ORIGINAL ARTICLE

The Upgrade of Hereditary Cancer Surveillance Schedule by Valka District Population Screening Data

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Summary

Introduction. The concept of hereditary cancer is one of the most important achievements in modern oncology. It has major scientific implications as well as high practical value in surveillance, prevention and adjustment of treatment for hereditary and familial malignancies. Identification of the persons-at-risk allows recommending a follow-up schedule for timely diagnostics of the corresponding cancers.

Aim of the Study is to evaluate the need for hereditary cancer surveillance program in Latvia and to adjust the surveillance schedule by population screening data.

Materials and methods. The study was performed as population screening in the Valka district, evaluating the family cancer history of 18642 respondents. Hereditary cancers were diagnosed by internationally accepted clinical criteria. Descriptive statistical analysis was carried out by CIA software.

Results. There were 885 persons, fulfilling the clinical diagnostic criteria of hereditary and familial cancer syndromes. The full spectrum of hereditary malignancies was identified thus indirectly characterising the familial background of oncological diseases in the local population. The cancer burden among blood relatives was high for all syndromes, exceeding 8.6%. The mean age of cancer diagnostics was significantly different among the syndromes, ranging 38.0–72.0 years.

Conclusions. The presence of familial background in all most frequent cancer locations and the high cancer burden in the affected kindreds justify the need for familial cancer surveillance. The data about the age of cancer manifestation can be used to adjust the follow-up schedule for most syndromes. Specific recommendations are elaborated and described in the article.

Key words: hereditary cancer, population screening, cancer surveillance.

INTRODUCTION

At present, it is considered that 5–10% of tumours might have hereditary basis – an inherited gene mutation that significantly increase the risk of cancer (12). Hereditary cancers frequently arise early in life (6). In order to prevent hereditary cancer or at least to diagnose it early, follow-up programs could be offered to persons subjected to increased hereditary cancer risk.

AIM OF THE STUDY

To evaluate the need for hereditary cancer surveillance program in Latvia and to adjust the surveillance schedule by population screening data.

MATERIALS AND METHODS

The investigation was designed as population screening for hereditary cancer within the frames of the project “The development of hereditary cancer prophylaxis in Estonia and Latvia” co-financed by European Union Interreg IIIB Neighbourhood programme. The population screening was carried out in the Valka district. There were 18642 respondents in the study (76.6% of the Valka district adult population). Adult

persons voluntarily filled out questionnaire concerning family cancer history. No recruitment restrictions were applied for upper age level, gender, ethnicity, presence or absence of cancer, cancer stage and other diagnoses. The participants of the study were asked if his / her relatives (father, mother, grandparents, siblings, children, grandchildren, aunts, uncles and other blood relatives) have had any tumour. If any positive answers were given the participants were asked about the localisation of the tumour. The data about the age of patient at the time of tumour diagnosis were obtained. If the patient has died because of the tumour the death age was ascertained as well. Additional questions were asked about the treatment modalities (e.g. radiation therapy and chemotherapy, extent of operation) of affected persons in order to verify the presence of malignant tumour and to specify its location.

The analysis was performed in the Hereditary Cancer Institute. Cases corresponding to the international diagnostic criteria of any hereditary cancer syndrome (Table 1) were identified and invited for additional medical consultation.

