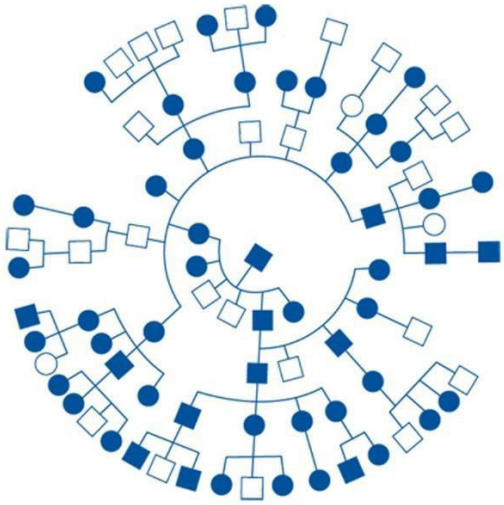
# Annual Report

# 2020

## 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 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.

## 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, 2020

| Syndrome | Number of individuals registered 01-01-2020 |
|---|---|
| Lynch syndrome | 3595 |
| Familial Adenomatous Polyposis | 3082 |
| Familial Atypical Multiple Mole Melanoma | 4645 |
| Hereditary prostate cancer | 1311 |
| Peutz-Jeghers syndrome | 50 |

### 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 2020 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) in 2019 and 2020. This information is meant both for treating physicians as well as for patients. Updated information about hereditary prostate cancer will follow in 2021.

## 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 2020.

Ykema BLM, Nagtegaal ID, Kuhlmann K, van Berkel AM, van Leerdam ME; Dutch T1 CRC Working Group. Compliance with mismatch repair testing in pT1 colorectal cancer diagnosed before the age of 70 years. Virchows Arch. 2021 Online ahead of print.

Monahan KJ, Bradshaw N, Dolwani S, Desouza B, Dunlop MG, East JE, Ilyas M, Kaur A, Lalloo F, Latchford A, Rutter MD, Tomlinson I, Thomas HJW, Hill J; Hereditary CRC guidelines eDelphi consensus group. 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(3):411-444

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.The Management of Peutz-Jeghers Syndrome: European Hereditary Tumour Group (EHTG) Guideline. J Clin Med. 2021;10:473.

Goggins M, Overbeek KA, Brand R, Syngal S, Del Chiaro M, Bartsch DK, Bassi C, Carrato A, Farrell J, Fishman EK, Fockens P, Gress TM, van Hooft JE, Hruban RH, Kastrinos F, Klein A, Lennon AM, Lucas A, Park W, Rustgi A, Simeone D, Stoffel E, Vasen HFA, Cahen DL, Canto MI, Bruno M; International Cancer of the Pancreas Screening (CAPS) consortium. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. Gut. 2020 Jan;69(1):7-17.

Arne Gc Bleijenberg, Joep Eg IJspeert, Yasmijn J van Herwaarden, Sabela Carballal, María Pellisé, Gerhard Jung, Tanya M Bisseling, Iris D Nagtegaal, Monique E van Leerdam, Niels van Lelyveld, Xavier Bessa, Francisco Rodríguez-Moranta, Barbara Bastiaansen, Willemijn de Klaver, Liseth Rivero, Manon Cw Spaander, Jan Jacob Koornstra, Luis Bujanda, Francesc Balaguer, Evelien Dekker. Personalised surveillance for serrated polyposis syndrome: results from a prospective 5-year international cohort study. Gut. 2020;69(1):112-121

