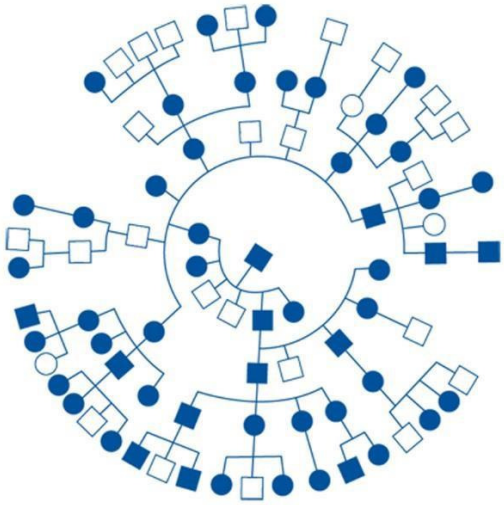
Annual Report

2021

The Netherlands Foundation for the Detection of Hereditary Tumors

Stichting Opsporing Erfelijke Tumoren (StOET)



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MISSION

The mission of the Foundation for the Detection of Hereditary Tumors (StOET) is to prevent unnecessary death by early detection of hereditary tumors. To achieve this, the national registry offers its support in the management of patients genetically predisposed to the development of cancer. The registry helps to identify all persons within an affected family and to provide information regarding their greatly increased risk of cancer and the importance of preventive surveillance examinations. It also monitors the quality of care and adherence to the necessary lifelong surveillance. In addition, the Foundation is a port of call for patients and families. The registry promotes scientific research with the joint aims of improving screening programs and increasing our understanding of hereditary tumors. All activities described in this annual report were designed to help accomplish the above mission.

1. GENERAL ISSUES

Monique van Leerdam as the Medical Director

Since January 2019, Monique van Leerdam MD, PhD, and gastroenterologist, has become the new medical director. She has a long record of excellent research in Lynch syndrome and polyposis syndromes. Prof. Dr van Leerdam is head of the Department of GI-Oncology at the National Cancer Institute (Antoni van Leeuwenhoek) in Amsterdam. In addition to her appointment as Medical Director of the registry, she is the head of the Family Cancer Clinic at Leiden University Medical Center.

Protection of privacy in accordance with new European legislation: AVG

The Registry keeps a record of medical data relating to patients and risk-bearing family members. The processing of such data has been subject to the General Data Protection Regulation (AVG) since May 25, 2018. The AVG sets out the conditions under which personal and medical data can be processed and also defines the rights of subjects involved. In agreement with the AVG, the STOET will only initiate registration once the person concerned has given written permission. In 2018 the Supervisory Committee for the Protection of Privacy was abolished and instead a privacy officer was appointed at the StOET, with a mandate to ensure that the rules on privacy are adhered to. Since December 2020 the StOET has a new privacy officer, Marie-José Bonthuis, with experience in other large database consortia. If a person registered with the StOET wishes to exercise his or her rights in accordance with the AVG, this can be done by sending a message to the following email address: privacy@stoet.nl.

Secure communication solutions

E-mail is an indispensable part of communication for the StOET and the specialists (and in some cases with patients). In 2019 ZorgMail Secure e-mail has been implemented which means that the StOET can receive and deliver e-mails with privacy-sensitive information in a the most secure environment possible.

European Society for Gastrointestinal Endoscopy (ESGE) guidelines

In 2019 the European Society for Gastrointestinal Endoscopy (ESGE) initiated two new guidelines regarding endoscopic surveillance of hereditary gastrointestinal tumors. The medical director of the StOET, Monique van Leerdam, was head of both guidelines. A pan-European group of experts performed the literature search, made a summary of the literature and wrote the guidelines. 1. Endoscopic Management of Lynch syndrome and familial risk of colorectal cancer: European Society of Gastrointestinal Endoscopy (ESGE) guideline.

2. Endoscopic management of polyposis syndromes: European Society of Gastrointestinal Endoscopy (ESGE) Guideline.

The European Hereditary Tumor Group

In 2006, the so-called Mallorca group was initiated by Hans Vasen and Gabriela Möslein. This group successfully developed an active network of specialists working in different fields, all of whom were involved in the prevention, diagnosis and treatment of hereditary GI tumor syndromes. The main aims of the group were (1) to conduct collaborative studies, (2) to establish guidelines and (3) to set up databases. Over the years these collaborations have led to numerous publications and guidelines, focusing mainly on Lynch syndrome and polyposis. The group also initiated the "Three Country Study" (3CS) (Christoph Engel et al.), which evaluated the effectiveness of colonoscopic surveillance by collecting the results of screening from LS registries in Germany, Finland and the Netherlands (see later in this report). Ten years into its existence, a decision was taken to formalize and transform the Mallorca group into a more open group which now also addresses other GI hereditary cancers. This group was named the European Hereditary Tumor Group (Chair: Gabriela Möslein). Due to the COVID pandemic there was no official meeting in 2020. In 2021 only a virtual meeting was organized. The meeting of the International hereditary working group; InSIGHT is postponed.

