The NSW & ACT Hereditary Cancer Registers

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BACKGROUND

The NSW & ACT Hereditary Cancer Registers (HCR) offer registration to people from families at risk for hereditary cancer.

OBJECTIVE

This article describes the Hereditary Cancer Registers and provides information to the treating health professional to register patients at risk of hereditary cancer to the HCR.

DISCUSSION

The HCR collaborates with treating doctors and familial cancer clinics to play an important role in the management of people at risk of hereditary bowel cancer.

Up to 15% of all bowel cancer patients report a family history of the condition.[1] A smaller proportion of bowel cancer patients have a family history consistent with syndromes that follow typical autosomal dominant inheritance patterns. The management of people with an inherited predisposition to develop early onset bowel cancer requires careful coordination with the best outcome for patients shown to occur when linked to a hereditary cancer register.[2] This allows patients and their family members to be followed and monitored with respect to cancer screening, prevention, and the early detection of disease symptoms.[3]

The first hereditary bowel cancer registers were established over 75 years ago.[2] Individuals opting for registration have been shown to have a reduced risk for colorectal cancer (CRC) by virtue of the fact that patients are educated about their condition, advised and reminded about screening procedures, and advised when prophylactic surgery is most appropriate.[3] National Health and Medical Research Council guidelines recommend referral of appropriate consenting individuals to hereditary bowel cancer registers.[4] The NSW & ACT Hereditary Cancer Registers (HCR) were established in 1990 by The Cancer Council New South Wales.

The Hereditary Cancer Registers

The HCR assists with the management of individuals from families at high risk for certain types of hereditary cancers. There is an advisory committee of consumers and specialist clinicians. Conditions covered by the registers are:

- hereditary nonpolyposis colorectal cancer syndrome
- familial adenomatous polyposis
- Peutz-Jeghers syndrome
- juvenile polyposis, and
- other polyposis syndromes.

The syndromes

HNPCC

Hereditary nonpolyposis colorectal cancer syndrome (HNPCC) is characterised by the

early onset of CRC and other epithelial cancers. The average age of CRC onset is under 45 years.[5] Accurate prevalence data are lacking, but a recent Danish population based assessment reports HNPCC to be 1.7% of the total CRC burden.[6]

In HNPCC there is a tendency for early onset, right sided synchronous or metachronous cancers, as well as atypical pathology.[7] Tumours from individuals with HNPCC display a genetic phenotype known as microsatellite instability. Microsatellite instability is characteristic of a deficiency in a DNA repair process known as 'DNA mismatch repair'. Individuals with HNPCC living in the Netherlands have a lifetime colorectal cancer risk of 80%[8] compared with, for example, a lifetime (by 75 years) risk of 4.2–5.8% in the general New South Wales (NSW) population.[9] Individuals diagnosed with HNPCC are also at risk of developing extracolonic cancers such as cancer of the endometrium (a 40% lifetime risk compared with a 1.1% risk in the NSW population[9]). In addition, studies have shown there is also increased risk of cancer of the ovary, ureter, stomach and kidney (renal pelvis).[10] Clinical diagnosis of HNPCC is suspected if family history meets the Amsterdam criteria.[11]

There should be at least three relatives with CRC, and all the following Amsterdam criteria should be present:

- one should be a first degree relative of the other two
- at least two successive generations should be affected
- at least one CRC should be diagnosed before the age of 50 years, and
- familial adenomatous polyposis should be excluded in the CRC case.

These original criteria have now been modified to include other associated tumours as well as, or in place of, CRC.[12]

Jarvinen[13] evaluated the efficacy of screening via a controlled trial showing that regular colonoscopies reduced the rate of CRC, CRC death and overall mortality in patients with HNPCC. Such evidence emphasises the importance cancer screening and surveillance plays in the care of individuals with this condition. At risk individuals are advised to have a 1–2 yearly colonoscopy from 25 years of age (earlier in some families). Screening for other cancers may also be advised.

