Chronic disease prevention in general practice

Applying the family history

BACKGROUND
The family history has a potentially important role in general practice for risk prediction and tailored disease prevention for several common chronic diseases.

OBJECTIVE
This article discusses the potential role of the family history in general practice including current risk assessment guidelines and approaches to supporting family history taking.

DISCUSSION
Family history reflects shared genetic and environmental risks and can be used to identify individuals at increased risk of common chronic disease who may benefit from tailored preventive management. General practitioners need to develop skills in taking a full family history, creating a pedigree and using this to determine disease risk. Future developments in this area include family history screening tools, computerised risk assessment and, in the longer term, identification of common genetic mutations that are reflected in a person's family history.

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The past decade has seen dramatic advances in our understanding of the genetics of common chronic disease, however it will be some time before this translates into clinically relevant genetic tests that predict disease risk. Historically, the family history has been used in general practice as both a psychosocial and risk assessment tool.[1] However, it has not been applied in a systematic way to tailor disease prevention in general practice.

Family history and chronic disease risk

The presence of a possible family history is an important risk factor for many common chronic diseases. Ischaemic heart disease,[2] type 2 diabetes,[3] cancers,[4–6] diabetes,[3] osteoporosis,[7] atopy,[8] and mental illness[9] are all associated with family history. Family history of a common chronic disease is associated with a 2–5 fold relative risk of developing the condition, and increases with the number of affected relatives and early age of onset.[10] A family history of a specific disease usually reflects the combined effects of genetic susceptibility, shared environmental exposures and common behaviours among relatives.

The family history is already used by clinical geneticists to identify families with Mendelian inherited subsets of disease such as BRCA1 and BRCA2 mutations in families with breast and ovarian cancer. However, while we await the identification of specific and more common genetic polymorphisms that might be used to assess an individual's disease risk, the family history can be used for risk assessment to tailor disease prevention strategies.

In the United Kingdom and the United States, through the National Service Frameworks[11] and the Center for Disease Control (CDC) Family History Initiative,[12,13] there have been recent recommendations for primary care practitioners to use the family history to support specific disease prevention. The underlying principles behind these recommendations for each disease are as follows:

- the disease represents a substantial public health burden
- family history is an established risk factor with known prevalence
- there are effective interventions for primary and secondary prevention
- there is awareness and accurate reporting of disease status among relatives.

The National Preventive and Community Medicine Committee of The Royal Australian College of General Practitioners regularly produces and updates evidence based guidance through the publication of *Guidelines for preventive activities in general practice* ('red

book').[14] These guidelines make several recommendations for the application of the family history in Australian general practice covering various chronic conditions including ischaemic heart disease, hypertension, breast, ovarian and colorectal cancers, melanoma, depression and osteoporosis *(Table 1)*.

Applying the family history for risk prediction

As a general rule, family history is associated with significant disease risk in the following circumstances:

- multiple family members are affected by a condition
- affected family members are close (ie. first or second degree) in relationship
- premature onset of a condition.[10]

The CDC has proposed using this approach to stratify individuals into high, moderate or average risk categories.[15] According to this approach, a family history that renders someone at moderate or high risk is defined as:

- at least one affected first degree relative, or
- two affected second degree relatives on the same side of the family.

Average risk is defined as:

- one affected second degree relative, or
- no report or unsure of family history.

For some conditions, these criteria have been adapted and extended to create specific screening guidelines and recommendations based on family history. However, there is a danger that these criteria are too simplistic and could misclassify individuals as being at increased risk with minimal family history. The 'red book' guidelines seek to be more specific for each condition but again take the broad approach of risk stratification which then determines tailored risk management strategies (*Table 1*).[14]

Psychosocial consequences of family history taking

The potential harms of discussing a patient's family history to predict risk need to be considered. A systematic review of the consequences of disease risk prediction demonstrates important individual differences that moderate the effects of 'threatening information' including coping strategies and the way in which the risk assessment is performed.[16] This review suggests that some distress in response to information about increased disease may be helpful, increasing participation in further surveillance and following advice aimed at reducing risk. Therefore, the family history may in fact act as a motivator to behaviour change. A recent study exploring the use of family history in disease prevention showed that inflated risk perceptions did not negatively affect screening behaviours related to breast cancer, and might even promote them.[17]

Concerns about the impact on ability to obtain insurance are often expressed in this context. However, it is important to realise that taking a family history in general practice does not create new information about disease risk, unlike undergoing a predictive genetic test. Insurance companies will often ask the same family history information from applicants, however, currently, rarely inflate premiums on this basis alone.