2. REGISTRATION

2.1 Registration of new family members

The number of subjects referred for registration has been stable for many years. Table 1 shows the current numbers of registered individuals, listed according to hereditary cancer syndrome.

Table 1. Number of individuals registered at the StOET on January 1st, 2021

Syndrome	Number of individuals registered 01-01-2021	Number of individuals registered 01-01-2021 but deceased
Lynch syndrome/ Familial Colorectal cancer	3724	530
Familial Adenomatous Polyposis/ poliposis	2582	461
Familial Atypical Multiple Mole Melanoma	4658	980
Familial prostate cancer	1308	517
Peutz-Jeghers syndrome	61	12

2.2. Reminder system

The StOET has a reminder system with the aim of guaranteeing the progress of lifelong screening. In practice this entails the sending of a message from the StOET to the treating specialist in which it is made clear that a certain patient is (again) eligible for screening examinations. The specialist then sends the result of the examination to the registry (or a copy of the letter to the general practitioner) and informs the StOET regarding scheduling of the next screening round.

In 2021 all specialists caring for persons registered at the StOET were informed in this way. If it emerged that a particular individual had withdrawn from screening, action was taken. First the

patient received a reminder to attend the examination from the specialist. In case of no response, the general practitioner was then asked to remind the patient of the importance of periodic examinations. This approach helps prevent the loss of patients from screening who might later present with complaints that in many cases are due to a carcinoma.

2.3 Information about the different hereditary syndromes.

All information about the different hereditary syndromes has been updated on the website (www.stoet.nl) over the last years and in 2021. This information is meant both for treating physicians as well as for patients. Updated information about familial prostate cancer will follow in 2022.

3. EVALUATION OF SURVEILLANCE

As stated in our mission, the registry promotes scientific research with the aim of improving surveillance programs. Below you will find studies related to surveillance conducted or published in 2021.

4. EDUCATION, PUBLICATIONS AND PATIENT INFORMATION

In the course of 2020 and 2021 due to the COVID19 pandemic many presentations and patient information days were cancelled.

The presentation for the Lynch Polyposis Patient association was organized as a virtual meeting in November 2020 and 2021. In addition, many articles were published with the aim of increasing knowledge regarding hereditary cancer (see below). The leaflets produced by the StOET on various hereditary forms of cancer were updated where necessary. The StOET website is updated regularly by Evelyn Groeneveld.

5 ORGANIZATION

5.1. Board

Dr. R. van Doorn (chairman), dermatologist, Leiden University Medical Center, Leiden
Dr. W.H. de Vos tot Nederveen Cappel, gastroenterologist, Isala Clinics, Zwolle
Prof. Dr. M. Mourits, gynaecologist, University Medical Centre Groningen, Groningen
Dr. A. Wagner, clinical geneticist, Erasmus Medical Centre, Rotterdam
Prof. Dr. P. Tanis, professor of colorectal surgery, Erasmus Medical Center, Rotterdam
Prof. Dr. J. Morreau, pathologist, Leiden University Medical Center, Leiden

5.2. Registry staff

Dr. M.E. van Leerdam, gastroenterologist, Medical Director
Drs. M. van Heck, organization, communication, finances (until March 2021)
I.S.J. van Leeuwen-Cornelisse, medical social worker
C. van der Kaa, registration Lynch syndrome
A. van Oostrum MSc, registration Lynch syndrome (until June 2021)
I.E.M. Voncken, registration Polyposis (until May 2021)
H.L. van Randeraad, registration Hereditary Melanoma and Hereditary Prostate cancer
E. Groeneveld, management assistant (as from January 2021)
L. van Leeuwen, registration Lynch syndrome (as from September 2021)
D. van Tol, registration Lynch syndrome (as from June 2021)

5.3. Data Privacy Officer
Mr. M.J. Bonthuis

5.4. Research Commission
Dr. P. van Duijvendijk, surgeon, Gelre Hospital, Apeldoorn
Prof. dr. E. Dekker, gastroenterologist, Amsterdam University Medical Centre, Amsterdam
Dr. A.M. Leliveld, oncological urologist, University Medical Centre Groningen, Groningen
Prof. Dr. M. Bekkenk, dermatologist, Amsterdam University Medical Centre, Amsterdam
S. ten Broeke, clinical geneticist in training, University Medical Centre Groningen, Groningen

6. PUBLICATIONS

Variation in the risk of colorectal cancer in families with Lynch syndrome: a retrospective cohort study.
International Mismatch Repair Consortium. Lancet Oncol. 2021 Jul;22(7):1014-1022.

