REVISTA PORTUGUESA DE Oncologia

PERMANYER

Check for updates

ORIGINAL ARTICLE

Testing positive after genetic testing for hereditary cancer: what's next?

Resultado positivo num teste genético para cancro hereditário: quais os próximos passos?

Isália Miguel[1,8,18], Sandra Bento[2,8,18], Sara Câmara[3,18], Susy Costa[4,18], Luzia Garrido[4,18], Maria Almeida[5,18], João Silva[6,18], Isadora Rosa[7,8], Paula Rodrigues[8], Carolina Carvalho[9], Pedro Souteiro[10], Rosa Neto-Silva[11], Sandra Silva-Soares[12], Miguel Ornelas-Azevedo[13], Gabriela Sousa[14], Diana Simão[15], Tamara Milagre[16], Graça Freitas[17], and Fátima Vaz[1,8,18]*

[1]Serviço de Oncologia, IPO Lisboa, Lisboa; [2]Serviço de Oncologia, ULS da Lezíria, Santarém; [3]Serviço de Ginecologia, SESARAM, Funchal; [4]Clínica de Mama, ULS São João, Porto; [5]Serviço de Genética, ULS de Braga, Braga; [6]Serviço de Genética, IPO Porto, Porto; [7]Serviço de Gastrenterologia, IPO Lisboa, Lisboa; [8]Clínica de Risco Familiar, IPO Lisboa, Lisboa; [9]Serviço de Oncologia, ULS Alto Ave, Guimarães; [10]Serviço de Endocrinologia, IPO Porto, Porto; [11]Serviço de Gastrenterologia, SESARAM, Funchal; [12]Serviço de Medicina da Reprodução, ULS São João, Porto; [13]USF Arca d'Água, ULS São João, Porto; [14]Serviço de Oncologia, IPO Coimbra, Coimbra; [15]Serviço de Oncologia Médica, ULS São José, Lisboa; [16]Associação EVITA - Cancro Hereditário; [17]Antiga Diretora Geral da Saúde; [18]Grupo de Cancro Hereditário da Sociedade Portuguesa de Oncologia. Portugal

Abstract

Background: *The growing integration of genetic testing into clinical oncology practice has led to the identification of a growing number of individuals carrying pathogenic variants associated with hereditary cancer.* **Objectives:** *These cases require a multidisciplinary and personalized approach; however, access to structured follow-up care remains unstandardized in Portugal.* **Methods:** *To discuss existing organizational models and establish consensus on an optimal infrastructure, the Hereditary Cancer Group of the Portuguese Society of Oncology organized a workshop in September 2023, involving representatives from various healthcare units across the country.* **Results:** *This document, arising from that meeting, proposes the implementation of a structured follow-up model for individuals at genetic risk of cancer. It aims to ensure equitable access to specialized care and to strengthen collaboration with General and Family Medicine. This coordination faces significant challenges, including the transmission of genetic information and limited access to imaging prescriptions, such as magnetic resonance imaging. Despite advances in molecular testing for hereditary cancer diagnosis, the clinical follow-up infrastructure – particularly in terms of multidisciplinary teams, genetic information management, equipment availability, and human resources – has not kept pace. Nevertheless, several centers have begun establishing multidisciplinary teams comprising various medical specialties, specialized nurses, and other health professionals who play a key role in managing patients' care pathways. A central priority is to define the role of the case navigator and ensure continuous patient contact throughout the care journey. This document presents a set of proposals aimed at fostering care organization and integration, technological solutions, the implementation of case navigators, and the dissemination of updates from European reference networks nationwide.*

Keywords: *Hereditary cancer. Genetic testing. Multidisciplinary care. Healthcare coordination.*

Correspondence:
Isália Miguel
E-mail: imiguel@ipolisboa.min-saude.pt

Date of reception: 15-07-2025
Date of acceptance: 30-07-2025
DOI: 10.24875/RPO.25000008

Available online: 13-10-2025
Rev. Port. Oncol. 2025;8(3):108-117
www.rponcologia.com

Resumo

Introduçao: *A crescente integração dos testes genéticos na prática clínica em Oncologia tem permitido identificar mais indivíduos com variantes patogénicas associadas ao cancro hereditário.* **Objetivos:** *Estes casos exigem uma abordagem multidisciplinar e personalizada, mas o acesso a cuidados de seguimento estruturados continua por normalizar em Portugal.* **Métodos:** *Com o objetivo de discutir modelos organizativos e estabelecer consenso sobre uma infraestrutura ideal, o Grupo de Cancro Hereditário da Sociedade Portuguesa de Oncologia promoveu, em setembro de 2023, um workshop com representantes de várias unidades de saúde do país.* **Resultados:** *Este documento, resultante do encontro, propõe um modelo de acompanhamento estruturado para indivíduos com risco genético de cancro, promovendo acesso equitativo a cuidados especializados e reforçando a colaboração com a Medicina Geral e Familiar. Essa articulação enfrenta desafios, como a transmissão de informação genética e limitações na prescrição de exames, nomeadamente ressonâncias magnéticas. Apesar da evolução nos testes moleculares, os recursos necessários ao seguimento clínico – nomeadamente equipas multidisciplinares, gestão da informação genética, acesso a equipamentos e recursos humanos – não acompanharam esse progresso. Ainda assim, vários centros estão a criar equipas multidisciplinares, compostas por diversas especialidades médicas, enfermeiros especializados e outros profissionais, que têm sido fundamentais na gestão do percurso destes doentes. Uma das prioridades é definir quem assume o papel de gestor de caso e como garantir um contacto contínuo com o doente ao longo do percurso assistencial. Este documento apresenta propostas que visam promover a organização e integração de cuidados, soluções tecnológicas, o gestor de cuidados e a disseminação das atualizações das redes europeias de referência.*

