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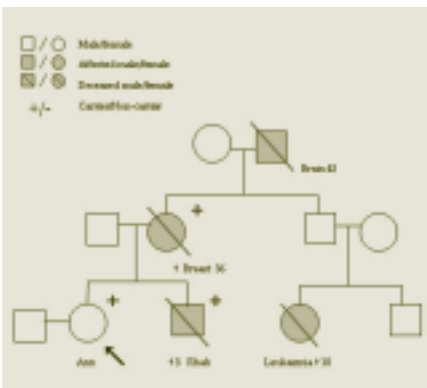


Figure 3: Example of a LFS pedigree

Publications

Ahmed AKJ, Hahn DEE, Hage JJ, Bleiker EMA, Woerdeman LAE. *Temporary banking of the nipple-areola-complex in 97 skin sparing mastectomies. Plastic and Reconstructive Surgery (in press)*

Douma KF, Bleiker EM, Aaronson NK, Cats A, Gerritsma MA, Gundy CM, Vasen HF. *Long-term compliance with endoscopic surveillance for familial adenomatous polyposis. Colorectal Dis 2010;12:1198-1207*

PSYCHOSOCIAL ISSUES IN CANCER GENETICS

This research line is being conducted in close collaboration with the NKI-AVL family cancer clinic. It comprises a number of studies which are focused on two psychosocial themes in genetic counseling for cancer: 1) the uptake and long-term psychosocial impact of risk-reducing behavior.; and 2) early detection of psychosocial problems and the development of psycho-educational interventions.

Psychosocial aspects of genetic testing in families at high risk of multiple tumors at various sites and ages The aim of this 4 year, multi-center, cross-sectional study is to investigate the uptake of genetic testing for Li-Fraumeni Syndrome (LFS) and Von Hippel-Lindau Disease (VHL), the psychosocial consequences of (not) undergoing genetic testing, and compliance with recommended surveillance programs. Data collection has been completed. In total, 243 individuals (78%) completed a self-report questionnaire.

The [study on LFS families](#) included 18 families with a p53 germline mutation. Eligible family members were invited to complete a self-report questionnaire assessing motives for (not) undergoing genetic testing, LFS-related distress and worries, and health-related quality of life. Uptake of presymptomatic testing was 55% (65/119). Of the total group, 23% reported clinically relevant levels of LFS-related distress. Carriers were not significantly more distressed than non-carriers or than those with a 50% risk who did not undergo genetic testing. Those with a lack of social support were more prone to report clinically relevant levels of distress (OR 1.3; 95% CI 1.0-1.5). Thus, although preventive and treatment options for LFS are limited, more than half of the family members from known LFS families choose to undergo pre-symptomatic testing. An unfavorable genetic test result, in general, does not cause adverse psychological effects. Nonetheless, it is important to note that a substantial proportion of individuals, irrespective of their carrier status, exhibit clinically relevant levels of distress which potentially warrant psychological support.

In the [study on VHL](#), we assessed compliance with the surveillance program for VHL. Of the 84 (77%) participants, 78 (93%) indicated having received an advice to undergo periodic surveillance. Of these, 71 (91%) reported being fully compliant with that advice. In 64% of the cases, this advice was only in part conform the published guidelines. Based on the medical files, between one-quarter and one-third of individuals did not undergo surveillance as recommended in the guidelines for central nervous system (CNS) lesions, and one-half for visceral lesions. Screening delay for CNS lesions was associated with 'hospital' and 'advice for surveillance that deviates from the guidelines' ($p < .01$). These results indicate that the majority of the participants report having received advice to undergo periodic surveillance. They also report being fully compliant with that advice. However, for the majority, the advice given is only partially consistent with published guidelines. Furthermore, delay in surveillance was observed for a substantial number of individuals. Efforts should be undertaken to stimulate guideline-based screening advice, and to minimize screening delay.

Screening for psychosocial problems at the family cancer clinic The aim of this 4 year KWF-study is to develop and evaluate a screening questionnaire as an aid in identifying individuals experiencing significant psychosocial problems associated with cancer genetic counseling. In 2009, this multidimensional questionnaire was developed according to EORTC guidelines for questionnaire module development: 1) generation of relevant issues, 2) operationalization of these issues into a set of items, and 3) questionnaire pre-testing. In 2010, this questionnaire has been evaluated for its reliability, validity, sensitivity, specificity and positive predictive value for detecting psychosocial problems and psychosocial support needs. For this validation study, new counselees who attend the NKI-AVL family cancer clinic for purposes of counseling and testing are invited to complete the screening questionnaire (by means of a touch screen computer) just prior to their second visit to the family cancer clinic (thus after an informative intake session), and at follow-up (three weeks after their final counseling). At both assessment points, the counselees are also being interviewed by a trained psychosocial worker who uses a semi-structured interview ('gold standard') to determine the problem areas that warrant further services. In total 130 have now completed both the screening questionnaire and the clinical interview with a

psychosocial worker. When this screening questionnaire proves to be sufficiently valid, a trial will be conducted, to evaluate the effectiveness of the questionnaire on: decreasing onco-genetic related psychosocial problems, and increasing effective communication between counsellors and clients, the awareness of problems of counselees, and appropriate referrals.