Familial adenomatous polyposis

Familial adenomatous polyposis (FAP) is usually characterised by the presence of hundreds to thousands of adenomatous polyps that carpet the entire colon and rectum. Typically these develop in the late teenage and early adult years. The most accurate prevalence data for FAP has been determined in the Danish population – based on registry data of 508 affected individuals – to be about one in 21 000.[3]

People with FAP are likely to develop bowel cancer before the end of their fifth decade of life unless a prophylactic colectomy has been performed. Other features of the syndrome include: desmoid tumours (occurring in 5–10% of FAP patients), benign retinal lesions (congenital hypertrophy of the retinal pigment epithelium), benign epidermoid cysts, osteomas of the mandible, and dental anomalies.[14] Familial adenomatous polyposis is caused by a germline mutation in the adenomatous polyposis coli (APC) gene.[15] More recently, a second gene – Mut Y Homolog (MYH) has been identified. This is believed to account for the proportion of patients that do not harbour APC germline mutations.[16] Genetic testing is available for this condition, although a causative gene mutation cannot be identified in all families.

Screening is recommended for those with FAP or those at risk from 10 years of age

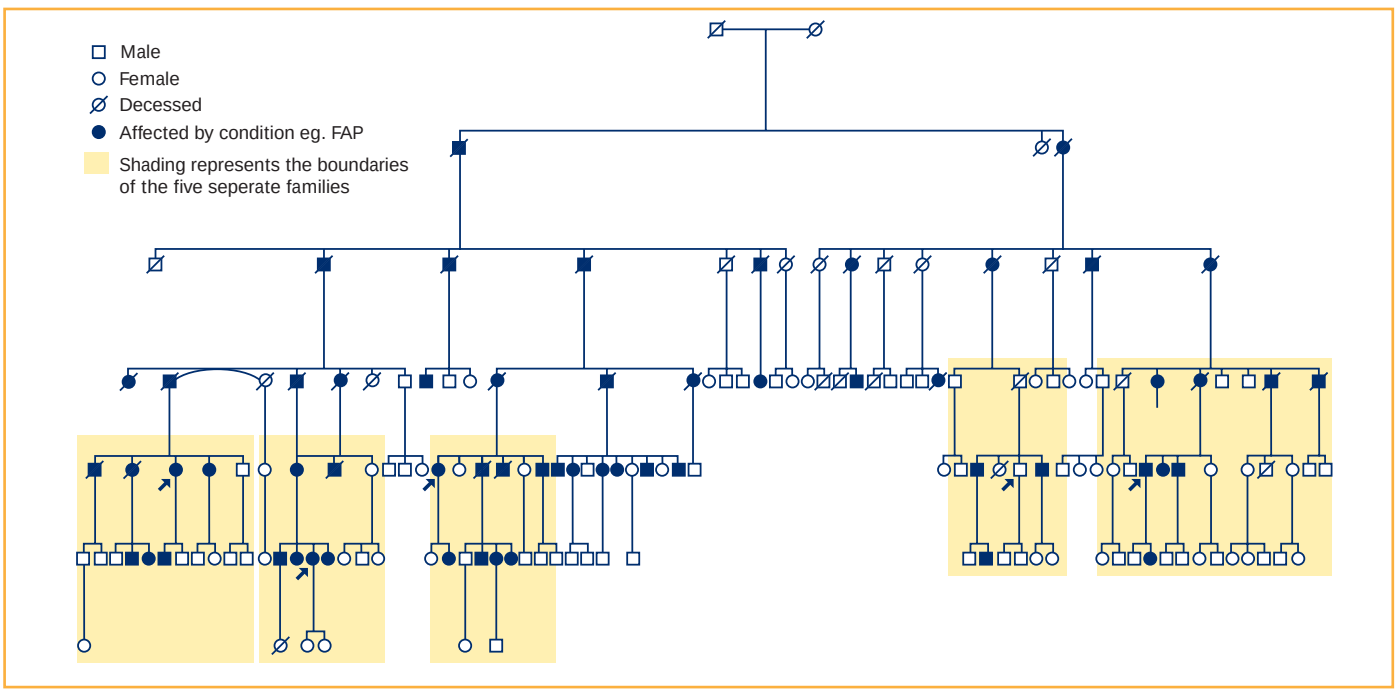

Figure 1. Pedigree showing linking of disparate families

with regular sigmoidoscopy being the preferred option.[17] Prophylactic colectomy is necessary, but the timing of this depends on the degree of polyposis. Screening for other cancers may also be advised.