Palavras-chave: *Cancro hereditário. Teste genético. Cuidados multidisciplinares. Coordenação em saúde.*

Introduction

The growing integration of genetics into clinical oncology practice has led to an increase in the number of individuals (both cancer survivors and those without prior oncological diagnoses) identified with genetic variants associated with hereditary cancer. These individuals require a multidisciplinary approach to manage their cancer risk, and various structures have been established across national institutions. However, not all patients, across the country, have access to integrated follow-up care. A national study presented in 2019, involving 611 respondents from 31 healthcare units, found that 45% of hospital units had specific structures for monitoring families at risk of hereditary cancer[1]. The same survey suggested that most of the National Health Service (Sistema Nacional de Saúde [SNS]) hospitals have the technical capacity to address and monitor major hereditary cancer syndromes. However, there appears to be a lack of common national organization to ensure care accessibility and effective coordination among various healthcare structures, including the primary care setting.

This study was driven by the need to harmonize two realities:

1. Existing evidence on the potential impact of cancer risk management in reducing morbidity and mortality in these individuals[2-5], as well as its effect on quality of life and family adjustment[6].
2. Challenges on the healthcare system due to the progressive increase in pathogenic variant (PV) carriers requiring specialized care. This increase is a consequence from the recent improvement in molecular genetic testing and the routine implementation of multigene panels[7]. In centers implementing programs based on the Mainstream Genetics model[8,9], the referral pathway for at-risk relatives to genetic consultations is not uniform.

The universe of hereditary cancer families is heterogeneous, and risk management may involve multidisciplinary teams with multiple specialties, including in the case of rare syndromes (e.g., Birt-Hogg-Dubé, Cowden, Li-Fraumeni), implying collaboration across multiple healthcare structures.

Objectives

General objective

The objective of the study was to develop a national framework ensuring a comprehensive and coordinated approach for the accurate identification and appropriate follow-up of individuals carrying PVs associated with hereditary cancer risk, across the country.

Specific objectives

- Promote the development of evidence-based follow-up guidelines.
- Clarify the roles of various medical specialties and other health care professionals, as well as of the structures needed to ensure timely access to genetic counseling, testing, and risk management.
- Define care pathways for these individuals.

Methods

Although health structures, in different formats, already provide care for hereditary cancer families and individuals, there is a critical need to share experiences and knowledge across different stakeholders, to harmonize access to adequate care across the National Health Service (currently comprising local health units and the IPO Hospital Group) and private units.

On the 29th September 2023, the Hereditary Cancer Group (HCG) of the Sociedade Portuguesa de Oncologia (SPO) organized a workshop in Lisbon to discuss the existing organizational models and proposals to improve care. The workshop format allowed the discussion of the pre-existing models of care in the different health structures across the country (presented in the first half), and also for a general discussion intending that, at the end, a proposal for a national framework regarding structure and core guidelines for the appropriate follow-up of these individuals was done.

The HCG invited healthcare workers from across the country, as well as patient associations and representatives from the National Oncological Plan (PNDO-DGS). Due to challenges in coordination with Primary Care, specialists in General and Family Medicine from across the country were also invited.

Results

Participants

Forty-four healthcare professionals (from public and private hospitals and from Primary Care Units) and three patient associations participated, sharing data and discussing existing organizational models in Portugal (Supplementary material, I and II). Furthermore, present were the then SPO President (Prof. Dr. Miguel Abreu), the former Director-General of Health (Dr. Graça Freitas), and Prof. Dr. Isabel Fernandes, representing the National Program for Oncological Diseases (PNDO_DGS).

Scope and strategic definition

The opening session highlighted the need to characterize the target population and to evaluate the current clinical practice. This would allow the strategic planning to ensure an equitable, patient-centered governance model.

For the current version of this document, (Portuguese version available in: www.cancrohereditario.pt/pt/eventos/gestao-de-risco-e-seguimento-dos-individuos-portadores-de-variantes-patogenicas-associadas-a-cancro-hereditario/), seven institutions provided aggregate data on individuals identified with PVs associated with hereditary cancer risk. In those 7 centers (IPO Lisboa, IPO Porto, IPO Coimbra, ULS S. João, ULS Alto Ave, Hospital Nelio Mendonça and ULS de Braga), a total of 8,105 individuals with PVs were identified, with the majority being mutations in *BRCA1*, *BRCA2*, and *PALB2* genes (4,171), 1,835 in mismatch repair (*MMR*) genes (associated with Lynch syndrome), 662 in genes linked to colorectal polyposis syndromes, 131 in *TP53*, 129 in *CDH1*, 52 in *PTEN*, and 1,132 in other moderate- and high-penetrance genes associated with hereditary cancer risk.