Preventive total gastrectomy The aim of this cross-sectional, multi-center study is to investigate the experiences with, and consequences of gastroscopy screening and prophylactic total gastrectomy in CDH1 mutation carriers. Mutations in the CDH1 gene are associated with a 70% lifetime risk for diffuse gastric cancer and an additional 40% risk for lobular breast cancer in women. The following research questions are being addressed: (1) What is the impact of prophylactic gastrectomy on quality of life and future planning? (2) What factors influence the decision and timing of prophylactic gastrectomy? (3) Which sociodemographic, clinical and psychological factors are associated with quality of life after gastrectomy?, and (4) What can we recommend to improve the health care in individuals from CDH1 families? Six families were identified with a CDH1 mutation. All individuals with a CDH1 gene mutation have been invited to complete a self-report questionnaire and to participate in a semi-structured interview. A comparison group of individuals who underwent a total gastrectomy because of cancer are also being invited to complete the self-report questionnaire. In total, 25 of the 31 CDH1 mutation carriers returned the questionnaires (81%). Of these, 20 individuals had undergone prophylactic total gastrectomy. First results show that 'the level of energy' is the most important factor determining functioning and quality of life after prophylactic gastrectomy: 65% of the participants experienced reduced excessive fatigue. Shortly after the surgery, difficulties in food-intake led to substantial weight loss. Respondents consider the dumping syndrome and reduced appetite syndrome as the most impairing functional complaints. About 40% report moderate to severe impairment in daily activities. Respondents are, in general, satisfied with the multidisciplinary health-care that is offered to them, however, they only stated that they could have benefited from better dietary counseling.

Surveillance of the pancreas in high risk individuals The aim of this study is to investigate the psychological burden of participating in a pancreatic cancer (PC-) surveillance program. Since 2006, a multi-center prospective study is investigating the effectiveness of PC-surveillance (EUS and MRI) in high-risk individuals. High-risk individuals are defined as (1) first degree relatives (FDR) of patients with familial pancreatic cancer (FPC) and (2) carriers of a PC-prone gene mutation. PC-prone gene mutations include CDKN2A (Familial Atypical Multiple Mole Melanoma (FAMMM)-syndrome), LKB1 (Peutz Jegers syndrome), BRCA1 (Hereditary Breast and Ovarian Cancer (HBOC) syndrome), BRCA2 (HBOC), and p53 (Li-Fraumeni syndrome). Carriers of a BRCA1/2 mutation or p53 mutation are only eligible when they meet additional criteria. In 2009, a psychosocial study arm was added to this multicenter surveillance study. The specific research questions of the psychosocial arm, are: 1) What is the perceived burden of participation in a PC-surveillance program, 2) what are the motivations to participate in such a program, 3) to what extent are those participating in the surveillance program worried about developing cancer, and 4) which factors are associated with anxiety experienced after an EUS-MRI-based surveillance program. Currently, with a cross sectional design, individuals are invited to complete a questionnaire four weeks after receiving their surveillance results. Sixty-nine individuals (85%) completed the questionnaire (54% female; mean age 52 yrs). Surveillance was reported as "very to extremely uncomfortable" by 15% for MRI, and 12% for EUS. Most frequently reported reason to participate was that surveillance might lead to PC detection in a curable stage. In 27 respondents (39%) EUS and/or MRI detected an abnormality including cysts and 1 suspicious solid lesion, which was resected. In total 29% is "often" or "almost always" concerned about developing cancer. Six respondents (9%) have clinical levels of depression and/or anxiety. Perceived advantages of surveillance outweighed disadvantages according to 88% of respondents. The finding of 'abnormal results', resulting in a shorter screening-interval (n=7) or surgery (n=1) was not related to a higher level of anxiety. In the total group, levels of anxiety and depression are comparable to those of the general population. From a psychosocial point of view PC surveillance in high-risk individuals seems feasible.

Publications (continued)

Douma KF, Bleiker EM, Vasen HF, Gundy CM, Aaronson NK. *Quality of life and consequences for daily life of familial adenomatous polyposis (FAP) family members. Colorectal Dis* 2010

Douma KF, Bleiker EM, Vasen HF, Gundy CM, Gerritsma MA, Aaronson NK. *Psychological distress and quality of life of partners of individuals with familial adenomatous polyposis. Psychooncology* 2010

Lammens CR, Bleiker EM, Aaronson NK, Wagner A, Sijmons RH, Ausems MG, Vriends AH, Ruijs MW, van Os TA, Spruijt L, Gomez Garcia EB, Cats A, Nagtegaal T, Verhoef S. *Regular surveillance for Li-fraumeni syndrome: advice, adherence and perceived benefits. Fam Cancer* 2010;9:647-654

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Lammens CR, Bleiker EM, Verhoef S, Hes FJ, Ausems MG, Majoor-Krakauer D, Sijmons RH, van der Luijt RB, van den Ouweland AM, van Os TA, Hoogerbrugge N, Gomez Garcia EB, Dommering CJ, Gundy CM, Aaronson NK. *Psychosocial impact of Von Hippel-Lindau disease: levels and sources of distress. Clin Genet* 2010;77:483-491

Lammens CRM. *Living with Li-Fraumeni Syndrome & Von Hippel-Landau disease. Thesis* 2010

Nieuwenhuis MH, Douma KF, Bleiker EM, Bemelman WA, Aaronson NK, Vasen HF. *Female fertility after colorectal surgery for familial a denomatous polyposis: a nationwide cross-sectional study. Ann Surg* 2010;252:341-344

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