Table 2. Overview of common familial diseases in family medicine[26,28]

Clinical scenario	Investigations/referral	Comments
All patients	Where possible, take a three-generational family history including: • First-degree relatives (children, siblings, parents) on both sides of the family • Second-degree relatives (aunts, uncles and grandparents) on both sides of the family Consider using the *Family History Questionnaire* as part of the medical history	Key information in the family history: • Ethnic background (ancestry and culture) • Adoption • Age at diagnosis • Age and cause of death • Birth defects • Stillbirths and miscarriages
Hereditary haemochromatosis (HH) Patients with one or more of: • Liver disease of unknown cause, including those with suspected alcoholic liver disease • all first degree relatives with haemochromatosis or with a known mutation in the *HFE* gene • Patients with conditions that could be a complication of HFE (diabetes mellitus, atypical arthritis, cardiomyopathy, erectile dysfunction or chronic fatigue)	Test for fasting transferrin saturation and serum ferritin concentration. If fasting transferrin saturation >45% or fasting ferritin >250 µg/L on more than one occasion, test for *HFE* mutations If a *HFE* mutation is identified, discuss options for genetic testing and referral for genetic counselling of at-risk family Children of *C282Y* heterozygotes should only be tested if the other parent has the *C282Y* mutation. Testing children in affected families is generally not recommended until age 18 years unless symptomatic. Other first-degree relatives of *C282Y* heterozygotes should be tested with iron studies. If these are positive, discuss genetic testing and referral for genetics counselling	In Australia, the MBS covers *HFE* gene testing for patients with: • Raised ferritin or transferrin saturation levels on more than 1 occasion; or • First-degree relative diagnosed with HH or with two *HFE* mutations.
Neurofibromatosis (NF) Patients with: NF1: • multiple café au lait spots, • inguinal/axillary freckling • multiple neurofibromas NF2: • bilateral vestibular schwannomas; • gradual hearing loss, • balance problems • tinnitus	Genetic testing NF1 Not necessary for diagnosis after birth Prenatal genetic testing possible only when the family specific gene mutation is known Genetic testing NF2 Pre-symptomatic genetic testing is available to blood relatives of individuals in whom a mutation has been identified.	Autosomal dominant pattern of inheritance 50% of cases due to sporadic mutation
Skin cancer increased risk • family history of melanoma in first-degree relative • fair complexion • a tendency to burn rather than tan • presence of freckles, light eye colour, light or red hair colour • age >30 years (>50 years most at risk) • presence of solar lentigines • past history of non melanoma skin cancers (age <40 years higher risk) • people with childhood high levels of ultraviolet exposure • episodes of sunburn in childhood	Annual skin examination Advice on self examination	Genetic testing in research phase

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Skin cancer – high risk • multiple atypical or dysplastic naevi and who have a history of melanoma in themselves or in a first degree relative	• Preventive advice, • Examination of skin (with or without photography) • Advice on self examination	Review every 3–12 months
Prostate cancer – high risk • Men with one or more first-degree relatives diagnosed under age 65 years • Men with a first-degree relative with familial breast cancer (*BRCA1* or *BRCA2*)	• Respond to requests for screening by informing patients of risks and benefits of screening	Note that routine screening of the general population for prostate cancer is not recommended[28] unless: • the man specifically asks for it; and • he is fully counselled on the pros and cons
Breast cancer – moderately increased risk • One first-degree relative diagnosed with breast cancer before the age of 50 (without the additional features of the potentially high-risk group) • Two first-degree relatives, on the same side of the family, diagnosed with breast cancer (without the additional features of the potentially high-risk group) • Two second-degree relatives, on the same side of the family, diagnosed with breast cancer, at least one before age 50 years (without the additional features of the potentially high-risk group)	Clarify risk at http://canceraustralia.gov.au/clinical-best-practice/gynaecological-cancers/familial-risk-assessment-fra-boc Breast awareness Consider referral to or consultation with a family cancer clinic for further assessment and management Mammogram at least every 2 years from age 50–69 years Annual mammograms from age 40 may be recommended if the woman has a first-degree relative <age 50 years diagnosed with breast cancer	In this increased risk group the relative risk of breast cancer up to age 75 years is between 1:8 and 1:4. (<4% of the female population) Note that for routine screening in the general population mammography is recommended every 2 years for women 50–69 years old