Operational structures in Portugal

To establish the starting point for discussion, several health professionals from already implemented operational structures in the country presented data regarding their experience. Speakers from IPO Lisboa (Isália Miguel, Isadora Rosa, and Paula Rodrigues), ULS São João (Susy Costa, Luzia Garrido, Sandra Silva-Soares), ULS Alto Ave (Carolina Carvalho), Dr. Nélio Mendonça Hospital (Sara Camara, Rosa Neto-Silva), and IPO Porto (Pedro Souteiro and João Silva) structured their presentations as follows:

1. How is the follow-up of individuals with positive genetic tests organized in your center?
2. How do PV carriers access follow-up care?
3. Are healthy PV carriers included in follow-up care?
4. What challenges do you identify?

The information collected is summarized in table 1.

Table 1. A Portuguese national portrait regarding cancer risk management

Question	Response
1. How is the follow-up of individuals with positive genetic tests organized?	Across various centers, specialized structures–Familial Cancer Risk Clinics, Oncogenetics consultations – have been established to monitor individuals either based on the predominant oncologic phenotype, or identified hereditary syndrome within their families (e.g., breast/ovarian/prostate cancer; gastrointestinal tumors; melanoma; pediatric hemato-oncology; pediatric gastroenterology; endocrinology syndromes, and others included in Medical Oncology management). In some institutions, multidisciplinary case discussions are regularly scheduled to address complex or atypical cases; review Variants of uncertain significance, and update management guidelines (e.g., Multidisciplinary Oncogenetics Group meetings, regular discussions between clinicians and molecular biologists). However, the extent to which individuals with a positive genetic test–particularly those without a cancer diagnosis–are effectively integrated in follow-up by existing structures remains unclear.
2. How do PV carriers access follow-up care?	Access is typically facilitated through referral by the oncogenetics clinic or the physician responsible for the genetic diagnosis, directing patients to familial cancer risk clinics or specific consultations, either within the same institution or to centers where such follow-up is available. Despite the growing number of individuals identified as at-risk and the complex, multidisciplinary nature of their care needs, hospitals did not have a proportional increase in specialized resources (infrastructure, equipment, and human resources). Consequently, healthcare professionals must coordinate internally or refer patients to other centers to ensure appropriate follow-up.
3. Are healthy PV carriers included in follow-up care?	In general, it is assumed that all carriers with a cancer diagnosis are followed through oncology consultations, with varying levels of integration into institutional surveillance and risk-reduction frameworks. For unaffected carriers (without a previous cancer diagnosis), follow-up is offered in many centers via structured familial risk clinics or specific medical oncology, endocrinology, and/or pediatric consultations. Some centers initially focused on patients with cancer and a positive genetic test, but are now working to expand follow-up services to include asymptomatic carriers.
4. What challenges have been identified?	Inadequate physical infrastructure; Shortage of dedicated human resources (e.g., clinical geneticists, gastroenterologists, anesthesiologists, specialized nurses); Increasing demand for genetic testing, challenging timely access and response; High cost of genetic testing; Difficulties in implementing surveillance protocols, particularly for endoscopic procedures (especially those requiring anesthesia), radiological exams (due to equipment limitations and long waiting times), and access to specialized consultations; Reluctance or refusal of some carriers to inform at-risk relatives of their genetic status; Lack of clear discharge criteria or referral pathways from specialized clinics; Insufficient surgical capacity and long waiting times for risk-reducing (prophylactic) surgeries.

IPO Lisboa

Since 2006, specific consultations (breast, ovarian, prostate, colorectal, and melanoma) have functioned within a specific structure dedicated to these patients: the Cancer Family Risk Clinic (Clínica de Risco Familiar [CRF]). At CRF, the different groups share space, administrative services, and collaboration with specialized Nursing, Medical Genetics, Psychology and Molecular Biology. Common to all CRF multidisciplinary groups is the close coordination with the molecular diagnostics team, enabling individualized interventions in systemic therapy decisions and risk-reducing surgeries (for both cancer patients and healthy carriers). The core team at CRF integrates multidisciplinary groups with several other medical specialities (Breast Surgeons, Gynecological Oncology, Plastic and Reconstructive Surgery, Urology). IPO Lisboa is part of the European Genturis network[10] in thematic Groups 2 (Lynch syndrome and polyposis), 3 (Breast and Ovarian) and 4 (other hereditary syndromes).