Patient perceptions of the importance of their family history will reflect their personal experience of the disease, including premature death or disability of a family member, and perceived patterns of illness relating to gender or age at death.[18] This is important to consider when discussing familial disease risk with patients. Exploring a patient's understanding and beliefs about personal vulnerability due to their family history is important in communicating risk and supporting shared decision making about the management of their disease risk.[18]

Taking a family history in general practice

To conduct a risk assessment, ideally a full three generational pedigree should be taken that asks about parents, aunts, uncles, siblings and grandparents on both sides of the family. Age at diagnosis should be identified, at least to within 5 years if possible. Ethnic background should also be considered. For example, people of Jewish background have a higher prevalence of breast and ovarian cancer predisposing mutations in BRCA1 and BRCA2; people of Afrikaan descent have a much higher prevalence of familial hypercholesterolaemia. Therefore, a family history of specific conditions may have more significance in certain ethnics groups.

The validity of self reported family history should also be considered. A Canadian study showed that reports of cancer sites in first degree relatives were generally accurate (breast 99%, ovary 100%, colon 93%), although information was less accurate about second degree relatives and age of diagnosis.[19] Intra-abdominal cancers are easily confused, for example 'stomach cancer' may reflect any intra-abdominal malignancy including liver metastases. If there is uncertainty, it can be helpful to ask patients to discuss their family history with their relatives in an attempt to gain more accurate information.

Drawing a pedigree is an important skill in summarising the family history, allowing disease risks to be determined and communicating this information with other health professionals. It can also be readily updated if new diagnoses occur in the family. *Figure 1* demonstrates how to draw a pedigree including the use of standard symbols.

Family history screening in general practice

General practitioners may require up to 30 minutes to record a three generational pedigree, far in excess of the time available for most consultations.[20] If using the family history in screening and prevention for common chronic disease is to be feasible in Australian general practice, a simple, brief screening tool that can be applied to the entire population is required to identify patients who may benefit from a more detailed pedigree and risk assessment. Although there have been some family history questionnaires developed,[21] no brief screening instrument has been validated for this purpose.

Family history assessment tools

There is growing interest in the development of family history tools that support the collection of family history information and, in some cases, create pedigrees and conduct risk assessment.[22] These tools include self administered paper questionnaires or computer programs, some of which are aimed at consumers and others for general practitioners. The CDC Family History Initiative has developed an electronic tool for use by consumers to create their own pedigree that they can then discuss with their primary care physician, therefore potentially absolving the GP of this time consuming task.

Table 1. Current screening and management guidelines incorporating family history as a risk predictor[14]

Screening guidelines	Management guidelines
Breast and/or ovarian cancer	
Moderate risk if: • One or two first degree relatives diagnosed with breast/ovarian cancer <50 years • Two first or second degree relatives on the same side of the family diagnosed with breast/ovarian cancer High risk if: • Three or more first or second degree relatives on the same side of the family diagnosed with breast/ovarian cancer • Two or more first degree relatives on the same side of the family diagnosed with breast/ovarian cancer including any one of: – bilaterality – diagnosed at 40 years or less – breast and ovarian cancer in the same person – breast cancer in a male • One first or second degree relative diagnosed at 45 years or less, plus another relative on the same side of the family with sarcoma diagnosed at 45 years or less • Breast cancer gene mutation identified in a family member	• Mammography from 40 years compared to 50 years for population risk • High risk women may carry BRCA1 or BRCA2 mutations and should be offered genetic testing. Refer to genetics service • If found to be positive for BRCA1 or BRCA2, also at high risk of ovarian cancer and thus ongoing surveillance is required
Colorectal cancer	
Slightly higher risk if: • One relative with colorectal cancer diagnosed at 55 years or over Moderately higher risk if: • One first degree relative with colorectal cancer diagnosed less than 55 years • Two first or second relatives on the same side of the family with colorectal cancer diagnosed at any age Potentially high risk if: • Three or more first or second degree relatives on the same side of the family diagnosed with colorectal cancer or suspected HNPCC • Two or more first or second degree relatives on the same side of the family diagnosed with colorectal cancer including any of: – multiple colorectal cancers in the one person – colorectal cancer diagnosed in a family member less than 50 years – more than one relative with endometrial cancer or ovarian cancer – one or more relative diagnosed with colorectal cancer with a large amount of adenomas spread throughout large bowel – presence of a high risk mutation identified in a family member	• Faecal occult blood testing (FOBT) at least every 2 years from 50–80 years of age • Colonoscopy every 5 years from 50–80 years (for those at moderately high risk), or 10 years less than age of first diagnosis of colorectal cancer in the family • Refer to genetics service for discussion regarding possibility of genetic testing • Colonoscopy every 1–2 years over 25 years of age for potentially high risk patients • Recommendations vary according to type of colorectal cancer (eg. FAP vs. HNPCC)
Melanoma	
Increased risk if: • All patients, including children, should be advised to adopt protective measures from the sun • Screening and skin self examination are recommended for high risk individuals • High risk features include: – multiple banal or dysplastic naevi with a family history of melanoma – dysplastic naevi in first degree relative	• Start screening high risk individuals in early teenage years on an annual basis • Stay alert for lesions with malignant features in intervening years • Education regarding protection from sun from birth