Other polyposis syndromes

Other polyposis syndromes covered by the HCR include Peutz-Jeghers syndrome, juvenile polyposis and hyperplastic polyposis syndrome. All these conditions include the risk of colonic polyps and regular screening is recommended.

Von Hippel-Lindau syndrome

Von Hippel-Lindau syndrome (VHL) is an inherited condition characterised by an abnormal growth of blood vessels. Complications from the syndrome are possible from birth.[18] Renal cell carcinomas are common in patients with VHL.[19] Birth incidence has been estimated in a British study to be one in 36 000 live births.[20] The nature of VHL means that multiple regular screening assessments are recommended. Screening tests such as ophthalmological review, medical resonance imaging of brain and spine, and abdominal ultrasound are recommended.[18] Thus, VHL patients can benefit greatly from a coordinated screening reminder service offered by a register. The VHL register is currently being developed at the HCR.

The HCR's services

The HCR provides a range of services to registrants including:

- screening reminders
- provision of information and education
- newsletters
- information days
- links to support groups and services, eg. the Cancer Helpline
- information about genetic counselling and genetic testing with links to familial cancer clinics (FCC)
- booklets providing information about the conditions covered by the registers including treatment and screening protocols, and
- assistance with informing relatives of their risk.

The HCR also operates the Cancer Verifications Service for FCCs that confirms reported cases of cancer within a family by accessing the NSW Central Cancer Registry data. Another key objective of the HCR is to conduct research to improve services for, and understanding of, hereditary cancer conditions.

The HCR has networks with registers in other regions so that interstate and international family members can be located and informed of their risk. Further, the HCR has been shown to be in a unique position whereby it can trace people's families to link disparate family members.

Figure 1 shows a case example of a pedigree where several families have presented to registers independently. Cross matching of pedigrees has shown that the families are in fact linked in the way shown. All families registering with the HCR are checked against other families registered to check for relatedness. This can be particularly useful when genetic testing is offered, as the known gene mutation may have already been identified in another section (or branch) of the family, saving both time and money.

Case study

In 2000, Mrs Y presented to her GP with iron deficiency anaemia and rectal bleeding. Consultation with a gastroenterologist revealed a carpeting of adenomas throughout the colon and rectum and a smattering of upper gastrointestinal tract adenomas. Mrs Y underwent a total colectomy to substantially reduce her risk of developing CRC. Following treatment, her GP arranged registration with the HCR and Mrs Y was provided with a regular reminder service to ensure that she undertook appropriate surveillance measures to reduce her residual cancer risk. The HCR has provided ongoing advice to Mrs Y's treating physicians about the recommended guidelines for FAP surveillance. Mrs Y had not had genetic testing at the time of registration, so the HCR referred her to an FCC for genetic counselling and testing. Genetic testing revealed a mutation in exon 15 of the APC gene and this allowed for predictive testing to be offered to Mrs Y's other at risk family members (siblings and any offspring aged 12 years or over) via the FCC. Predictive testing will clarify the family members' risk status to ensure appropriate surveillance measures in those persons with the genetic predisposition and to prevent unnecessary screening in those without. The HCR was able to assist Mrs Y in informing her relatives of their hereditary cancer risk and the option for genetic testing. For at risk relatives residing interstate, the HCR facilitated transfer of information to the appropriate FCC and state based registers.

Registrations

As at 30 June 2004, the HCR had 768 individuals from 414 families registered. Of these registrants, 285 individuals were at risk of FAP, 424 at risk of HNPCC, and less than 20 at risk for the other polyposis syndromes.

Referrals to the HCR are made mostly via FCCs but also from treating doctors, other registers and the Cancer Council NSW Helpline. Over recent years, referrals from GPs or treating doctors have been decreasing, with referrals from FCCs on the rise (*Figure 2*). This accords with the development of these specialised services in NSW.