Breast, ovarian, and prostate cancer family risk consultation

Access to the consultation is made through referral from other clinics and units from IPO Lisboa and from other external public or private units. This multidisciplinary group includes dedicated nursing for patient and family management throughout the process, and also oncologists, geneticists, and the molecular diagnostics group (an integral part of the multidisciplinary team). Based on evidence and actionable results, most tests prescribed in 2023 for breast, ovarian, and prostate cancer patients included genes *ATM*, *BARD1*, *BRCA1*, *BRCA2*, *CDH1*, *CHEK2*, *PALB2*, *PTEN*, *RAD51C*,

RAD51D, *STK11*, *TP53*, and *MMR* genes. The detection rate was approximately 10-11%. For reanalyses (multigene panel reanalyses in patients previously tested only for *BRCA1/2),* the positivity rate was 8% (30/386) (2023 data). The surveillance protocol for these carriers was presented, along with Genturis[10-12], European Society for Medical Oncology (ESMO)[11], and National Comprehensive Cancer Network (NCCN)[13] recommendations, included in the internal protocols.

Colorectal cancer family risk consultation

The colorectal cancer family risk consultation follows patients with non-polyposis and polyposis hereditary syndromes. Lynch syndrome is associated with an autosomal dominant defect in the MMR system, leading to accelerated carcinogenesis and early-onset cancers (colorectal, endometrial, ovarian, gastric, small intestine, urothelial, central nervous system [CNS], pancreatic, and biliary). Surveillance significantly reduces colorectal cancer risk. The surveillance protocol for these carriers was presented, along with ESMO[14], NCCN[15], and EHTG/ESCP[16] recommendations. In APC-associated polyposis, a defect in the Wnt signaling pathway results in an autosomal dominant syndrome with an 80-100% lifetime colorectal cancer risk and extracolonic manifestations (small intestine, CNS, thyroid, liver, stomach, and pancreas). The institutional surveillance protocol was presented and compared with NCCN recommendations[14].

ULS São João (Porto)

This local health unit has an Oncogenetics consultation that works in coordination with various teams involved in diagnostics and surveillance. ULS São João is the only public center in Portugal offering access to Preimplantation Genetic Testing for Monogenic (PGT-M) Disorders. It is also a Genturis center[10] for thematic Groups 1 (Neurofibromatosis), 2 (Lynch syndrome and polyposis), 3 (Breast and Ovarian), and 4 (other hereditary syndromes).

Oncogenetics consultation

Patients are referred to the ULS São João Oncogenetics outpatient unit, either from other services of ULS São João or from external public or private health services. After identifying carriers (affected or unaffected), they are referred to various High-Risk Consultations based on the identified PV. The Breast and Ovarian Cancer High-Risk Consultation, managed by surgical oncologists, follows individuals with syndromes associated with PVs in *BRCA1*, *BRCA2*, *PALB2*, *CDH1* (females), *PTEN*, *CHEK2* (females), *ATM* (females), *BRIP1*, *RAD51C*, *RAD51D*, and *BARD1*. The Gastrointestinal Tumors High-Risk Consultation, also managed by surgical oncologists, follows individuals with syndromes associated with PVs in *CDH1* (both sexes), *CHEK2*, *ATM*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *APC*, *MUTYH*, and *STK11*. The Medical Oncology High-Risk Consultation, managed by oncologists, follows individuals with syndromes associated with PVs in *ATM* (males), *CHEK2* (males), *DICER1*, *FH*, *FLCN*, *NF1*, *TP53*, *PTEN*, *RB1*, *RET*, SDHs, SUFU, and VHL.

In 2019, a Multidisciplinary Oncogenetics Group Consultation was established to discuss criteria for expanding genetic studies in families with undiagnosed hereditary syndromes and surveillance protocols for carriers of variants in moderate- and low-penetrance genes. The multidisciplinary group includes dedicated nurses, oncologists, geneticists, and surgical oncologists responsible for High-Risk Consultations. Carriers of variants of unknown significance (VUS) are reassessed every 2-3 years, with VUS reclassification requested from the original laboratory at no additional cost. Surveillance follows ERN-Genturis[10,11,16-30], ESMO[11,14], and NCCN[13,15] guidelines. Pediatric carriers are followed in High-Risk Pediatric Hemato-Oncology and Gastroenterology.

PGT-M

ULS São João is the only public center in Portugal performing PGT-M for PV carriers at risk of transmitting variants to the offspring. It receives nationwide patients, who are eligible for the procedure. Dr. Sandra Silva-Soares explained why genetic counseling is important to inform couples about transmission risks and available interventions (e.g., prenatal diagnosis or PGT-M). Early referral (inter-hospital or via email: umr@ulss-joao.min-saude.pt) with clinical details, variant reports, and carrier data was emphasized. For variants in unauthorized pre-implantation genes, approval from the National Council for Medically Assisted Reproduction (Comissão Nacional de Procriação Medicamente Assistida, [CNPMA] - www.cnpma.org.pt/) is required and then handled by the reproductive medicine center after verifying inclusion criteria. Most new gene variants require pre-genetic tests and embryonic diagnostics at Universitaire Ziekenhuis Brussel (not feasible in Portugal).

Key challenges include:

- Age limit for women (40 years) for assisted reproductive techniques in the SNS.
- A 14-month waiting list for treatment.
- Inability to perform PGT-M for independent reproduction due to the inability to create pre-genetic tests for variant identification in embryos (donor genetic information unavailable in the SNS).
- Individuals with healthy children without the PV lack eligibility for the procedure in the SNS.