Table 1. Current screening and management guidelines incorporating family history as a risk predictor[14] (continued)

Screening guidelines	Management guidelines
Type 2 diabetes Increased risk if: • First degree relative with type 2 diabetes • Hypertension present • Indigenous Australian, Pacific Islander, Chinese, or from Indian subcontinent – begin screening at 35 years of age	• Begin screening at 55 years of age in general population, every 3 years • Begin screening at 45 years in at risk patients; and 35 years for those with at risk ethnicity, annually • Measure plasma glucose, preferably fasting • Confirm with oral glucose tolerance test • Encourage risk factor reduction: low fat diet, weight loss, increased physical activity
Cardiovascular disease Increased risk if: • Family history of premature heart disease in a first degree relative: <55 years in a man, <65 years in a woman • Familial hypercholesterolaemia or familial combined hyperlipidaemia is present in the family • Indigenous Australian	• Screen blood pressure of all adults from 18 years, at least every 2 years; or annually for those with multiple risk factors • Screen cholesterol levels of all healthy adults without risk factors from 45 years of age, every 5 years • Screen cholesterol levels of at risk patients from 18 years of age, annually • Consider drug treatment given: – increased cholesterol levels in conjunction with family history of premature CVD or other risk factors – poor response to lifestyle changes – elevated cholesterol due to familial hypercholesterolaemia
Hereditary haemochromatosis Increased risk if: • First or second degree relative of an affected person • First or second degree relative of someone with an identified mutation in the hfe gene • Diabetes, atypical arthritis, cardiomyopathy	• Transferrin saturation test: if >45%, DNA test • Serum ferritin concentration: if raised on more than one occasion, DNA test • DNA typing for all first and second degree relatives of an index case
Cystic fibrosis Increased risk if: • Family history of cystic fibrosis • Partner is affected or a known carrier of cystic fibrosis (risk to offspring) • Consanguineous relationship with northern European ancestry	• Refer to genetics service for discussion about genetic testing
Hameoglobinopathies and thalassaemia Increased risk if: • Southern mediterranean or southeast Asian background • Family history of haemoglobinopathy	• In high risk ethnic population, screen all pregnant women
Osteoporosis Increased risk if: • Premature menopause (<45 years) • Family (especially maternal) history of hip fracture	• Advise about risk factor modification: healthy diet high in calcium, smoking cessation, falls prevention counselling • Consider HT in postmenopausal women

Table 1. Current screening and management guidelines incorporating family history as a risk predictor[14] (continued)

Screening guidelines	Management guidelines
Fragile X syndrome Increased risk if: • Male or female with intellectual disability, developmental delay or learning disability of unknown cause • Male with autism-like features • Family history of undiagnosed intellectual disability or Fragile X syndrome • Previous Fragile X cytogenetic test that was negative or inconclusive • Woman with a personal or extended family history of ID, DD or learning disability	• Arrange, or refer to genetic service to arrange testing via karyotyping (cytogenetic studies) via blood sample
Mental illness Increased risk if: • Family and/or personal history of depression • Family history of suicide	• Maintain a high level of clinical awareness of those at increased risk