Table 1. The applied diagnostic criteria of hereditary cancer

Hereditary syndrome	Diagnostic criteria
Definitive hereditary non-polyposis colorectal cancer (HNPCC)	Amsterdam II criteria: <ul style="list-style-type: none"> • At least 3 relatives affected by HNPCC associated cancer (colorectal, endometrial, small bowel, ureteric, renal pelvis); at least one should be first-degree relative of the other two AND • At least two successive generations should be affected AND • At least one cancer should be diagnosed before age 50 AND • Familial adenomatous polyposis (FAP) should be excluded
Suspected HNPCC (sHNPCC)	At least 2 first degree relatives with HNPCC associated cancer (colorectal, endometrial, small bowel, ureteric, renal pelvis) AND at least one cancer is diagnosed before age 50
Familial colorectal cancer, variety 1 (FCC1)	Colorectal cancer in at least 2 first degree relatives after the age of 50. HNPCC and FAP should be excluded
Familial colorectal cancer, variety 2 (FCC2)	Colorectal cancer in at least 2 second degree relatives at any age. HNPCC and FAP should be excluded
Hereditary breast cancer (HBC)	At least 3 breast cancer patients in family at any age AND one of those patients is first degree relative to other two or second degree relative through male
Suspected HBC, variety 1 (sHBC1)	At least one of the following criteria: 1) Breast cancer diagnosed under the age of 40; 2) Medullary or atypical medullary breast cancer; 3) Male breast cancer; 4) Bilateral breast cancer, one of them diagnosed under the age of 50.
Suspected HBC, variety 2 (sHBC2)	Two breast cancers among first degree relatives (or second through male) at any age
Hereditary ovarian cancer (HOC)	At least 3 ovarian cancer cases in family at any age AND one of those patients is first degree relative to other two or second degree relative through male
Suspected HOC (sHOC)	Two ovarian cancer cases among first degree relatives
Hereditary breast/ovarian cancer (HBOC)	At least 3 breast/ovarian cancer patients in family at any age AND one of those patients is first degree relative to other two or second degree relative through male
Suspected HBOC, variety 1 (sHBOC1)	Breast and ovarian cancer in the same individual at any age
Suspected HBOC, variety 2 (sHBOC2)	Two breast or ovarian cancers among first degree relatives (or second through male) at any age
Hereditary endometrial cancer (HEC)	At least 3 first degree relatives with endometrial cancer and at least one of them diagnosed before age of 50
Suspected HEC (sHEC)	Two first degree relatives with endometrial cancer and at least one of them diagnosed before age of 50
Familial endometrial cancer (FEC)	At least 3 first degree relatives with endometrial cancer at any age
Suspected FEC, variety 1 (sFEC1)	At least 2 first degree relatives with endometrial cancer at any age
Suspected FEC, variety 2 (sFEC2)	At least 2 second degree relatives with endometrial cancer at any age
Familial lung cancer (FLC)	At least 3 first degree relatives with lung cancer at any age
Suspected FLC (sFLC)	Two first degree relatives with lung cancer at any age
Hereditary stomach cancer (HSC)	At least 3 first degree relatives with stomach cancer at any age
Suspected HSC (sHSC)	Two first degree relatives with stomach cancer at any age
Hereditary prostate cancer (HPC)	At least 3 blood relatives with prostate cancer at any age OR 2 blood relatives with prostate cancer diagnosed before age of 55 in both of them
Suspected HPC (sHPC)	Two blood relatives with prostate cancer at any age OR Case of prostate cancer diagnosed before age of 55
Familial brain tumour (FBtT)	At least 3 first degree relatives with brain tumour at any age
Suspected FBtT (sFBtT)	Two first degree relatives with brain tumour at any age

Familial haematological tumours (FHemT)	At least 3 first degree relatives with malignant haematological tumour at any age
Suspected FHemT (sFHemT)	Two first degree relatives with malignant haematological tumour at any age
Familial pancreatic tumour (FPan)	At least 2 first-degree relatives with pancreatic tumour or melanoma at any age
Familial cancer of urinary bladder (FBlaC)	At least 3 first degree relatives with urinary bladder cancer at any age
Suspected FBlaC (sFBlaC)	Two first degree relatives with urinary bladder cancer at any age

The diagnosis was updated according to additional data presented by participants. Additional data obtained during consultations were applied in order to identify inter-related families. In this way, the possibility to include any person repeatedly in the analysis due to several kindred relationships was eliminated. Written preventive recommendations were given as well.