ULS Alto Ave (Guimarães)

Until 2019, high-risk patients had to be referred to a different city to access genetic testing at the Medical Genetics Consultation at ULS Braga. In 2020, ULS Alto Ave implemented two hereditary cancer risk consultations: one for gastrointestinal syndromes (2020); for the other syndromes a Cancer Family Risk consultation was set up in 2021. In 2022, ULS Alto Ave had its own Medical Genetics consultation that allows for better access to genetic testing. The Cancer Family Risk consultation, managed by Medical Oncology, initially managed only patients with positive genetic tests and prior oncological diagnoses. Since 2023, it has included healthy carriers with positive genetic tests in surveillance. An internal document, disseminated through ULS Alto Ave, outlines objectives, prescribed multigene panels, and the informed consent for genetic testing (based on a national guideline from the Directorate-General of Health, DGS).

Dr. Nélio Mendonça hospital (Funchal)

Since 2018, the Breast and Ovarian Cancer Family Risk Consultation has collected data on carriers of genetic predispositions or relevant family histories, even if untested. After 2019, with Medical Genetics collaboration, proactive testing was implemented in diagnostic and predictive settings. Before, since 2011, a Polyposis and Family Risk Consultation was operating with similar objectives (specific surveillance for high-risk patients). On June 20, 2022, the Family Risk Clinic was officially established, including both teams plus Medical Genetics. Clinical links are identified within the hospital (Dermatology, Imaging, Plastic Surgery, etc.) and collaborate with the Family Risk Clinic in patient management. A nurse with specialized training in this area was assigned to the clinic, managing genograms, genetic archives, and an email account that serves as an interface with patients and other healthcare professionals.

IPO Porto

The IPO Porto Genetics Consultation coordinates with the Genetics Laboratory and with the various other consultations involved in managing the risk of PV carriers associated with hereditary cancer. The Endocrinology-Family Risk Consultation was presented as an example.

Endocrinology-family risk consultation

Several endocrine neoplasms (medullary thyroid carcinomas, pheochromocytomas/paragangliomas, pituitary, and parathyroid tumors) can occur in familial genetic syndromes. The Endocrinology Family Risk Consultation at IPO Porto started its activity in 2022, in coordination with the Medical Genetics Service, which refers asymptomatic carriers identified through cascade family screening. Surveillance for hereditary endocrine neoplasms requires clinical, imaging, and analytical monitoring, often involving dynamic laboratory tests in endocrinology. Centralizing these individuals in a dedicated consultation has standardized procedures through surveillance protocols, promoted clinical research, and balanced early neoplasm detection with avoiding iatrogenic and psychologically stressful diagnostic procedures.

Role of nursing

Two nurses (from ULS São João and IPO Lisboa) emphasized nurses' role in managing the care needs of at-risk individuals throughout their care pathway. Experiences at the two institutions differ slightly. At ULS São João, the nurse participates in the Breast Oncology Group Consultation, identifies patients eligible for genetic testing, and serves as a liaison with the multidisciplinary team, and participates in the referral to High-Risk Consultations. At ULS São João, the nurse also identifies priority cases for timely genetic diagnosis to optimize therapeutic decisions, manages cascade testing for at-risk relatives, and maintains family records as per current Portuguese legislation. The concept of a "nurse navigator" was explored.

At IPO Lisboa, the nursing team collaborates with the medical team to prioritize requests, ensuring timely genetic diagnosis for patients with short-term

therapeutic implications. Beyond creating initial files and genograms, they facilitate coordination between consultations (e.g., scheduling risk consultations after identifying a cancer-associated variant), manage cascade testing for at-risk relatives, and collaborate, during the follow-up in surveillance protocol compliance. The nursing team participates in the core team with the Molecular Pathology Unit, and has a close collaboration with the Psychology Unit, assessing distress in *BRCA1/2* carriers.

Medical genetics

Medical Genetics specialists are essential for pre- and post-test counseling and for developing surveillance plans. In most healthcare structures, they do not participate in active follow-up of PV carriers and their surveillance, after test results. They remain involved in identifying relatives, managing reproductive options (e.g., PGT-M), and participating in multidisciplinary case discussions, variant analysis, and guideline development[31].

Discussion

The open discussion highlighted the following points:

Coordination with general and family medicine (GFM)

Given that GFM has more training in prevention and health promotion than most hospital medical specialties; its collaboration is not only desirable but mandatory. GFM's holistic approach spans the entire life cycle, including preventive care for those at increased risk, such as the individuals addressed in this document. Keeping up with specialized, updated knowledge can be challenging for GFM, requiring ongoing dialogue with colleagues specializing in these conditions, especially given the low prevalence of PV carriers associated with hereditary cancer in each of the patient files under the care of a specific GFM. GFM faces three main challenges in managing preventive care for PV carriers:

- Difficulty in the communication of clinical information to patients regarding their genetic risk
- Challenges in maintaining updated specialized knowledge about genetic risk and the low number of PV carriers in each patient list.
- Barriers to accessing complementary diagnostic and therapeutic resources (CDTRs) and integrating care.

