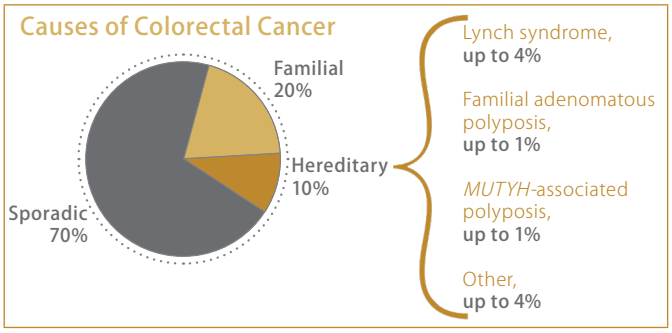
THE PATHCARE NEWS

INTERNATIONAL GENETIC TESTING FOR HEREDITARY COLORECTAL & ENDOMETRIAL CANCER

Approximately **10%** of all colorectal cancers (CRC) are hereditary. Patients who carry a pathogenic germline variant in a CRC-related gene have an increased risk of developing CRC, as well as other cancers.



Hallmarks of hereditary colorectal and endometrial cancer
• CRC at < 50 years
• Endometrial cancer at < 60 years
• Bilateral breast cancer
• CRC/endometrial cancer and a Lynch syndrome (LS)-related cancer[+] diagnosed separately or at the same time
• Tumour with mismatch repair deficiency or high-level microsatellite instability
• CRC/endometrial cancer and ≥ 1 first-degree relative with any LS-related cancer diagnosed before age 50 years
• CRC/endometrial cancer and ≥ 2 first-degree relatives with any LS-related cancers regardless of age of cancer diagnosis

[+] colorectal, endometrial, ovarian, stomach, small bowel, urinary tract, biliary tract, prostate, brain, sebaceous adenomas, sebaceous carcinomas, keratoacanthomas, pancreatic

Genetic testing may confirm a diagnosis and help guide treatment and management decisions. Identification of a disease-causing variant would also guide screening, testing and early diagnosis of at-risk relatives.

INVITAE - International send away service

PathCare offers a referral service to Invitae Laboratory in the USA. Invitae offers an extensive genetic test menu over a broad range of clinical areas, including hereditary cancer:

https:// www.invitae.com/en/physician/category/CAT000015/

Invitae offers testing via single-gene or multi-gene panels at a fixed patient-pay price, with the additional benefits of re-requisitioning a sample for additional genes at no extra cost, and free-of-charge family variant testing to blood relatives, if requested within 150 days of the initial patient's report.

The cost of any Invitae hereditary cancer panel (regardless of the number of genes tested) is **299 US Dollars*** (cost in Rands is dependent on the exchange rate). As this is a patient-pay option, Invitae bills the patient directly for these tests. PathCare charges an international handling fee (**R950***) which is paid upfront when providing the sample.

The turnaround time for Invitae tests is approximately **4 weeks**.

The following panels are available at Invitae (please note that these tests are specifically designed to identify heritable germline mutations and are NOT appropriate for the detection of somatic mutations in tumour tissue):

1. LYNCH SYNDROME PANEL

This test analyses 5 genes associated with Lynch syndrome.

Lynch syndrome, also called hereditary non-polyposis colon cancer (HNPCC), increases the risk of many types of cancer, particularly colorectal. Women with this disorder also have an increased risk for endometrial and ovarian cancer. Lynch syndrome is the most common cause of adult-onset hereditary colorectal and endometrial cancers. Individuals with Lynch syndrome are also carriers of autosomal recessive constitutional mismatch repair deficiency (CMMR-D).

Disorders tested using this panel:
- Lynch syndrome
- Congenital tufting enteropathy
- Constitutional mismatch repair deficiency (CMMR-D) syndrome

2. FAMILIAL ADENOMATOUS POLYPOSIS TEST

This test analyses the *APC* gene.

Pathogenic variants in this gene can cause *APC*-associated polyposis conditions, which include familial adenomatous polyposis (FAP), attenuated FAP (AFAP), and gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS). These disorders are primarily associated with the development of numerous colonic and/or gastric polyps and colon or gastric cancer.