The following approach to analysis was undertaken. After the respective cases were diagnosed by clinical hereditary/ familial cancer syndrome, the population frequency was calculated as the ratio between the number of diagnosed cases and the studied group. In order to characterise the course of malignant tumour, the data about the age of tumour diagnostics and age of tumour-related death were retrieved from the questionnaires and subjected to descriptive statistical analysis using CIA software (1). The cancer burden was calculated in a descriptive approach as the ratio between affected persons and the whole number of blood relatives in the affected blood line. The estimates were performed for all hereditary and familial cancer syndromes. In cases when the diagnosis was substantiated on peculiar characteristics of a single case in accordance with the criteria provided in Table 1, the number of relatives was counted in the whole kindred.

The project was accepted by the Central Committee of Medical Ethics. Written informed consent was obtained from all participants.

RESULTS

Analysing 18642 family cancer histories, 885 persons fulfilled the clinical diagnostic criteria of hereditary cancer syndromes. The syndromes were characterised by the population frequency, the index cancer burden in blood relatives, age of tumour diagnostics and age of tumour-related death as shown in Table 2. The population frequency of individual syndromes ranged 0.005 – 0.628%. The most common cancers as breast, lung, colorectal and gastric cancer were characterised also by the highest population frequencies of the respective hereditary cancer syndromes, reaching 1.181% for breast-involving syndromes, 0.569% for familial lung cancer, 0.510% for hereditary and familial gastric cancer and 0.273% for colorectal cancer-involving syndromes. The index cancer burden was generally high invariably exceeding 8.6% (in sHBC1) and reaching high values in common syndromes: 30.1% in HNPCC, 25.5% in familial lung cancer and 25.2% in hereditary stomach cancer. In combination with the mostly close values of the age of cancer diagnostics and age of tumour-related death, the high cancer burden confirmed the significance of the problem. The cancer burden was also evidently greater than the cumulative incidence of the respective tumours in EU population (2). The frequency of non-index cancers in the identified pedigrees also was analysed. In contrast to the index cancer burden, the frequency of breast, ovarian cancer or brain tumours in HNPCC pedigrees did not exceed the cumulative incidence in EU (2). The brain tumour burden was 0.7%; (95% CI = 0.1–0.3%) in HNPCC and 0.8% (95% CI = 0.2–2.7%) in sHNPCC. No ovarian cancer cases were reported in HNPCC, but in sHNPCC the ovarian cancer burden in female blood relatives was 0.7% (0.1–4.1%). The breast cancer burden in females was 1.2% (95% CI = 0.2–6.4%) in HNPCC and 3.0% (95% CI = 1.2–7.4%) in sHNPCC.

Table 2. Characteristics of hereditary and familial cancer syndromes in local population