The "unnatural" history of colorectal cancer in Lynch syndrome: Lessons from colonoscopy surveillance.
Ahadova A, Seppälä TT, Engel C, Gallon R, Burn J, Holinski-Feder E, Steinke-Lange V, Möslein G, Nielsen M, Ten Broeke SW, Laghi L, Dominguez-Valentin M, Capella G, Macrae F, Scott R, Hüneburg R, Nattermann J, Hoffmeister M, Brenner H, Bläker H, von Knebel Doeberitz M, Sampson JR, Vasen H, Mecklin JP, Møller P, Kloor M. Int J Cancer. 2021 Feb 15;148(4):800-Review.

Progress Report: New insights into the prevention of CRC by colonoscopic surveillance in Lynch syndrome.
Vasen HFA.Fam Cancer. 2022 Jan;21(1):49-56. Review.

Duodenal Adenomas and Cancer in MUTYH-associated Polyposis: An International Cohort Study.
Collaborative Group on Duodenal Polyposis in MAP, Thomas LE, Hurley JJ, Sanchez AA, Aznárez MR, Backman AS, Bjork J, Capella G, Clark SK, Colas C, Dekker E, Dolwani S, Ghorbanoghli Z, Gonn M, Gonzalez Romero S, Hes FJ, Jundi H, Kelland S, Latchford AR, Brito HL, Lynch PM, Meuser E, Mork ME, Mort M, Garcia MN, Nielsen M, Parc Y, Ricci MT, Saurin JC, Tuin KV, Vasen H, Vilar E, Vinet O, Vitellaro M, Walton SJ, West HD, Sampson JR.Gastroenterology. 2021 Feb;160(3):952-954.e4.

Genotype-phenotype correlations for pancreatic cancer risk in Dutch melanoma families with pathogenic CDKN2A variants.
Overbeek KA, Rodríguez-Girondo MD, Wagner A, van der Stoep N, van den Akker PC, Oosterwijk JC, van Os TA, van der Kolk LE, Vasen HFA, Hes FJ, Cahen DL, Bruno MJ, Potjer TP.J Med Genet. 2021 Apr;58(4):264-269. doi: 10.1136/jmedgenet-2019-106562. Epub 2020 Jun 1.PMID: 32482799 Free PMC article.

Associations of Height With the Risks of Colorectal and Endometrial Cancer in Persons With Lynch Syndrome.
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Clinical Perspective on Proteomic and Glycomic Biomarkers for Diagnosis, Prognosis, and Prediction of Pancreatic Cancer.
Hanna-Sawires RG, Schiphuis JH, Wuhrer M, Vasen HFA, van Leerdam ME, Bonsing BA, Mesker WE, van der Burgt YEM, Tollenaar RAEM.Int J Mol Sci. 2021 Mar 6;22(5):2655.

Report of the fifth meeting of the European Consortium 'Care for CMMRD' (C4CMMRD), Leiden, The Netherlands, July 6th 2019.
Suerink M, Wimmer K, Brugieres L, Colas C, Gallon R, Ripperger T, Benusiglio PR, Bleiker EMA, Ghorbanoghli Z, Goldberg Y, Hardwick JCH, Kloor M, le Mentec M, Muleris M, Pineda M, Ruiz-Ponte C, Vasen HFA.Fam Cancer. 2021 Jan;20(1):67-73.

A genetic variant in telomerase reverse transcriptase (TERT) modifies cancer risk in Lynch syndrome patients harbouring pathogenic MSH2 variants.
Wiik MU, Evans TJ, Belhadj S, Bolton KA, Dymerska D, Jagmohan-Changur S, Capellá G, Kurzawski G, Wijnen JT, Valle L, Vasen HFA, Lubinski J, Scott RJ, Talseth-Palmer BA.Sci Rep. 2021 May 31;11(1):11401.

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The Management of Peutz-Jeghers Syndrome: European Hereditary Tumour Group (EHTG) Guideline.
Wagner A, Aretz S, Auranen A, Bruno MJ, Cavestro GM, Crosbie EJ, Goverde A, Jelsig AM, Latchford A, Leerdam MEV, Lepisto A, Puzzono M, Winship I, Zuber V, Möslein G.J Clin Med. 2021 Jan 27;10(3):473. Review.

When and How To Use Endoscopic Tattooing in the Colon: An International Delphi Agreement.
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Can innovation in endoscopic therapy alter clinical outcomes in patients with familial adenomatous polyposis?
van Leerdam ME, Latchford A.Endosc Int Open. 2021 Aug 23;9(9):E1445-E1446.
Universal Immunohistochemistry for Lynch Syndrome: A Systematic Review and Meta-analysis of 58,580 Colorectal Carcinomas.
Eikenboom EL, van der Werf-'t Lam AS, Rodríguez-Girondo M, Van Asperen CJ, Dinjens WNM, Hofstra RMW, Van Leerdam ME, Morreau H, Spaander MCW, Wagner A, Nielsen M.Clin Gastroenterol Hepatol. 2022 Mar;20(3):e496-e507.

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Hanna-Sawires RG, Schiphuis JH, Wuhrer M, Vasen HFA, van Leerdam ME, Bonsing BA, Mesker WE, van der Burgt YEM, Tollenaar RAEM.

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