Disorders tested using this test:
- Familial adenomatous polyposis
- Attenuated familial adenomatous polyposis
- Gastric adenocarcinoma and proximal polyposis of the stomach

3. COLORECTAL CANCER GUIDELINES-BASED PANEL

This panel analyses 19 genes associated with a significantly elevated risk of hereditary CRC. The genes included in this panel are medically actionable and have published, evidence-based management guidelines. It does not include genes with preliminary evidence of an association with CRC.

Disorders tested using this panel:
- Lynch syndrome
- Familial adenomatous polyposis
- Attenuated familial adenomatous polyposis
- MUTYH-associated polyposis
- Peutz-Jeghers syndrome
- Juvenile polyposis syndrome
- Serrated polyposis syndrome
- Li-Fraumeni syndrome
- Cowden and Cowden-like syndrome
- Oligodontia-colorectal cancer syndrome
- Constitutional mismatch repair deficiency

Invitae Family Variant Testing

When a family member has been tested through Invitae and a pathogenic/likely pathogenic variant has been identified, free-of-charge targeted family variant testing is available to blood relatives of this patient within 150 days of the initial patient's report. The PathCare International referral service handling & courier fee (R950) **will** still apply to family testing. The original report from Invitae (including the RQ number) will need to accompany these samples. Adequate genetic counselling is also recommended, as this testing may be offered to at-risk unaffected family members.

When to order a smaller or larger panel?

It is recommended that you select your panel according to a detailed 3-generation family history. It is also important to consider that more targeted genetic testing leads to fewer incidental or difficult to interpret findings. For patients who test negative on a smaller panel, there is always the option to re-requisition their sample to a larger panel in the same clinical area, at no additional cost within 150 days of the initial report.

Medical aid coverage of genetic testing

International genetic testing is more affordable than local genetic testing but is usually NOT covered by medical aid.

We therefore offer the patient-pay option for the above mentioned comprehensive international gene panels as a more affordable option for those patients who are unable to get authorisation for local testing from their medical aids and would still like to go ahead with testing. As this is a patient-pay option, it is advised that you discuss the cost implications with your patients prior to ordering international genetic testing.

Genetic Counselling

It is internationally recognised and strongly recommended that genetic testing be offered in the context of appropriate pre- and post-test genetic counselling by a genetics professional.

PathCare does not offer a clinical genetic counselling service but is able to provide you with contact details for genetic counsellors in South Africa. Please contact our Genetics Team for a list of HPCSA-registered genetic counsellors who you can refer your patients to. We understand that there are limited genetic counselling services in South Africa, however, most genetic counsellors would be able to arrange online consultations if necessary.

Please feel free to contact our **Genetics Team** if you have any questions on:

☎ (021) 596 3655

✉ geneticconsult@pathcare.org

Quick Guide To Testing

(Please use the PathCare Cancer Genetic Request Form for all requests)

	Lynch Syndrome Panel (5 genes)	Familial Adenomatous Polyposis Test (1 gene)	Colorectal Cancer Guidelines-Based Panel (19 genes)
Gene/s tested	*MLH1, MSH2, MSH6, PMS2, EPCAM*	*APC*	*APC, AXIN2, BMPR1A, CHEK2, EPCAM,GREM1, MLH1, MSH2, MSH3, MSH6,MUTYH, NTHL1, PMS2, POLD1, POLE,PTEN, SMAD4, STK11, TP53*
Cost* (Patient-pay, not covered by medical aid)	299 US Dollars* + international referral service handling fee R950*		
TAT	~4 weeks		
Sample type	Blood (EDTA) Buccal swab available on request (Sample failure may occur. In rare occasions, a repeat sample may be requested)		
Additional benefits	Family variant testing at no additional charge, following pre-test counselling, for all blood relatives of patients who undergo gene or panel testing for a hereditary condition at Invitae and are found to have a pathogenic or likely pathogenic variant. The PathCare handling fee (R950) **will**, however, still apply. This order must be placed within 150 days of the original patient's test report.		
	Re-requisition: If you don't get the answers you need from the initial test, you can add additional genes or panels within the same clinical area within 150 days at no additional charge.		

** Costs are subject to change. Prices are correct and valid as of September 2023*