The definition needs an agreed structure and process for HITH, not just a mission statement, as the platform on which clinical interventions can occur, be further developed or be studied. It should establish how the HITH service becomes a legal and clinical extension of the hospital. As a result, it must address medical care: specifically, whether a hospital-affiliated, formal, separate, clinical HITH unit constitutes the basis for HITH care.

Caplan et al's meta-analysis chips away a little further into the future form of hospitals and HITH, the way a sculptor chisels at a marble block to reveal important new aspects of the image that lies within.

Competing interests: No relevant disclosures.

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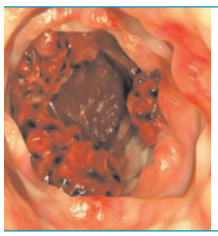

The Australasian Colorectal Cancer Family Registry

Reducing the impact of colorectal cancer

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Colorectal cancer (CRC) is one of the most common cancers in Australia, with a risk in people under the age of 75 years of one in 18 for men and one in 26 for women. Each year, about 15 000 Australians are diagnosed with CRC, and about 4000 die from it.[1] The 5-year survival from CRC is 62%, which is considerably worse than, for example, breast cancer, which has a 5-year survival of 88%.[2]

A genetic predisposition is suspected to underlie up to a third of all CRCs.[3] However, only 5% of CRCs are known to be caused by mutations in cancer predisposition genes.[4] Substantial advancement in understanding the aetiology, prevention and treatment of CRC, as well as reducing mortality, requires comprehensive personal, family and epidemiological data and biospecimens (DNA and tumour tissue) for large numbers of people across the full spectrum of risk. The Australasian Colorectal Cancer Family Registry (ACCFR) provides this resource.[5]

The ACCFR was established for collaborative research into the prevention and treatment of CRC and is our region's largest and best characterised family-based resource of data and biospecimens. It began in 1993 as the Victorian Cancer Family Study, funded by VicHealth. Since 1997, the ACCFR has been part of the Colon Cancer Family Registry (CCFR), an international consortium across Australia, New Zealand, the United States and Canada that is funded by the US National Institutes of Health. The CCFR is the largest family-based worldwide resource for studies of CRC and associated cancers, and the ACCFR comprises about a third of it. More than 11 500 people from 1800 families in Australia and New Zealand have been recruited to the ACCFR, through the Victorian Cancer Registry (960 case families), family cancer clinics in Brisbane, Sydney, Melbourne, Adelaide, Perth and Auckland (580 multiple-case families), or the Victorian electoral roll (270 control families). Maintenance of the ACCFR includes conducting follow-up surveys every 5 years to update data regarding personal and family cancer history, CRC screening (by faecal occult blood test or colonoscopy), colonoscopic polypectomy and other bowel surgeries.

The ACCFR acts as a research enabler, with access to data and biospecimens provided equitably to internal and external researchers. Gaining access requires submission of a proposal with a detailed research plan. Written informed consent is obtained from all study participants, with protocols approved by the relevant institutional human research ethics committee. To date, most studies have used data collected at baseline. As people recruited as cases through family cancer clinics have deliberately been oversampled for familial risk, the ACCFR differs from other cancer cohorts in novel ways. For example, unaffected family members have similar familial risk profiles to affected family members, and can be used as controls. People recruited as population controls and those recruited as CRC cases from the Victorian Cancer Registry, who are selected irrespective of CRC family history, are useful for identifying a range of risk factors for all CRCs, not only those that are inherited.

Genotype data in the ACCFR enable studies of the risk-modifying effects of genetic and non-genetic factors. They have been used for a range of gene-discovery research, including classic linkage studies, genome-wide association studies, and whole-exome and whole-genome studies using next-generation sequencing. Furthermore, participants with CRC at recruitment are prospectively followed up to provide information about potential risk factors for any subsequent cancers that arise. The ACCFR also facilitates novel behavioural and psychosocial research to understand participants' health care utilisation.

Among other achievements, the ACCFR has been used to:

- elucidate CRC risk factors and their interactions with gene mutations and family history;[6]
- establish age-, sex- and gene-specific cancer risks;[7]
- describe a new subtype of CRC — "familial colorectal cancer type X";[8]
- discover new susceptibility genetic variants;[9]
- facilitate molecular and pathological characterisation of CRC;[10]
- determine cancer risks after a previous diagnosis of CRC;[11]
- demonstrate that screening is both underused and overused, based on CRC risk;[12] and
- demonstrate that people at high risk of CRC are declining testing for high-risk genes because of health insurance concerns.[13]

Also, in a collaboration with general practitioners, the ACCFR investigators have established the new Centre of Research Excellence (CRE) for Reducing the Burden of Colorectal Cancer by Optimising Screening: Evidence to Clinical Practice, supported by the National Health and Medical Research Council. This CRE aims to provide GPs with the tools to predict patients' CRC risk and refer them accordingly.

The ACCFR is now a prospective family cohort study. As such, it is positioned to provide definitive information on CRC risk and risk modification, which can inform translation into clinical practice and health care policy and improve population health. It will do this by combining DNA science with behavioural research, surveillance and early-intervention therapeutic strategies. The risk of CRC is heterogeneous, and screening requirements vary according to the level of risk. The ACCFR will provide a model to predict who is at highest risk and in need of the most intensive surveillance, so that resources can be used rationally. In this way, risk assessment will inform risk management, with optimisation of health outcomes.

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