Improving identification of Familial Breast & Colorectal Cancer & *how do we implement* in General Practice?

Nadeem Qureshi
Division of Primary Care
Familial breast cancer

The classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care
How big an issue?

• **Breast cancer**: lifetime risk 8-10
• 1 in 5 cases have a **family history**
• Up to 3% breast cancers in **women** due to BRCA1 & BRCA2 mutation
• Up to 15% breast cancers in **men** due to BRCA1 & BRCA2 mutation (& prostate cancer)
• BRCA1 mutation: 60-90% lifetime breast cancer risk; 40-65% ovarian cancer risk
Dominant inheritance

- **Pattern**
  - Affected people in each generation
  - Males and females affected in approx. equal numbers
  - All forms of transmission seen, including male to male transmission

- **Dominant**: Needs only one copy of a gene pair to be altered to cause the disease
Rationale for management: *risk stratification*

<table>
<thead>
<tr>
<th>Breast cancer risk category</th>
<th>Definition of category</th>
<th>Probability of a breast cancer genetic mutation (BRCA1, BRCA2 or TP53 mutation)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Near population risk</strong></td>
<td>Lifetime breast cancer risk from aged 20</td>
<td>less than 3%</td>
</tr>
<tr>
<td></td>
<td>Breast cancer risk between age 40 and 50 years</td>
<td>less than 3%</td>
</tr>
<tr>
<td><strong>Moderate risk</strong></td>
<td>less than 17% (equivalent to less than 1 in 6)</td>
<td>a risk of 3–8%</td>
</tr>
<tr>
<td></td>
<td>17% or a greater but less than 30% (equivalent to greater than 1 in 4)</td>
<td></td>
</tr>
<tr>
<td><strong>High risk</strong></td>
<td>30% or greater (equivalent to greater or equal to 1 in 3)</td>
<td>a risk of greater than 8%</td>
</tr>
</tbody>
</table>
FH recommendations

• Detailed family history (FHx):
  – women with concerns about breast cancer risk
  – clinically relevant e.g. HRT, on registration

• What information to collect:
  – Age at which diagnosed
  – Relationship to affected (paternal; maternal)
  – Ethnicity
  – Nature of cancer
  – Gene mutation in family

How collect & interpret family history information?
- discuss later
Primary care management

Woman presents with concerns regarding family history, or concerns are raised in consultation (e.g., breast symptoms, HRT or oral contraceptive pill use)

Has a faulty gene been identified in the family?

Yes

Offer direct referral to tertiary care

No

Does 1st and 2nd degree maternal or paternal family history show any breast cancer?

Yes

No

Is there ONLY ONE relative diagnosed with breast cancer over age 40?

Yes

No

Does the woman have at least one tick in Box A?

Yes

Offer referral to secondary care

No

Is the woman aged 40–49 years?

Yes

Inform woman she will not generally be offered additional mammography

No

Does the woman have one tick in Box B?

Yes

Is there a paternal history of breast cancer?

Yes

No

Are there any unusual cancers in family? (see below) or is there Jewish ancestry?

Yes

Seek advice from secondary care contact about level of risk and appropriateness of referral

No

Manage in primary care
- Offer appropriate information (see Box 1, page 11)
- Offer support mechanisms to women with ongoing concerns not being referred

Box A: Referral criteria from primary care to secondary care: women likely to be at more than raised risk (see page 5)

A tick in any box indicates a positive referral

<table>
<thead>
<tr>
<th>Condition</th>
<th>Box A Criteria</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female breast cancers only</td>
<td>One 1st degree relative and one 2nd degree relative diagnosed before average age 50</td>
<td></td>
</tr>
<tr>
<td>Male breast cancer</td>
<td>One 1st degree male relative diagnosed at any age</td>
<td></td>
</tr>
<tr>
<td>Bilateral breast cancer</td>
<td>One 1st degree relative where 1st primary diagnosed before age 50 for bilateral breast cancer, each breast has the same cause</td>
<td></td>
</tr>
<tr>
<td>Breast and ovarian cancer</td>
<td>One 1st or 2nd degree relative with ovarian cancer at any age and one 1st or 2nd degree relative with breast cancer at any age (one should be a 1st degree relative)</td>
<td></td>
</tr>
</tbody>
</table>

Information to remember when taking a family history:
- All relatives must be on one side of the family and be blood relatives of the consultee and of each other.
- First-degree relatives: mother, father, daughter, son, sister, brother.
- Second-degree relatives: grandparent, grandchild, aunt, uncle, niece and nephew; half sister and half brother.
- Third-degree relatives: great grandparent, great grandchild, great aunt, great uncle, first cousin, grand nephew and grand niece.
- Paternal history: two or more relatives diagnosed with breast cancer on father’s side of family.