Christoph Engel, Aysel Ahadova, Toni T Seppälä, Stefan Aretz, Marloes Bigirwamungu-Bargeman, Hendrik Bläker, Karolin Bucksch, Reinhard Büttner, Wouter T de Vos Tot Nederveen Cappel, Volker Endris, Elke Holinski-Feder, Stefanie Holzapfel, Robert Hüneburg, Maarten A J M Jacobs, Jan J Koornstra, Alexandra M Langers, Anna Lepistö, Monika Morak, Gabriela Möslein, Päivi Peltomäki, Kirsi Pylvänäinen, Nils Rahner, Laura Renkonen-Sinisalo, Karsten Schulmann, Verena Steinke-Lange, Albrecht Stenzinger, Christian P Strassburg, Paul C van de Meeberg, Mariette van Kouwen, Monique van Leerdam, Deepak B Vangala, Juda Vecht, Marie-Louise Verhulst, Magnus von Knebel Doeberitz, Jürgen Weitz, Silke Zachariae, Markus Loeffler, Jukka-Pekka Mecklin, Matthias Kloor, Hans F Vasen, German HNPCC Consortium, the Dutch Lynch Syndrome Collaborative Group; Finnish Lynch Syndrome Registry. Associations of Pathogenic Variants in MLH1, MSH2, and MSH6 With Risk of

Colorectal Adenomas and Tumors and With Somatic Mutations in Patients With Lynch Syndrome. Gastroenterology. 2020;158(5):1326-1333

## 4. EDUCATION, PUBLICATIONS AND PATIENT INFORMATION

In the course of 2020 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. 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 Magdalena van Heck and Evelyn Groeneveld.

## 5. OTHER STUDIES/ PUBLICATIONS

Myriam Chalabi, Lorenzo F Fanchi, Krijn K Dijkstra, José G Van den Berg, Arend G Aalbers, Karolina Sikorska, Marta Lopez-Yurda, Cecile Grootscholten, Geerard L Beets, Petur Snaebjornsson, Monique Maas, Marjolijn Mertz, Vivien Veninga, Gergana Bounova, Annegien Broeks, Regina G Beets-Tan, Thomas R de Wijkerslooth, Anja U van Lent, Hendrik A Marsman, Elvira Nuijten 8, Niels F Kok, Maria Kuiper, Wieke H Verbeek, Marleen Kok, Monique E Van Leerdam, Ton N Schumacher, Emile E Voest, John B Haanen. Neoadjuvant immunotherapy leads to pathological responses in MMR-proficient and MMR-deficient early-stage colon cancers. Nature Medicine. 2020;26(4):566-576

Jasper L A Vleugels, Lianne Koens, Marcel G W Dijkgraaf, Britt Houwen, Yark Hazewinkel, Paul Fockens, Evelien Dekker, DISCOUNT study group. Suboptimal endoscopic cancer recognition in colorectal lesions in a national bowel screening programme. Gut. 2020;69(6):977-980

Miriam P van der Meulen, Ida J Korfage, Else-Mariëtte B van Heijningen, Harry J de Koning, Monique E van Leerdam, Evelien Dekker, Iris Lansdorp-Vogelaar, working group on the guideline for colonoscopy surveillance. Interpretation and adherence to the updated risk-stratified guideline for colonoscopy surveillance after polypectomy - a nationwide survey. Endoscopy International Open. 2020;8(10):E1405-E1413

Arne G C Bleijenberg, Monique E van Leerdam, Marloes Bargeman, Jan Jacob Koornstra, Yasmijn J van Herwaarden, Manon Cw Spaander, Silvia Sanduleanu, Barbara A J Bastiaansen, Erik J Schoon, Niels van Lelyveld, Evelien Dekker, Joep E G IJspeert. Substantial and sustained improvement of serrated polyp detection after a simple educational intervention: results from a prospective controlled trial. Gut. 2020;69(12):2150-2158

Bleijenberg AG, IJspeert JE, van Herwaarden YJ, Carballal S, Pellisé M, Jung G, Bisseling TM, Nagetaal ID, van Leerdam ME, van Lelyveld N, Bessa X, Rodríguez-Moranta F, Bastiaansen B, de Klaver W, Rivero L, Spaander MC, Koornstra JJ, Bujanda L, Balaguer F, Dekker E. Personalised surveillance for serrated polyposis syndrome: results from a prospective 5-year international cohort study. Gut. 2020;69:112-121.