The difficulty in transmitting clinical information about genetic risk results from legal limitations on recording genetic information in electronic health records. The requirement to separate genetic information to prevent discrimination, as stipulated in current legislation [Law No. 12/2005 of January 26 (Personal Genetic Information and Health Information) and its regulation, Decree-Law No. 131/2014 of August 29], complexifies the follow-up for carriers without prior cancer diagnoses, as no platforms or archives enable electronic sharing between genetics or risk clinics and GFM. Although confidential notes can be added to electronic medical records, these are only accessible to the registering physician, hindering follow-up if the physician leaves the practice. A proposal during the discussion was to seek feedback from the Shared Services of the Ministry of Health (SPMS) to enable controlled access to genetic information in the electronic health record, restricted to those managing patient risk in hospital or primary care settings, ensuring secure data use.

GFM faces barriers to prescribing necessary CDTRs (some only available or requested at the hospital level like MRI) for early cancer detection and care integration. To address these, bidirectional training on primary care and hospital procedures, identifying contact points, and coordinating hereditary cancer risk management should be implemented, specifying what can be done in primary care, what can be shared, what must be hospital-based (e.g., risk-reducing surgeries), and what can primarily be managed in primary care (e.g., follow-up of women with a *BRCA1/2* PV post-risk-reducing surgeries). The current reform of the National Health Service, with the generalization of the Local Health Unit model, can solve this problem, liberalizing access to complementary diagnostic means, making these accessible to GFM.

Coordination in care of high risk individuals

Some hereditary cancer syndromes are so complex that, to manage risk in individuals affected, good coordination between a Risk Clinic and Primary Care would not be enough. Indeed, for some patients, the system has to work in a national network (e.g., only one public hospital offers PGT-M). This underscores the need for agreed-upon follow-up guidelines, awareness of available network services, and criteria for effective referrals to other centers when necessary.

Infrastructure

The increasing identification of individuals with positive genetic tests has not been accompanied by proportional increases in structural resources for their follow-up, particularly regarding multidisciplinary structures, genetic information management, access to equipment [breast MRI, abdominal MRI/MRCP, whole-body MRI, colonoscopy equipment and operating rooms], and human resources. This has led some Medical Genetics or Oncology services, where mainstream genetics programs are implemented, to send positive cases to centers with established multidisciplinary groups. However, these reference centers also face exponential increases in identified at-risk individuals and have serious difficulties in accommodating promptly externally referred patients.

Indeed, there is an increasing pressure on existing structures, but new teams have also been progressively implemented in places where they did not previously exist, such as ULS Alto Ave, Dr. Nélio Mendonça Hospital, ULS Trás-os-Montes e Alto Douro, ULS Almada-Seixal, and ULS Braga (the latter two in 2024). These units initially focused on managing cancer patients, considering their genetic specificities, but some have progressively extended their scope to unaffected relatives with positive tests.

The minimum infrastructure facilities needed for healthcare institutions identifying these patients were discussed. No consensus was reached on whether a dedicated physical space was necessary. While ideal for archiving, administrative support, patient care managers (e.g., nurse navigators or other patient navigators), and multidisciplinary meetings, space limitations may make this unfeasible. Functional team coordination was deemed essential. Each site should define a team considering clinical guidelines and patient's needs, tailored to the structure's specifics and leveraging its professional resources. These teams include various specialties, varying by hereditary syndrome follow-up needs. Ideally, the patient's physician should be part of these teams, which should include specialists as "connecting links" across services and structures involved in the patient's care pathway.

Patient care manage/patient navigator

Specialized nursing plays a critical role in managing the care pathway of these patients and their families, as highlighted during the meeting. After identifying a PV and developing a surveillance plan, the patient care manager addresses questions and operationalizes the plan over time. While nursing typically assumes this role, other professionals (e.g., genetic counselors, psychologists) also fulfill this role in some centers. The priority is defining who serves as the patient care manager in each healthcare unit and how patients can contact them throughout their care journey, ensuring guidance beyond scheduled consultations and procedures. Each patient should receive a card identifying their care manager and contact details, including the email of the multidisciplinary team's structure.

Guidelines

Given the multiplicity of hereditary syndromes and follow-up guidelines from various national and international societies (e.g., Gastroenterology, Gynecologic Oncology) (ERN-Genturis[10,11,16-30], ESMO[11,14], NCCN[13,15]), it is proposed that ERN-Genturis [10,11,16-30] and ESMO[11,14] guidelines be followed where available, resorting to others for specific cases not covered. Existing national guidelines are included in multidisciplinary case discussions but are rarely organized into comprehensive guidelines. Several multidisciplinary structures have approved surveillance protocols, though their frequent updating is challenging. The importance of an updated, individualized, and dynamic surveillance plan for each patient, serving as a "passport" for navigating healthcare structures, was emphasized. This dynamism reflects both guideline updates and changes in patient risk (e.g., post-risk-reducing surgeries)[32].

