed?

Europe needs to sustain investment in cancer research, paying closer attention to the endocrine aspects of cancer which are currently underrepresented in the different EU funding schemes. This includes basic, preclinical and clinical research, and understanding the long-term effects of cancer and its treatment, including the impact on quality of life.

The EndoCompass Research Roadmap recommends the following research priorities:

1. Improve evidence on hormone-based treatment for ER-positive breast cancer
We need clearer evidence on how different hormone-based therapies affect cancer risk and outcomes. This includes reclassifying progestins (synthetic hormones used in hormone replacement therapy and contraception) by receptor activity and reassessing where specific hormone ligands may be beneficial. There is also a need to improve public understanding of breast cancer risks linked to hormone replacement therapy (HRT). Research should also explore treatment strategies beyond direct oestrogen receptor targeting, including approaches that address interactions between hormone signalling pathways.

2. Address treatment resistance in prostate cancer
Investment should focus on strategies to disrupt persistent androgen receptor (AR) signalling and improve treatment of advanced prostate cancer. This includes identifying biomarkers and alternative therapeutic targets. We also need more research into how metabolic health influences disease progression and response to metabolism-related drugs. Another priority is to investigate how immune-targeting strategies can improve the effectiveness of immunotherapy in prostate cancer.

3. Improve monitoring and care for those with long-term endocrine complications after cancer treatment
A better understanding of endocrine complications after childhood cancer treatment or after the use of checkpoint inhibitors will help identify survivors at risk of toxicity so they can avoid unnecessary treatment later in life. Priorities include hypothalamic-pituitary dysfunction, thyroid disease, bone health and obesity management. Oncofertility risks, including sperm damage and the health of children born to cancer survivors, should be assessed through large, long-term studies.

4. Improve early diagnosis and personalised care in familial endocrine cancer syndromes
Research should improve the diagnosis and long-term management of familial endocrine cancer syndromes (rare hereditary endocrine disorders). This should start with support for international registries and biobanks, which allow researchers to study larger cross-border populations to identify disease triggers and refine screening strategies. Earlier diagnosis should be supported through education for non-specialists and shared decision-making tools. There is also an opportunity to offer more personalised care based on genotype–phenotype correlations and risk prediction. Research should also address psychosocial impacts, survivorship needs and reproductive health for affected children and adults and their families.

5. Embed precision medicine and metabolic factors into cancer research
Endocrine-related cancer research should investigate the patient-level factors that influence disease behaviour and treatment response. This includes developing models that mimic human tumour biology to understand how tumours form and progress at different ages and in different tissues. These models can also be used to test new treatment strategies.

For more information on proposed research priorities in this area, please refer to EndoCompass project: research roadmap for endocrine causes and consequences of cancer.

Investing in hormone health is one of the most effective ways for Europe to prevent and manage disease, support healthy ageing and sustain its health systems and economy.

The endocrine community calls on policymakers to deliver the EndoCompass recommendations and ensure a healthier, more resilient Europe.

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To discuss the recommendations in this paper or related policy engagement activities, please contact ESE or ESPE emailing: **info@ese-hormones.org** or **secretariat@eurospe.org**

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Find out more about the EndoCompass Research Roadmap : ese-hormones.org/endocompass.

This document is an extract from *The EndoCompass Research Roadmap – Policy Priorities for Better Hormone Health in Europe*, a wider set of policy recommendations for improving hormone health across Europe. Read the full paper: ese-hormones.org/endocompass-policy-paper

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*Reference numbers follow the numbering used in the full paper.

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