Syndrome	PF	Cancer burden, %		Age of diagnosis, years		Age of death, years	
		F	95% CI	Interval	Mean (95% CIM)	Interval	Mean (95% CIM)
HBC	0.011	40.0 ¹	19.8–64.3 ¹	40–55	47.5 (37.1–57.8)	50–60	54.7 (50.0–59.4)
sHBC1	0.628	8.6	7.2–10.2	20–70	38.0 (36.2–39.7)	26–78	44.7 (41.7–47.7)
sHBC1	0.628	16.3 ¹	13.8–19.1 ¹	20–70	38.0 (36.2–39.7)	26–78	44.7 (41.7–47.7)
sHBC2	0.343	31.8 ¹	27.5–36.4 ¹	25–82	51.8 (48.9–54.6)	25–66	60.9 (56.7–65.1)
HBOC	0.011	60.0 ¹	31.3–83.2 ¹	34–82	61.0 (46.9–75.0)	58–85	71.4 (54.9–87.9)
sHBOC1	0.032	19.3 ¹	9.2–36.3 ¹	40–60	48.8 (44.2–53.3)	47–69	54.3 (42.3–66.3)
sHBOC2	0.156	30.8 ¹	25.0–37.3 ¹	18–86	56.6 (51.8–61.4)	23–87	66.1 (61.2–71.0)
HOC	0.005	33.3 ¹	12.1–64.6 ¹	34–70	49.7 (4.0–95.4)	72	72
sHOC	0.021	36.4 ¹	19.7–57.0 ¹	45–70	54.2 (46.4–61.9)	47–72	57.2 (50.1–64.3)
HNPCC	0.059	30.1	23.3–38.0	30–77	54.2 (50.2–58.2)	28–89	61.7 (54.2–69.2)
CRC	0.107	15.8	10.7–22.5	36–77	59.3 (53.8–64.8)	28–89	61.5 (52.9–70.0)
Ut		22.4 ¹	14.8–32.3 ¹	30–65	48.4 (43.4–53.4)	37–72	NA
sHNPCC		15.5	11.6–20.3	27–82	53.7 (49.1–58.3)	28–88	55.5 (49.5–61.5)
CRC	0.107	10.6	7.4–14.8	28–82	55.2 (49.1–61.3)	32–88	56.7 (49.9–63.5)
Ut		9.6	5.7–15.8 ¹	27–72	50.5 (43.0–58.0)	28–73	51.2 (33.1–69.3)
FCC	0.107	17.0	12.8–22.3	41–89	72.0 (67.3–76.7)	52–90	76.3 (73.1–79.5)
HEC	0.027	41.5 ¹	27.8–56.6 ¹	40–75	52.1 (47.2–57.0)	44–76	57.7 (49.6–65.8)
sHEC	0.139	32.2 ¹	25.7–39.4 ¹	30–81	48.5 (44.4–52.6)	35–87	58.7 (53.6–63.8)
FEC/ sFEC1	0.139	30.0 ¹	23.8–37.1 ¹	52–90	66.2 (63.5–69.9)	54–91	72.4 (69.4–75.4)
sFEC2	0.048	32.4 ¹	22.4–44.2 ¹	26–82	57.6 (49.9–65.3)	26–83	63.3 (54.7–71.9)
FLC d/s	0.569	18.4	16.4–20.7	18–90	57.9 (55.9–59.9)	13–90	61.2 (58.5–62.1)
FLC	0.070	25.5	19.3–32.8	35–78	56.0 (53.0–59.0)	36–79	57.1 (54.1–60.1)
sFLC	0.499	17.2	15.0–19.7	18–90	58.5 (56.1–60.9)	13–90	61.2 (59.1–63.3)
HSC	0.113	25.2	20.6–30.4	30–83	56.9 (53.4–66.3)	30–90	58.3 (55.3–61.3)
sHSC	0.397	16.0	13.8–18.5	34–95	62.5 (60.1–64.8)	37–96	65.6 (63.4–67.6)
HPC d/s.	0.118	22.2 ²	16.5–29.0 ²	35–75	57.7 (53.3–62.1)	37–80	60.7 (55.0–66.4)
HPC	0.005	21.4 ²	7.6–47.6 ²	70–74	72.0 (67.0–76.9)	76	NA
sHPC	0.113	22.2 ²	16.4–29.4 ²	35–75	56.8 (52.8–60.8)	59.7	54.6–64.8
FBlaC	0.064	22.8	14.9–33.2	60–87	70.7 (66.7–74.7)	65–92	75.7 (71.6–79.8)
FHemT	0.091	16.3	12.1–21.2	3–88	47.5 (38.9–56.1)	4–86	49.8 (40.5–59.1)
FPan	0.054	14.7	9.1–22.9	51–72	61.6 (57.3–65.9)	51–83	63.4 (58.2–68.6)
FBtT d/s.	0.102	16.5	12.5–21.5	2–77	43.9 (35.0–52.8)	2–77	47.8 (39.7–55.9)
FBtT	0.016	32.3	18.6–49.9	59–60	59.7 (58.2–61.2)	50–65	59.7 (54.3–65.1)
sFBtT	0.086	14.4	10.4–19.5	2–77	41.8 (32.0–51.5)	2–77	45.2 (35.9–54.5)