Table 1. Hereditary cancer registers in Australia

State	Conditions covered	Address	Telephone
New South Wales/ Australian Capital Territory	FAP, HNPCC, polyposis syndromes, VHL	Locked Bag 9000 Potts Point NSW 1335	02 9334 1807 02 9334 1794
Queensland	FAP, polyposis syndromes	Qld Clinical Genetics Services Level 4, Block 65 Royal Children's Hospital Herston Qld 4029	07 3636 5117
South Australia	FAP, HNPCC, polyposis syndromes, other familial cancers	Familial Cancer Unit (FCU) Women's and Children's Hospital 72 King William Road North Adelaide SA 5006	08 8161 6995
Victoria	FAP, HNPCC, breast, breast/ovary	The Cancer Council Victoria 1 Rathdowne Street Carlton Vic 3053	03 9635 5176 03 9635 5374 03 9635 5414
Western Australia	FAP, HNPCC, polyposis syndromes, breast/ovary	Genetic Services of WA 374 Bagot Road Subiaco WA 6008	08 9340 1603 08 9340 1713
Tasmania	FAP, HNPCC, polyposis syndromes	PO Box 1963 Launceston Tas 7250	03 6348 7006

How the HCR can assist treating doctors

The HCR can assist GPs and specialist treating doctors to assess the level of cancer risk in an individual with a family history of bowel cancer. The HCR can provide written resources for determining the level of risk as well as surveillance guidelines for hereditary bowel cancer syndromes. General practitioners and specialist treating doctors can register their patients with the HCR to assist them maintain their screening schedule. Once registered, patients are provided with screening reminders, tailored and up-to-date information, regular newsletters, public information events and links to support networks. Individuals may also benefit from referral to FCCs who can offer genetic counselling and genetic testing. Sometimes referral to an FCC is appropriate in the first instance. The case study illustrates how the HCR can assist GPs and specialised treating doctors in providing care to this population.

In some families with a proven or suspected genetic predisposition to malignancy, genetic testing can be offered to determine which family members might be at increased risk of cancer. Genetic counselling and testing for cancer risk is available through FCCs.

Familial cancer clinics

Familial cancer clinics, funded by state departments of health, are established in all Australian states to provide risk assessment and advice for those with concerns about a family history of cancer. They are multidisciplinary and may involve geneticists, genetic counsellors and other medical specialists such as oncologists, surgeons and gastroenterologists. They work closely with all hereditary cancer registers.

Hereditary cancer registers in Australia

Hereditary cancer registers exist to cover all states in Australia (*Table 1*). Each register may offer varying services for some or all hereditary cancer conditions.

How to register individuals with the HCR

General practitioners and specialist doctors can register individuals with the HCR directly. It is preferable for individuals to be seen by their local FCC so they may access the available expertise. Individuals suitable for registration with the HCR include:

- those with a strong family history of bowel cancer (eg. family history that satisfies the Amsterdam criteria)
- those with an early age of onset of bowel cancer (eg. under 40 years of age), and
- those from families with the conditions described above.

Individuals may be offered the choice to register their details with the HCR, with registration involving written informed consent to be included on the register and the offer of a screening reminder service. Registration involves the completion of the registration and consent form by the individual and clinician. Once registered, individuals receive the full range of services of the HCR including information booklets specific to their condition.

Conclusion

The HCR collaborate with treating doctors and FCCs to register families at risk for hereditary bowel cancer. Since its inception in 1990, the HCR has experienced increasing numbers of registrations annually. The HCR is an example where central registration of hereditary cancer syndromes provides an effective, coordinated approach to the care of this population.

It is now evident that the HCR play an important role in the management of people at risk of hereditary cancer. The HCR has networks with registers both locally and internationally. Clinicians in doubt of the

appropriateness of a referral may contact their local FCC to discuss a patient's family history. Familial cancer clinics conduct risk assessment with genetic counselling and testing as appropriate. The HCR plans to expand in the future and include cancers other than bowel cancer, while also increasing research capacity.

Acknowledgments

The authors wish to thank Bruce Armstrong, current and previous staff of the HCR for their contribution to the work of the HCR, and Andrew Penman and The Cancer Council NSW for their support. The authors would like to acknowledge the support of the NSW Department of Health by providing access to the NSW Central Cancer Registry data, and the advice and support of the HCR Advisory Committee (Sally Auld, Sarah Doak, Kate Dunlop, Claire Groombridge, David Koorey, Colleen Macic, Jill Nehrybecki, Sheridan O'Donnell, Angela Overkov, Kathy Tucker, Robyn Ward, and Rachel Williams).

Conflict of interest: none declared.

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