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Breast cancer – potentially high risk • Women who are at potentially high risk of ovarian cancer • Two first- or second-degree relatives on one side of the family diagnosed with breast or ovarian cancer plus one or more of the following features on the same side of the family: • additional relative(s) with breast or ovarian cancer • breast cancer diagnosed before age 40 years • bilateral breast cancer • breast and ovarian cancer in the same woman • Ashkenazi Jewish ancestry • breast cancer in a male relative. • One first or second degree relative diagnosed with breast cancer at age 45 years or younger plus another first or second degree relative on the same side of the family with sarcoma (bone/soft tissue) at age 45 years or younger • Member of a family in which the presence of a high-risk breast cancer gene mutation has been established	Clarify risk at www. nbocc.org.au/fraboc Advise referral to a cancer specialist or family cancer clinic for risk assessment, possible genetic testing and management Ongoing surveillance strategies may include regular clinical breast examination, breast imaging with mammography, magnetic resonance imaging (MRI) or ultrasound and consideration of ovarian cancer risk	In this group, the relative risk of breast cancer up to age 75 years is between 1:8 and 1:4. (<1% of the female population)
Ovarian cancer – higher risk Family history of ovarian cancer, especially first-degree relatives and more than one relative (risk of about 3 times the population average) Presence of the breast cancer susceptibility gene 1 (*BRCA1*) or breast cancer susceptibility gene 2 (*BRCA2*)	Based on current evidence no screening is recommended Consider increased frequency of screening for breast and colorectal cancer in higher risk groups	Routinely screening for ovarian cancer using blood tests for cancer antigen (CA) 125, or transabdominal or transvaginal ultrasound provides no benefit. Note that those who have used the oral contraception, or carried a pregnancy to term have a lower (about half) the risk of the population average.
Colorectal cancer (CRC) category 1: average or slightly increased risk Asymptomatic people with: • no personal history of bowel cancer, colorectal adenomas or ulcerative colitis and no confirmed family history of CRC, or • one first- or second-degree relative with CRC diagnosed at age 55 years or older	FOBT every 2 years from 50 years of age	

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CRC category 2: moderately increased risk Asymptomatic people with: • one first-degree relative with CRC diagnosed before age 55 years, or • two first-degree or one first- and one second degree relative/s on the same side of the family with CRC diagnosed at any age (without potentially high-risk features as in Category 3)	Colonoscopy every 5 years from age 50 years, or at an age 10 years younger than the age of first diagnosis of CRC in the family, whichever comes first Sigmoidoscopy plus double-contrast barium enema or CT colonography (performed by an experienced operator) is acceptable if colonoscopy is contraindicated Consider offering FOBT	This group comprises about 1–2% of the population
CRC category 3: High risk Asymptomatic people with: • three or more first- or second-degree relatives on the same side of the family diagnosed with colorectal cancer (suspected Lynch syndrome, also known as hereditary non-polyposis CRC or HNPCC) or other Lynch syndrome-related cancers or • two or more first- or second-degree relatives on the same side of the family diagnosed with CRC including any of the following high-risk features; – multiple CRC in the one person – CRC before age 50 years – a family member who has or had Lynch syndrome-related cancer or • at least one first or second degree relative with CRC, with a large number of adenomas throughout the large bowel (suspected familial adenomatous polyposis (FAP)) or • somebody in the family in whom the presence of a high risk mutation in the adenomatous polyposis coli (APC) or one of the mismatch repair genes has been identified	Refer to bowel cancer specialist to plan appropriate surveillance Refer for genetic screening of affected relatives FAP: flexible sigmoidoscopy or Colonoscopy in attenuated FAP Recommended screening schedules are as follows; **Familial adenomatous polyposis** (APC mutation status unknown): every 12 months from age 12–15 years to age 30–35 years and every 3 years after age 35 years **Lynch syndrome:** 1–2 yearly from age 25 years or 5 years earlier than the youngest affected member of the family (whichever is earliest). Aspirin 100 mg/day is effective prophylaxis[31]	This group with a relative risk of 4–20, make up <1% of the population Note that members of proven FAP and Lynch syndrome families who are shown not to carry the family mutation are no longer at high risk and revert to the average-risk group and still require population based screening.
Type 2 diabetes – increased risk • Age >40 years • Aboriginal and Torres Strait Islander peoples	AUSDRISK every 3 years	Diabetes risk may be calculated using AUSDRISK.[28] This calculates a score related to the risk of developing diabetes over a 5-year period