¹ in female

² in male

Abbreviations in the Table: PF, population frequency; F, frequency; CI, confidence interval; CIM, confidence interval for the mean; HBC, hereditary breast cancer; sHBC1, suspected hereditary breast cancer, variety 1; sHBC2, suspected hereditary breast cancer, variety 2; HBOC, hereditary breast ovarian cancer; sHBOC1, suspected hereditary breast ovarian cancer, variety 1; sHBOC2, suspected hereditary breast ovarian cancer, variety 2; HOC, hereditary ovarian cancer; sHOC, suspected hereditary ovarian cancer; HNPCC, hereditary non-polyposis colorectal cancer; CRC, colorectal cancer; Ut, endometrial cancer; NA, not applicable; sHNPCC, suspected hereditary non-polyposis colorectal cancer; FCC, familial colorectal cancer; HEC, hereditary endometrial cancer; sHEC, suspected hereditary endometrial cancer; FEC, familial endometrial cancer; sFEC1, suspected familial endometrial cancer, variety 1; sFEC2, suspected familial endometrial cancer, variety 2; FLC, familial lung cancer; d/s, definitive and suspected; sFLC, suspected familial lung cancer; HSC, hereditary stomach cancer; sHSC, suspected hereditary stomach cancer; HPC, hereditary prostate cancer; sHPC, suspected hereditary prostate cancer; FBlaC, familial cancer of urinary bladder; FHemT, familial haematological tumours; FPan, familial pancreatic cancer; FBtT, familial brain tumour; sFBtT, suspected familial brain tumour

DISCUSSION

The Valka district population screening has confirmed the presence of hereditary or familial background in all major cancer localisations. The high cancer burden among blood relatives justifies the need for surveillance in the families-at-risk.

Hereditary breast-ovarian cancer is the most common hereditary cancer syndrome in Valka population. In all hereditary breast-ovarian cancer syndromes the index cancer burden among female blood relatives exceeds the respective cumulative frequencies in EU females (2) indicating the need for the surveillance. Although the cancer burden is different in various syndromes, e.g. sHBC1 and sHBC2, it does not characterize the biological properties of cancer, such as growth rate, therefore intensity of follow-up cannot be lowered in syndromes characterised by lower frequency of affected female blood relatives.

According to the literature, annual mammography remains the gold standard of follow-up of female, if her family cancer history corresponds to the criteria of hereditary breast cancer (5). The surveillance is recommended from 25–30 years of age (5, 12) and may include annual breast self-examination (12). Clinical and ultrasound (US) evaluation of breast twice per year also is suggested as well as additional fine needle aspiration or core biopsy if indicated clinically or by US data. In carriers of the *BRCA1/2* mutations, the main genetic background of hereditary breast-ovarian cancer, breast tumours tend to be of high grade and lack calcifications thus decreasing sensitivity of mammography therefore magnetic resonance imaging is considered for screening (6). Surveillance for ovarian cancer includes pelvic US examination and serum testing for tumour markers, e.g. CA125, recommended to start from 25 years of age (5). However, due to lack of recognisable precancerous changes in the ovaries none of methods have been shown to detect ovarian cancer in earlier stage than in symptomatic patients (6).

As revealed by the 95% confidence interval of the mean (CIM) age of tumour diagnostics, clinical tumour manifestation in local hereditary breast-ovarian cancer syndrome patient is expected after 35 years of age. The follow-up aiming at early, preclinical diagnostics must be started earlier. According to literature (5, 6, 12) and results of the present study the following schedule is recommended – annual breast self-examination, clinical and US examination twice per year from 25 years as well as mammography and MRI examination every year from 25 years age, if clinically hereditary breast-ovarian cancer syndrome is established. Transvaginal US examination and serum testing for tumour marker CA125 can be advised from 35 years of age as the lower border of 95% CIM for ovary-involving syndromes is generally higher.