Proposals/challenges

The main proposals to organize hereditary cancer risk management for at-risk patients and foster synergies among healthcare providers include:

- Integration of genetic testing teams dedicated to risk management.
- At the individual level, each patient should have updated information about their genetic status and risk management plan.
- Network between different health structures and between hospitals and primary care depend on technological solutions probably dependent on SPMS.
- Regardless of national consensus (e.g., from Portuguese societies or specific multidisciplinary groups), the SPO HCG should provide links to the

latest Genturis[10], ESMO[11,14], and NCCN[13,15] guidelines on its website.
- Implement the patient care manager role across centers.
- Each patient's genetic status and plan should ideally be expressed in a standardized document, like a passport, promoted by the SPO HCG.
- National centers in European networks (e.g., ERN-Genturis) should collaborate in disseminating relevant updates and opportunities for national collaboration.

Several structures involved in genetic testing and follow-up of patients with confirmed genetic risk were implemented after the September 2023 workshop (e.g., ULSTMAD and ULS Braga). Maintaining a good network communication is essential, as structures are overburdened (particularly in CDTR access). Sharing organizational experiences within the healthcare system is desirable to reduce duplication and optimize the management required for individuals at risk of hereditary cancer.

Following this initiative, in December 2023, DL No. 13227/2023 was published in the Diário da República, approving the National Cancer Control Strategy, Horizon 2030. For the 1st time, under the early detection pillar, it was included a national strategic determination to establish an expert panel to support the development of Oncological Screening Standards for Hereditary Syndromes associated with increased cancer risk, particularly for *BRCA1/2*-associated breast cancer and Lynch syndrome-associated colorectal cancer. This legislative measure, linked to the National Program for Oncological Diseases, is a critical step toward integrating oncological screening for hereditary syndromes into the national healthcare system.

Conclusion

The participation of various professional groups from different SNS structures and patient associations enabled the identification of limitations in hereditary cancer risk management in Portugal and the proposal of intervention areas. This process is dynamic, requiring ongoing intra- and inter-institutional communication channels and collaboration with scientific societies and patient associations to integrate guidelines on organization, infrastructure, and technical follow-up. The implementation of screening for two major adult hereditary cancer syndromes, as outlined in DL No. 13227/2023, is recognized as a decisive step toward integrating hereditary cancer risk management at the national level.

Funding

This article is supported by the SPO Group of Hereditary Cancer.

Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

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

References

1. Available from: https://www.medis.pt/mais-medis/cancro/cancro-hereditario-so-45-2 das-unidades-hospitalares-tem-estrutura-para-seguir-familias-e-doentes [Last accessed on 2024 Feb 15].
2. Roebothan A, Smith KN, Seal M, Etchegary H, Dawson L. Specialty care and counselling about hereditary cancer risk improves adherence to cancer screening and prevention in newfoundland and labrador patients with BRCA1/2 pathogenic variants: a population-based retrospective cohort study. Curr Oncol. 2023;30:9367-81.
3. Villani A, Shore A, Wasserman JD, Stephens D, Kim RH, Druker H, et al. Biochemical and imaging surveillance in germline TP53 mutation carriers with Li-Fraumeni syndrome: 11 year follow-up of a prospective observational study. Lancet Oncol. 2016;17:1295-305.
4. Barrow P, Khan M, Lalloo F, Evans DG, Hill J. Systematic review of the impact of registration and screening on colorectal cancer incidence and mortality in familial adenomatous polyposis and Lynch syndrome. Br J Surg. 2013;100:1719-31.
5. Dullens B, de Putter R, Lambertini M, Toss A, Han S, Van Nieuwenhuysen E, et al. Cancer surveillance in healthy carriers of germline pathogenic variants in BRCA1/2: a review of secondary prevention guidelines. J Oncol. 2020;2020:9873954.
6. Gomes P, Pietrabissa G, Silva ER, Silva J, Matos PM, Costa ME, et al. Family adjustment to hereditary cancer syndromes: a systematic review. Int J Environ Res Public Health. 2022;19:1603.
7. Calabrese A, von Arx C, Tafuti AA, Pensabene M, De Laurentiis M. Prevention, diagnosis and clinical management of hereditary breast cancer beyond BRCA1/2 genes. Cancer Treat Rev. 2024;129:102785.
8. Alves IT, Condinho M, Custódio S, Pereira BF, Fernandes R, Gonçalves V, et al. Genetics of personalized medicine: cancer and rare diseases. Cell Oncol (Dordr). 2018;41:335-41.
9. Beard C, Monohan K, Cicciarelli L, James PA. Mainstream genetic testing for breast cancer patients: early experiences from the Parkville Familial Cancer Centre. Eur J Hum Genet. 2021;29:872-80.
10. ERN GENTURIS. Available from: https://www.genturis.eu [Last accessed on 2024 Nov 09].
11. Sessa C, Balmaña J, Bober SL, Cardoso MJ, Colombo N, Curigliano G, et al. Risk reduction and screening of cancer in hereditary breast-ovarian cancer syndromes: ESMO Clinical Practice Guideline. Ann Oncol. 2023;34:3347.
12. McDevitt T, Durkie M, Arnold N, Burghel GJ, Butler S, Claes KB, et al. EMQN best practice guidelines for genetic testing in hereditary breast and ovarian cancer. Eur J Hum Genet. 2024;32:479-88.
13. NCCN Clinical Practice Guidelines - Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic; 2025. Available from: https://www.nccn.org