Unusual cancers:
- Bilateral breast cancer
- Male breast cancer
- Ovarian cancer
- Sarcoma at younger than age 45 years
- GI or childhood adrenal cortical carcinoma
- Complicated pattern of multiple cancers at young age

Box B: Referral criteria from primary care to secondary care: women likely to be at raised risk (see page 5)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Box B Criteria</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female breast cancers only</td>
<td>One 1st degree relative diagnosed before age 40</td>
<td></td>
</tr>
<tr>
<td>Male breast cancer</td>
<td>One 1st degree relative and one 2nd degree relative diagnosed after average age 50</td>
<td></td>
</tr>
</tbody>
</table>

1 Women with Jewish ancestry are around 5–10 times more likely to carry BRCA1 or BRCA2 mutations than women in non-Jewish populations.
Do they meet either of the following criteria?
- Diagnosis under 40 years
- Total family history meets criteria for referral to secondary care*

Are any of the following present in the family history?
- Bilateral breast cancer
- Male breast cancer
- Ovarian cancer
- Jewish ancestry
- Sarcoma in a relative younger than 45 years
- Glioma or childhood adrenal cortical carcinomas
- Complicated patterns of multiple cancers at a young age
- Paternal history of breast cancer (two or more relatives on the father's side of the family)

Seek advice from the designated secondary care contact

*Referral criteria to secondary care:
- One first-degree female relative diagnosed with breast cancer at younger than age 40 years or
- One first-degree male relative with breast cancer at any age or
- One first-degree relative with bilateral breast cancer where the first primary was diagnosed at younger than age 50 years or
- Two first-degree relatives, or one first-degree relative and one second-degree relative, diagnosed with breast cancer at any age or
- One first-degree or second-degree relative diagnosed with breast cancer at any age and one first-degree or second-degree relative diagnosed with ovarian cancer at any age (one of these should be a first-degree relative) or
- Three first-degree or second-degree relatives diagnosed with breast cancer at any age

Offer referral to secondary care

Do they meet the following criteria?
- Total family history meets criteria for referral to secondary care*

Offer referral to secondary care

Manage in primary care, and provide standard written information
Improving FHx collection

- Self-administered questionnaire
Interpreting Family History

• Decision support
Add Diseases Affecting Family Members
Please select a family member. To select a partnership, twins or the person to adopt the selected family member, hold down shift and select the other family member.
Primary care management

Woman presents with concerns regarding family history, or concerns are raised in consultation (e.g., breast symptoms, HRT or oral contraceptive pill use)

Has a faulty gene been identified in the family?

Yes

Offer direct referral to tertiary care

No

Does 1st and 2nd degree maternal or paternal family history show any breast cancer?

No

Manage in primary care
- Offer appropriate information (see Box 1, page 11)
- Offer support mechanisms to women with ongoing concerns not being referred

Most common referral path

Yes

Is there ONLY ONE relative diagnosed with breast cancer over age 40?

No

Are there any unusual cancers in family? (see below) or Is there a paternal history of breast cancer? or Is there Jewish ancestry?

No

Box A: Referral criteria from primary care to secondary care: women likely to be at more than raised risk (see page 5)

- Female breast cancers only
  - One 1st degree relative and one 2nd degree relative diagnosed before average age 50
  - Two 1st degree relatives diagnosed before average age 50
  - Three or more 1st or 2nd degree relatives diagnosed at any age

- Male breast cancer
  - One 1st degree male relative diagnosed at any age

- Bilateral breast cancer
  - One 1st degree relative where 1st primary diagnosed before age 50
  - For bilateral breast cancer, each breast has the same equal value as one relative

- Breast and ovarian cancer
  - One 1st or 2nd degree relative with ovarian cancer at any age and one 1st or 2nd degree relative with breast cancer at any age (one should be a 1st degree relative)

Box B: Referral criteria from primary care to secondary care: women likely to be at raised risk (see page 5)

- Female breast cancers only
  - One 1st degree relative diagnosed before age 40

- One 1st degree relative and one 2nd degree relative diagnosed after average age 50