In HNPCC pedigrees, the described life time risk of colorectal cancer in MMR gene mutation carriers reaches 80% (11). HNPCC is characterised by early age at onset of colorectal cancer (10); the mean age of diagnosis is approximately 44 years (11). Due to early

cancer development, the surveillance in HNPCC and in suspected HNPCC should include colonoscopy every 1–2 years beginning from 20–25 years and annually after 40 years of age (15).

In Valka HNPCC patients, the mean age of tumour diagnostics is significantly higher. The data of the present study might validate the offered recommendation plan, accounting also for early diagnostics in the few younger cases. Alternatively, the surveillance might be started later. In contrast, FCC probands should consider starting colonoscopy from 35 years of age but in 95% of cases it can be postponed even until 57 years. Thus, the possibility of late-onset familial cancer should be recognised.

According to the literature the risk of extracolonic tumours in HNPCC, e.g. endometrial cancer and ovarian cancer, could be high. The surveillance therefore should include endometrial aspiration or transvaginal ultrasound, and it is recommended for females beginning from 25–35 years of age (7, 15). The endometrial cancer burden among female blood relatives in the presented study is as high as 22.4%, 95% CI=14.8–32.3%. Therefore the proposed surveillance as mentioned above is advised also in the result of the performed research. The highest above mentioned age border would be more appropriate starting point.

In agreement with the published data (17) the results of Valka population screening do not justify surveillance for breast cancer as a part of HNPCC-related person follow-up. The risk of ovarian cancer in HNPCC families is estimated as 6.7–9% by the age of 70 (15, 17). However, the Valka population screening data do not substantiate surveillance for ovarian cancer as the frequency is low and does not exceed the cumulative incidence in EU women (2). Frequency of brain tumours in HNPCC families has been a matter of dispute (17). The Valka population screening data reveal frequency of brain tumours that is very close to the cumulative risk for brain tumour in EU (2). Taking into account this finding and the limited possibilities of early treatment, surveillance for brain tumour cannot be justified.

The cumulative risk of incident endometrial cancer in EU women is estimated as 1.5 (2). The cancer burden was significantly higher in all hereditary endometrial cancer groups, substantiating necessity of surveillance. In the whole hereditary endometrial cancer syndrome groups the lowest observed border of the 95% confidence interval of the mean age was 44.4 years. Starting the surveillance at the age of 35 would be appropriate in at least 95% of affected females. However, the youngest cases were diagnosed at 26 and 30 years of age. Therefore, it would be possible to consider the beginning of surveillance at the age of 25 by endometrial aspiration or transvaginal ultrasound. Prophylactic surgery can be considered in proved mismatch repair gene mutation carriers.

For lung cancer, screening benefit has been reported by some (8) but doubted by other groups (16). The cumulative risk of incident lung cancer in EU is estimated as 6.47 and 1.64 in males and females respectively (2).

The cancer burden was significantly higher both in FLC and sFLC in the Valka population. The mean age of lung cancer diagnostics was: in FLC 56.0 (95% CI=53–59) years, in sFLC 58.5 (95% CI=56.1–60.9) years of age. However, presence of younger lung cancer cases also could be revealed in family cancer history. Thus, the surveillance should be started either at 45 years or 10 years before the younger case of lung cancer in family, whatever comes first, and should consist of lung X-ray twice a year. As synergistic influence of smoking and hereditary factors has been observed (13), cessation of smoking should be strongly recommended for high risk persons.

Both HSC and sHSC in Valka district were characterised by remarkable gastric cancer burden: HSC, 25.2% (95% CI=20.6–30.4%) and sHSC, 16.0% (95% CI=13.8–18.5%) exceeding the cumulative risk of stomach cancer in EU: in females, 0.68 % and in males 1.62% (2). Therefore, surveillance and /or prevention programme is strongly indicated. The mean age of cancer diagnostics was: in HSC 56.9 (95% CI=53.4–66.3) years of age, in sHSC 62.5 (95% CI=60.1–64.8) years of age that represents part of the published interval ranging from 16 to 82 years of age (9). Therefore the surveillance programme should be started either at the age of 45 years or 10 years before the youngest gastric cancer case in family, whatever comes first.

