Assessing Risks for families with inherited cancers: an introduction to a new system

Kevin Hughes, MD
188 adult hereditary syndromes

- Benign 153
- Cancer 32
- Cancer plus benign 3

Adult hereditary syndromes: 188

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mendellian disorder</td>
<td>Familial arrhythmogenic right ventricular dysplasia</td>
</tr>
<tr>
<td>Abdominal aortic aneurysm</td>
<td>Familial combined hyperlipidemia</td>
</tr>
<tr>
<td>Abdominal obesity-metabolic syndrome</td>
<td>Familial dysautonomia</td>
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<tr>
<td>Acute pleuritis</td>
<td>Familial deficiency of tissue plasminogen activator</td>
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<tr>
<td>Adult polyarteric renal disease</td>
<td>Familial hyperaldosteronemia, type 1</td>
</tr>
<tr>
<td>Alport syndrome</td>
<td>Familial hypercholesterolemia</td>
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<tr>
<td>Amyloidosis V</td>
<td>Familial hypertriglyceridemia</td>
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<tr>
<td>Amyloidosis VI</td>
<td>Familial hypercholesterolemia with Wolff-Parkinson-White syndrome</td>
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<tr>
<td>Amyloidosis VII</td>
<td>Familial idiopathic prepubertal edema</td>
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<td>Antithrombin III deficiency</td>
<td>Familial hypoproteinemia</td>
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<tr>
<td>Apolipoprotein(a)</td>
<td>Familial mitral valve prolapse</td>
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<tr>
<td>Apoptosis (a)</td>
<td>Familial partial lipodystrophy</td>
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<tr>
<td>Atherosclerotic malformation of the brain</td>
<td>Familial pseudohypoparathyroid due to red cell leak</td>
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<tr>
<td>Arthrogryposis and scoliosis</td>
<td>Familial neurofibromatosis</td>
</tr>
<tr>
<td>Atherosclerotic susceptibility</td>
<td>Familial thoracic aortic aneurysan</td>
</tr>
<tr>
<td>Atrial cardiomyopathy with heart block</td>
<td>Familial ventricular tachycardia</td>
</tr>
<tr>
<td>Autoimmune polyendocrinopathy syndrome, type 1</td>
<td>Fibromuscular dysplasia of arteries</td>
</tr>
<tr>
<td>AD Early-Onset muscular dystrophy</td>
<td>Friedreich ataxia</td>
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<tr>
<td>AD Homochromatosis</td>
<td>Generalized juvenile polyposis with pulmonary AV fistula</td>
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<td>AD Pseudohypoparathyroid</td>
<td>Homochromatosis (classical and type 3)</td>
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<td>AD Pseudohypoparathyroid</td>
<td>Hepatitis B deficiency</td>
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<tr>
<td>AR dilated cardiomyopathy</td>
<td>Hereditary hemorrhagic telangiectasia, type 1</td>
</tr>
<tr>
<td>AR hypercholesterolemia</td>
<td>Hereditary hemorrhagic telangiectasia, type 2</td>
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<tr>
<td>AR nemaline myopathy</td>
<td>Hereditary neurocutaneous angiomatosis</td>
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<tr>
<td>AR Noonan syndrome</td>
<td>Hereditary pancreatitis</td>
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<tr>
<td>Bardet-Biedl syndrome</td>
<td>Herman-Lund syndrome</td>
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<td>Barth syndrome</td>
<td>Hidrotich-rich myoglobin</td>
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<td>Becker type muscular dystrophy</td>
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<td>Berardinelli-Neale congenital lipodystrophy</td>
<td>Homocysteinemia/homocystinuria</td>
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<td>Bloom syndrome</td>
<td>Hyperesotic periodic paroxysm</td>
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<td>Bloom syndrome</td>
<td>Hypertrophic cardiomyopathy</td>
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<tr>
<td>Brugada syndrome</td>
<td>Insulin receptor defect</td>
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<td>CADASIL</td>
<td>Insulin-resistant diabetes mellitus with acanthosis nigricans and hypertension</td>
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<td>Cardiac conduction defect</td>
<td>Intracranial berry aneurysan</td>
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<td>Cardiomyopathy-hypogonadism/colagenose syndrome</td>
<td>Juvenile homochromatosis</td>
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<td>Cerebral cavernous malformations</td>
<td>Kaars-Gerrits syndrome</td>
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<td>Cerebrovasculardisease with thin skin, alopecia</td>
<td>Leber ophtal alinity</td>
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<td>Cerebrovascular disease with thin skin, alopecia</td>