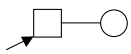
However, pedigree taking is perhaps not the most complicated part of the process. Disease risk assessment, particularly for some of the familial cancers, is a complex task, as demonstrated by the multiple risk criteria in guidelines.[13] General practitioners often overestimate the risk associated with family history.[23] The difficulties of implementing even simple guidelines in general practice are well described.[24] Computer decision support systems have been proposed as a potential method to enable GPs to create pedigrees and assess familial disease risk through the implementation of risk assessment guidelines.[25] Such a resource, known as the GRAIDS software, that provides individualised risk assessment and management advice to GPs for patients with a family history of breast, ovarian or colorectal cancers has recently completed a trial in the United Kingdom, the results of which will be available in 2006.[26] *Figure 2* shows a screenshot of this software. A similar tool is currently being developed and piloted for Australian general practice that covers a wider range of common chronic diseases including cancer, heart disease and diabetes.

Conclusion

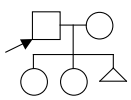
The family history should be used in general practice to support individual risk assessment and tailored disease prevention for common chronic diseases including cancer, heart disease

Step 1
Draw the symbol for the family member being seen. Indicate this person with an arrow, and enter any pertinent details (eg. name, age)

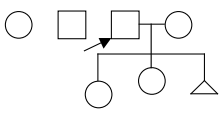
Step 2
Draw a line directly across to a symbol for a partner



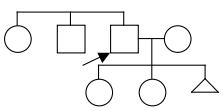
Step 3
Ask about the number of pregnancies pertaining to the couple. Draw a reverse 'T' from the partnership line and add the symbol for each child and pregnancy below it, joined by a vertical line



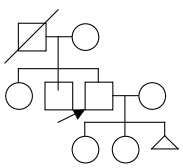
Step 4
Ask about brothers and sisters for each of the couple. Add the symbols along side the corresponding person



Step 5
Indicate the relationship between siblings by drawing a vertical line stemming from each symbol and joining them together with a horizontal line



Step 6
Add a vertical line from this sibship line, and add parents.
(Note: indicate deceased relatives using a diagonal line through the symbol and include details such as age at death, age of diagnosis)



Step 7
Repeat steps 4–6 for each parent to include aunts, uncles and grandparents on both sides of the family member you are seeing. The same information should be collected for the partner's side of the family

male □
female ○
pregnancy △

Figure 1. Taking a family history and drawing a pedigree
Source: The genetics file – a resource for general practitioners. Victoria: Genetic Health Services, 2003

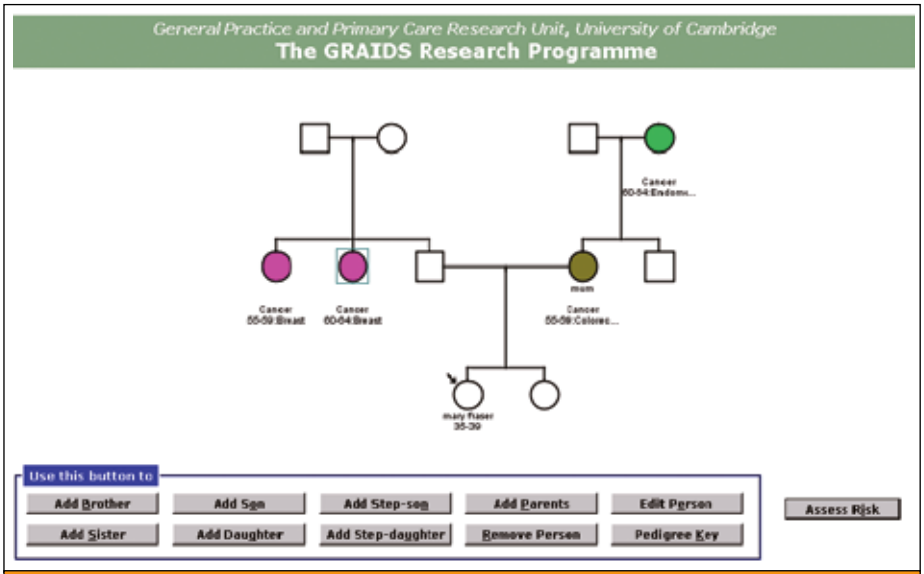


Figure 2. Screenshot of GRAIDS – a family history tool for GPs

and diabetes. This requires the development of new skills in taking a more detailed family history, constructing a pedigree and using this to determine personal disease risk. Further research is required to examine innovative methods to support disease risk assessment and develop family history screening tools for use in general practice.

Conflict of interest: none declared.

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