Brouwer JGM, Newcomb PA, Bisseling TM, Figueiredo JC, Hopper JL, Jenkins MA, Koornstra JJ, Lindor NM, Vasen HFA, Win AK, Kampman E, van Duijnhoven FJB. Height and Colorectal and

Endometrial Cancer Risk for Persons with Lynch Syndrome. Am J Epidemiol. 2020. Online ahead of print.

Eijkelboom AH, Brouwer JGM, Vasen HFA, Bisseling TM, Koornstra JJ, Kampman E, van Duijnhoven FJB. Diet quality and colorectal tumor risk in persons with Lynch syndrome.
Cancer Epidemiol. 2020 Online ahead of print.

Terlouw D, Suerink M, Singh SS, Gille HJJP, Hes FJ, Langers AMJ, Morreau H, Vasen HFA, Vos YJ, van Wezel T, Tops CM, Ten Broeke SW, Nielsen M. Declining detection rates for APC and biallelic MUTYH variants in polyposis patients, implications for DNA testing policy. Eur J Hum Genet. 2020 Feb;28(2):222-230.

Blatter R, Tschupp B, Aretz S, Bernstein I, Colas C, Evans DG, Genuardi M, Hes FJ, Hüneburg R, Järvinen H, Lalloo F, Moeslein G, Renkonen-Sinisalo L, Resta N, Spier I, Varvara D, Vasen H, Latchford AR, Heinimann K. Disease expression in juvenile polyposis syndrome: a retrospective survey on a cohort of 221 European patients and comparison with a literature-derived cohort of 473 SMAD4/BMPR1A pathogenic variant carriers. Genet Med. 2020 Sep;22(9):1524-1532.

Daans CG, Ghorbanoghli Z, Velthuizen ME, Vasen HFA, Offerhaus GJA, Lacle MM, Siersema PD, Ausems MGEM, Boonstra JJ. Increased prevalence of Barrett's esophagus in patients with MUTYH-associated polyposis (MAP). Fam Cancer. 2020 Apr;19(2):183-187.

## 6. ORGANIZATION

### 6.1. Board

Prof. Dr. W. Bemelman, chair, surgeon, Amsterdam Medical Center, Amsterdam
Prof. Dr. R. Hofstra, Head, Department of Clinical Genetics, Erasmus Medical Center, Rotterdam
Dr. R. van Doorn, Department of Dermatology, Leiden University Medical Center, Leiden
Dr. de Vos tot Nederveen Cappel, gastroenterologist, Isala Clinics, Zwolle
Prof. Dr. M. Mourits, gynaecologist, University Medical Centre Groningen, Groningen

### 6.2. Registry staff

Dr. M.E. van Leerdam, gastroenterologist, Medical Director
Drs. M. van Heck, organization, communication, finances
I.S.J. van Leeuwen-Cornelisse, medical social worker
C. van der Kaa, registration Lynch syndrome
A. van Oostrum MSc, registration Lynch syndrome
I.E.M. Voncken, registration Polyposis
H.L. van Randeraad, registration Hereditary Melanoma and Hereditary Prostate cancer

### 6.3. Data Privacy Officer

Mr. I. de Vries until 1/12/2020
Mr. M.J. Bonthuis starting from 1/1/2021

### 6.4. Research Commission

Dr. P. van Duijvendijk, surgeon, Gelre Hospital, Apeldoorn
Prof. dr. E. Dekker, gastroenterologist, AMC, Amsterdam
Dr. R. van Doorn, dermatologist, Leiden University Medical Centre, Leiden
Dr. A. Wagner, clinical geneticist, Erasmus Medical Center, Rotterdam

## ENCLOSURES

1. Presentations

1. ESGE meeting (virtual) Berlin April 2020; cancelled. Management of hereditary CRC syndromes.
2. Medicamenteuze behandel opties voor FAP en Lynch syndroom