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Type 2 diabetes – high risk Any one of following risk factors: • AUSDRISK score of 12 or more • all people with a history of a previous cardiovascular event (acute myocardial infarction or stroke) • women with a history of gestational diabetes mellitus • women with polycystic ovary syndrome • patients on antipsychotic drugs	Fasting blood sugar every 3 years	
Familial hypercholesterolaemia • Premature ischaemic heart disease (men aged <55 years, women aged <60 years) • First-degree relative with premature ischaemic heart disease (men aged <55 years, women aged <60 years) • Total cholesterol >7.5 or LDL-C >4.9 • First-degree relative with a total cholesterol >7.5 or LDL-C >4.9 • Tendon xanthomata or arcus cornealis at age <45 years	Genetic testing is available through specialist cardiac or Genetics Services	Assess their probability of having family history using the Dutch Lipid Clinic Network criteria or Modified UK Simon Broome criteria (28) Offer referral to a lipid disorders clinic if DLCN score >3 or the MUKSB suggests a possible family history
Fragile X and other causes of developmental delay Children or adults of either sex with one or more of the following features: • developmental delay including intellectual disability of unknown cause • autistic-like features • attention deficit hyperactivity disorder • speech and language problems • social and emotional problems, such as aggression or shyness • a female with a history of primary ovarian insufficiency or premature menopause (age <40 years) • adults with ataxia, balance problems and Parkinsonism • a relative with a fragile X mutation	Chromosomal analysis (chromosomal array or karyotype if array not available) and DNA test for fragile X syndrome (available on the MBS) in children and adults. Refer to Genetics Services for cascade testing of relatives	There is no known single gene that causes autism; genetic testing is not currently available. Diagnosis of Fragile X Syndrome can be made at any age. GPs ought to be aware of the risk of adult-onset conditions for carriers of Fragile X syndrome – Fragile X associated tremor ataxia (more so in males than females) and primary ovarian insufficiency in females – which can have a wide-ranging impact, not just on the child with Fragile X syndrome

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Hereditary thrombophilias • DVT <50 yrs • Spontaneous thrombosis in absence of recognised risk factors • Recurrent thrombosis • Family history of thrombosis • Thrombosis in unusual sites e.g. CNS, abdominal veins, upper limb • Stillbirth or fetal death in utero	Consider screening for thrombophilia	A thrombophilia screen (factor V Leiden, prothrombin variants, antithrombin III deficiency, protein C deficiency, protein S deficiency and activated protein C resistance) is available on the MBS only if the patient has: • A personal history of proven venous thromboembolism or pulmonary embolism, or • A 1˚ relative who has a proven defect of any of the above
Carrier screening for haemoglobinopathies People have increased risk if have ancestry/ethnic background from; Southern European, African (including Americas and Caribbean), Middle Eastern, Chinese, Indian subcontinent, Central and South East Asian, Pacific Islander, New Zealand Maori, South American and some northern Western Australian and Northern Territory Indigenous communities	Mean corpuscular volume, mean corpuscular haemoglobin, ferritin, haemoglobin electrophoresis and iron levels Seek advice from haematology or genetic services about DNA testing especially for alpha-thalassaemia carriers	Test couple prior to pregnancy or in first trimester

Adapted with permission from from Barlow-Stewart, K., et al. (2007). Genetics at a Glance, The Australian Government Agency, Biotechnology Australia: 1-6.

Many of the recommendations have been sourced from The Red Book- Guidelines for preventive activities in general practice, 8th edition, East Melbourne: Royal Australian College of General Practitioners, 2012.