From the surgical point of view, it is important to distinguish between hereditary diffuse stomach cancer (HDSC) and familial intestinal stomach cancer. HDSC is characterised by tendency to submucosal extension, by dismal prognosis as well as by marked difficulties in early endoscopic detection. Hence, prophylactic gastrectomy in proved mutation carriers can be considered as a gold standard, 5 years earlier than the youngest age of gastric tumour diagnosis in the family (4). Therefore *E-cadherin* gene (*CDH1*) evaluation must be offered if the kindred fulfilled the criteria of hereditary diffuse gastric cancer, due to described frequency of *CDH1* gene mutation in HDSC that ranges 30–50% (4). Taking into account the possible high number of HSC cases in Latvia, the prognosis and intervention possibilities as well as psychological and compliance considerations, it would be of utmost importance to set up the *CDH1* gene mutation analysis in combination with subsequent surgical prophylaxis. The minimal recommendations for the present situation or families lacking older medical documentation include clinical evaluation of family history and surveillance by frequent chromoendoscopy combined with biopsy. The endoscopy should be performed biannually (3, 4). At least 15 mucosal biopsies must be provided for histological evaluation (9).

Familial urinary bladder cancer was an example of late-onset familial cancer, characterised by high cancer burden (22.8%) in contrast to incident urinary bladder cancer frequency in EU estimated as 2.82% and 0.52% (2). Thus, surveillance also is recommended by urine cytology, beginning from 50 years of age and continuing annually.

Once familial pancreatic cancer syndrome is established there is a choice to undergo surveillance like endoscopic US, MRI or computed tomography. However, there is no acceptable screening protocol (18). Prophylactic pancreatectomy is not recommended in asymptomatic individuals belonging to familial pancreatic cancer high-risk families (14) due to insufficient data of efficiency as well as severe morbidity of offered procedure.

The frequency of affected persons among blood relatives in the definitive and suspected familial brain tumour and haematological tumour families is high. However, in contrast to the previously discussed types of inherited tumours, no reasonable surveillance program is available.

CONCLUSIONS

1. The presence of familial background in all most frequent cancer locations and the high cancer burden in the affected kindreds justify the need for familial cancer surveillance. The data about the age of cancer manifestation can be used to adjust the follow-up schedule for most syndromes.
2. The follow-up of hereditary breast-ovarian cancer should include breast self-examination, clinical and ultrasound examination from 25 years of age twice per year, mammography and MRI examination annually from 25 years of age, transvaginal examination and serum testing for tumour marker CA125 from 35 years of age.
3. In HNPCC/suspected, HNPCC the follow-up should include colonoscopy every two years from 25 years of age. Annual colonoscopy is indicated after 35 years of age in HNPCC/suspected HNPCC/FCC1/FCC2. For females, transvaginal ultrasound from 25 years of age should be included in cases of HNPCC and in suspected HNPCC. In female matching the criteria of hereditary and familial endometrial cancer syndrome it would be reasonable to start the surveillance programme at the age of 25 by the transvaginal ultrasound annually. Prophylactic hysterectomy is recommended to HEC syndrome patients with proved mismatch repair gene mutation.
4. In familial lung cancer the surveillance should be started at 45 years of age consisting of X-ray twice per year.
5. In hereditary stomach cancer syndrome, biannual chromoendoscopy surveillance combined with at least 15 biopsies is indicated from 45 years of age. *E-cadherin* gene (*CDH1*) evaluation should be set up as prophylactic gastrectomy can be recommended to *CDH1* gene mutation carriers.
6. The surveillance for familial urinary bladder cancer include urine cytology annually beginning from 50 years of age.
7. No reasonable surveillance schedule can be recommended for familial pancreatic cancer, familial brain tumour and familial haematological malignancies.

Conflict of interest: None

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