14. Stjepanovic N, Moreira L, Carneiro F, Balaguer F, Cervantes A, Balmaña J, et al. Hereditary gastrointestinal cancers: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2019;30:1558-71.
15. NCCN Clinical Practice Guidelines - Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric; 2024. Available from: https://www.nccn.org
16. Seppälä TT, Latchford A, Negoi I, Sampaio Soares A, Jimenez-Rodriguez R, Sánchez-Guillén L, et al. European guidelines from the EHTG and ESCP for Lynch syndrome: an updated third edition of the Mallorca guidelines based on gene and gender. Br J Surg. 2021;108:484-98.
17. Blair VR, McLeod M, Carneiro F, Coit DG, D'Addario JL, van Dieren JM, et al. Hereditary diffuse gastric cancer: updated clinical practice guidelines. Lancet Oncol. 2020;21:e386-97.
18. Tischkowitz M, Colas C, Pouwels S, Hoogerbrugge N, PHTS Guideline Development Group, European Reference Network GENTURIS. Cancer Surveillance Guideline for individuals with PTEN hamartoma tumour syndrome. Eur J Hum Genet. 2020;28:1387-93.
19. Crosbie EJ, Ryan NA, Arends MJ, Bosse T, Burn J, Cornes JM, et al. The Manchester International Consensus Group recommendations for the management of gynecological cancers in Lynch syndrome. Genet Med. 2019;21:2390-400.
20. van Leerdam ME, Roos VH, van Hooft JE, Balaguer F, Dekker E, Kaminski MF, et al. Endoscopic management of Lynch syndrome and of familial risk of colorectal cancer: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2019;51:1082-93.
21. Monahan KJ, Bradshaw N, Dolwani S, Desouza B, Dunlop MG, East JE, et al. Guidelines for the management of hereditary colorectal cancer from the British Society of Gastroenterology (BSG)/Association of Coloproctology of Great Britain and Ireland (ACPGBI)/United Kingdom Cancer Genetics Group (UKCGG). Gut. 2020;69:411-44.
22. Zaffaroni G, Mannucci A, Koskenvuo L, de Lacy B, Maffioli A, Bisseling T, et al. Updated European guidelines for clinical management of familial adenomatous polyposis (FAP), MUTYH-associated polyposis (MAP), gastric adenocarcinoma, proximal polyposis of the stomach (GAPPS) and other rare adenomatous polyposis syndromes: a joint EHTG-ESCP revision. Br J Surg. 2024;111:znae070.
23. van Leerdam ME, Roos VH, van Hooft JE, Dekker E, Jover R, Kaminski MF, et al. Endoscopic management of polyposis syndromes: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2019;51:877895.
24. Wagner A, Aretz S, Auranen A, Bruno MJ, Cavestro GM, Crosbie EJ, et al. The management of Peutz-Jeghers syndrome: European Hereditary Tumour Group (EHTG) guideline. J Clin Med. 2021;10:473.
25. Bakhuizen JJ, Hanson H, van der Tuin K, Lalloo F, Tischkowitz M, Wadt K, et al. Surveillance recommendations for DICER1 pathogenic variant carriers: a report from the SIOPE Host Genome Working Group and CanGene-CanVar Clinical Guideline Working Group. Fam Cancer. 2021;20:337-48.
26. Geilswijk M, Genuardi M, Woodward ER, Nightingale K, Huber J, Madsen MG, et al. ERN GENTURIS clinical practice guidelines for the diagnosis, surveillance and management of people with Birt-Hogg-Dubé syndrome. Eur J Hum Genet. 2024;32:1542-50.
27. Carton C, Evans DG, Blanco I, Friedrich RE, Ferner RE, Farschtschi S, et al. ERN GENTURIS tumour surveillance guidelines for individuals with neurofibromatosis type 1. EClinicalMedicine. 2023;56:101818.
28. Legius E, Messiaen L, Wolkenstein P, Pancza P, Avery RA, Berman Y, et al. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. Genet Med. 2021;23:15061513.
29. Frebourg T, Bajalica Lagercrantz S, Oliveira C, Magenheim R, Evans DG, European Reference Network GENTURIS. Guidelines for the Li-Fraumeni and heritable TP53-related cancer syndromes. Eur J Hum Genet. 2020;28:1379-86.
30. Binderup ML, Smerdel M, Borgwadt L, Beck Nielsen SS, Madsen MG, Møller HU, et al. von Hippel-Lindau disease: updated guideline for diagnosis and surveillance. Eur J Med Genet. 2022;65:104538.
31. Costa C, Lemos MS, Azevedo LF, Paneque M. Service provision of genetics health care in Portugal. J Community Genet. 2023;14:101-13.
32. Available from: https://www.gustaveroussy.fr/fr/programme-apres-cancer-interval [Last accessed on 2025 Feb 23].