- Two 1st degree relatives diagnosed after average age 50

Information to remember when taking a family history
All relatives must be on same side of family and be blood relatives of the consultee and of each other.
First-degree relatives: mother, father, daughter, son, sister, brother
Second-degree relatives: grandparent, grandchild, aunt, uncle, niece and nephew, half sister and half brother
Third-degree relatives: great-grandparent, great-grandchild, great aunt, great uncle, first cousin, grand nephew and grand niece
Paternal history: two or more relatives diagnosed with breast cancer on father's side of family

Unusual cancers
- Bilateral breast cancer
- Male breast cancer
- Ovarian cancer
- Sarcoma at younger than age 45 years
- Glioma or childhood adrenal cortical carcinoma
- Complicated patterns of multiple cancers at young age

Does the woman have at least one tick in Box A?

Yes

Offer referral to secondary care

No

Does the woman have one tick in Box B?

Yes

Is the woman aged 40–49 years?

No

Inform woman she will not generally be offered additional mammography

No

Does woman want risk counselling/risk management advice or consideration for prevention trials?

Yes

Seek advice from secondary care contact about level of risk and appropriateness of referral

No

Yes

1 Women with Jewish ancestry are around 5–10 times more likely to carry BRCA1 or BRCA2 mutations than women in non-Jewish populations.
Catherine Black (20-Feb-1970)

Summary
Offer referral to secondary care.

Box A Criteria (women likely to be at more than moderate risk)
- Has one female 1st degree relative and one female 2nd degree relative diagnosed with breast cancer before average age 50.
- Has three or more female 1st or 2nd degree relatives diagnosed with breast cancer at any age

Box B Criteria (women likely to be at moderate risk)
- Has two female 1st degree relatives diagnosed with breast cancer after average age 50.

Additional Criteria
- 1st and 2nd degree maternal or paternal family history shows breast cancer.
- Has unusual cancers in the family.
<table>
<thead>
<tr>
<th>Name</th>
<th>DOB</th>
<th>10 yr risk</th>
<th>FEV 10 yr risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brenda White</td>
<td>12-Jan-1940</td>
<td>11.91%</td>
<td>3.98</td>
</tr>
<tr>
<td>Bridget Green</td>
<td>02-Jul-1946</td>
<td>7.91%</td>
<td>2.67</td>
</tr>
<tr>
<td>Carol White</td>
<td>17-Oct-1963</td>
<td>7.08%</td>
<td>3.30</td>
</tr>
<tr>
<td>Catherine Black</td>
<td>20-Feb-1970</td>
<td>2.88%</td>
<td>2.34</td>
</tr>
<tr>
<td>Claire White</td>
<td>17-Oct-1963</td>
<td>19.08%</td>
<td>8.90</td>
</tr>
<tr>
<td>Denise Black</td>
<td>22-Nov-1990</td>
<td>0.04%</td>
<td>1.83</td>
</tr>
</tbody>
</table>
Process in feasibility study

CME session

Postal survey to women

Invite women during consultation

Family history entered into FaHRAS & risk information produced

Information to GP

Average risk (< 17% lifetime)

Moderate/high risk (17%+ lifetime)

Women posted risk status & breast awareness leaflet

Women posted risk status & breast awareness leaflet

GP discusses risk status, management, & referral
**GENETIC RISK OF BREAST CANCER STUDY: FAMILY HEALTH QUESTIONNAIRE**

**This section asks about your IMMEDIATE RELATIVES**

<table>
<thead>
<tr>
<th>Relationship to you (optional)</th>
<th>First name or year of birth</th>
<th>Did relative have breast cancer, ovarian cancer or prostate cancer? <em>Please state which cancer.</em></th>
<th>Age when cancer developed</th>
<th>If this person died, what was their age?</th>
<th>What was the cause of death?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Your mother</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your father</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your grandparents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your mother’s mother</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your mother’s father</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your father’s mother</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your father’s father</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Do not give information about family members who are not your blood relatives e.g. step- or foster-brothers or sisters or children/relatives by marriage.
Online Family History Questionnaire

FaHRAS for Primary Healthcare
[Familial Breast Cancer Risk Assessment]

1: Patient
2: Patient's Health
3: Relatives
4: Relative's Health
5: Any Other Information

Patient Details
Please enter the patient’s details below.

- Participant number:
- GP Name:
- Date Of Birth:
- Are they adopted:
- Are they a twin:

Next >>
Dear GP

{Patient name} {Date of birth} {Patient Address}

Breast Cancer Risk Assessment: Moderate/high risk of familial breast cancer

Action: Offer secondary care referral

Family History
The patient has been found to be at moderate risk of familial breast cancer by the Familial History Risk Assessment Software (FaHRAS).

