

Annex 10: Examples of prevention and early detection on the basis of cancer hereditary susceptibility testing with personalised preventive strategies

Breast cancer

Breast cancer is hormonally driven and chemoprevention is an attractive, albeit nonselective, management strategy. The selective oestrogen receptor modulator tamoxifen has been shown in a number of phase III randomised controlled trials to reduce the incidence of breast cancer by 16%-49% in high-risk females. A double-blind prospective randomised controlled trial of more than 19,000 postmenopausal women showed raloxifene, another selective oestrogen receptor modulator, to be an alternative, effective option, with fewer side effects in postmenopausal women at high risk of developing breast cancer.

Selective preventative strategies can be used in female carriers of mutations in the BRCA1 or BRCA2 genes, which give a 45–65% chance of developing breast cancer by the age of 70. These genes also increase the risk of ovarian, colon and prostate cancer. Individualised genetic testing for the BRCA genes is available for individuals with a strong family history of breast cancer. Prophylactic options for individuals found to be carriers include removal of breast tissue, oophorectomy or chemical oestrogen deprivation. A Cochrane review found that worry over breast cancer was significantly reduced following a mastectomy, and that it was effective in reducing the incidence of deaths from breast cancer.

Colorectal cancer

The accumulation of germline mutations triggers colorectal cancer (CRC) development. One percent of bowel cancers are caused by familial adenomatous polyposis coli (FAP), an autosomal dominant disorder with complete penetrance, where a mutation in the adenomatous polyposis coli (APC) gene causes truncation of the protein product and deregulation of the downstream Wnt signalling pathway. Formation of hundreds of polyps contributes to the frequent development of CRC by 40–50 years old. Genetic screening identifies carriers and allows consideration of prophylactic bowel resection. This use of personalised medicine has led to a 55% reduction in CRC incidence and improved overall survival in patients with FAP, though, as in surgical prophylaxis for breast cancer above, surgery does not guarantee complete prevention of cancer development.

A number of chemopreventative agents have been studied in CRC. An analysis of randomised controlled trials using aspirin for prevention of vascular events demonstrated that patients treated with aspirin developed fewer distant metastases and fewer fatal adenocarcinomas. A randomised controlled trial in carriers of hereditary non polyposis CRC showed that daily aspirin therapy reduces the incidence of primary CRC. Aspirin is a promising, but nonselective strategy. Stratified chemopreventative agents may be used in the future to delay or even prevent progression of polyps and reduce the need for drastic bowel surgery.