Reason for recommendation: has two first-degree relatives, or one first-degree and one second-degree relative, diagnosed with breast cancer at any age.

Recommendation
It is recommended that the patient be referred to the Breast Cancer Specialist Services for a further consultation. The patient has been posted a letter regarding her breast cancer risk status and has been asked to contact you to discuss her result.
Participant Feedback

“...since completing this form I have just been diagnosed with breast cancer and I am due to have a mastectomy on the 16th April. If it wasn't for your survey this would probably remained undetected. I cannot thank you enough for originally contacting me.”

- 46 years, high risk

“... it’s been identified that instead of starting mammograms at the age of 50, I’m starting them now at the age of 40 and it’s only through participating ... that that’s happened. And actually that might be a lifesaver.”

- 38 years, high risk
Further potential of FAHRAS
Case Scenarios from Colorectal Patients

**Patient 1**
Strong FH on maternal side;
- *Maternal uncle bowel dx: 50, d: 50ish*
- *Maternal Aunt bowel dx: 80ish, died*
- *Maternal Aunt breast dx:60ish d: 60ish,*
- *Maternal cousin bowel dx: 30, d: 30*
- *Maternal cousin bowel dx: 50 d: 50ish*
- *Another uncle died bowel not sure which side*

**Patient 2**
Strong FH on maternal side;
- *Mother breast cancer, dx: 62 d: 64*
- *Brother colon cancer, dx & d: 58*
- *Proband removal of polyps*
What to do if a patient has a family history of bowel and related cancers.

**Key**
- Green is low risk
- Orange is moderate risk
- Pink is moderate to high risk
- Red is high risk

<table>
<thead>
<tr>
<th>Number of close relatives with bowel cancer</th>
<th>Age of cancer diagnosis</th>
<th>Refer to FH clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (1\textsuperscript{st} degree)</td>
<td>= 45</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>&gt;45</td>
<td></td>
</tr>
<tr>
<td>1 (1\textsuperscript{st} degree)</td>
<td>Separate or multiple tumours at any age</td>
<td>✓</td>
</tr>
<tr>
<td>1 (1\textsuperscript{st} degree-polyps only)</td>
<td>More than one significant (&gt;10mm) polyp under 50yrs</td>
<td>✓</td>
</tr>
<tr>
<td>2 (same side or both parents)</td>
<td>Average age = 70</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>&gt;70</td>
<td></td>
</tr>
<tr>
<td>2 (same side)*</td>
<td>Average age &lt;50</td>
<td>✓</td>
</tr>
<tr>
<td>3 or more (same side)*</td>
<td>Any age</td>
<td>✓</td>
</tr>
<tr>
<td>Polyposis Coli</td>
<td>Positive family history</td>
<td>✓</td>
</tr>
</tbody>
</table>

*Related cancers: When there is, in addition to at least one bowel cancer, a history of endometrial, ovarian, gastric, biliary, renal, small bowel or brain cancer in other close relatives.

- A close relative is any first or second degree relative (parent, brother, sister, child, aunt, uncle, grandparent).
- The family history should be of affected \textbf{blood relatives} through either the \textbf{maternal or paternal side} of the family.
- For \textbf{enquiries} about a patient's family history, or if there is a history of unusual cancers, please contact the Clinical Genetics Service on: 0115 9627728.
Patient presents with a Family History of Bowel or related cancers

Assess family history

- Lower risk
  - Manage in Primary Care
  - Reassure
  - Advise on diet and lifestyle
  - Advise to report any symptoms or changes in Family History promptly

- Higher risk
  - Refer to Bowel FH clinic
  - Detailed risk assessment/discuss options according to level of risk
  - Colonoscopy (frequency varies)
  - Genetic testing
  - Participation in research studies

In Nottingham, referrals should be made to the Family History Clinic, Department of Surgery, E Floor, West Block, QMC.
Online Family History Questionnaire

FaHRAS for Primary Healthcare

[ Familial Breast Cancer Risk Assessment ]

New Assessment  Settings  Change Password  Users  Event Log

1: Patient  2: Patient’s Health  3: Relatives  4: Relative’s Health  5: Any Other Information

Patient Details

Please enter the patient’s details below.

- Participant number:
- GP Name:
- Date Of Birth:
- Are they adopted:
- Are they a twin:

Next >>