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<td>Cortisol 11-beta-hydroxylase deficiency</td>
<td>Limb-girdle muscular dystrophy, type 1B</td>
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<td>Crostata syndrome</td>
<td>Long QT1 (Romano Ward syndrome)</td>
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<tr>
<td>Dilated cardiomyopathy</td>
<td>Long QT2</td>
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<td>Dilated cardiomyopathy with wooly hair and lanterdema</td>
<td>Long QT4</td>
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<tr>
<td>Duchenne type muscular dystrophy</td>
<td>Long QT7 (Lange-Nielson syndrome)</td>
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<td>Dysferrochelamines</td>
<td>Long QT8</td>
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<tr>
<td>Ehlers-Danlos syndrome, type IV</td>
<td>Long QT7 (Anderson carboxyhydrinotic periodic paroxysm)</td>
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<td>Mal de Meleda</td>
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<td>Malnourished hyperthermia susceptibility 1</td>
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<tr>
<td>Ehlers-Danlos syndrome, type unspecified</td>
<td>Marfan syndrome</td>
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<td>Emery-Dreifuss muscular dystrophy</td>
<td>Maternally transmitted diabetes-neurofibromatosis</td>
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<td>Endocardial fibroelastosis</td>
<td>Maternal onset diabetes-neurofibromatosis</td>
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<td>Fabry disease</td>
<td>Maturity onset diabetes-neurofibromatosis</td>
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<td>Familial antiphospholipid syndrome</td>
<td>Maturity onset diabetes-neurofibromatosis</td>
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<td>MELAS</td>
<td>Moyamoya</td>
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<tr>
<td>Multiple endocrine dysplasia with early-onset diabetes mellitus</td>
<td>Myotonic dystrophy</td>
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<tr>
<td>Noonan syndrome</td>
<td>Myasthenia</td>
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<td>Non-endocrine polyendocrinopathy syndrome</td>
<td>Nephropathic cardiomyopathy</td>
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<tr>
<td>Neurofibromatosis, type 1</td>
<td>Neurofibromatosis, type 2</td>
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<tr>
<td>Niemann-Pick disease (types C and E)</td>
<td>Nocturnal myopathy</td>
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<tr>
<td>Noonan syndrome</td>
<td>Obesity and endocrinopathy due to impaired processing of prohormones</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>Obstructive sleep apnea</td>
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<tr>
<td>Pancreatic beta cell agenesis with neonatal diabetes mellitus</td>
<td>Paroxysms with sleep apnea and mental depression</td>
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<td>Paroxysmal familial von Willebrand syndrome</td>
<td>Paroxysmal familial ventricular fibrillation</td>
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<tr>
<td>PHACE association</td>
<td>Progeria</td>
</tr>
<tr>
<td>Pinell hyperplasia, insulin-resistant diabetes mellitus</td>
<td>Progressive familial heart block and 1 and 2</td>
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<tr>
<td>Plasminogen activator inhibitor 1</td>
<td>Protein C deficiency</td>
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<td>Plasminogen deficiency</td>
<td>Protein S deficiency</td>
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<td>Pseudoachromatosis, elasticum</td>
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<td>Schmidt syndrome</td>
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<td>Sjogren-Larsson syndrome</td>
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<td>Sneddon syndrome</td>
<td>Progressive familial heart block, 1 and 2</td>
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<td>Spontaneous coronary dissection</td>
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<td>Stress-induced polymorphic ventricular tachycardia</td>
<td>Progressive familial heart block, 1 and 2</td>
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<tr>
<td>Tangier disease</td>
<td>Progressive familial heart block, 1 and 2</td>
</tr>
<tr>
<td>Tardive thal muscular dystrophy</td>
<td>Protein C deficiency</td>
</tr>
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<td>Thalamic-responsive megakaryoblastic anemia syndrome</td>
<td>Protein S deficiency</td>
</tr>
<tr>
<td>Three M syndrome</td>
<td>Protein S deficient</td>
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<td>Thrombophiles due to deficiency of activated protein C</td>
<td>Protein S deficiency</td>
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<tr>
<td>Thrombophiles due to thrombomodulin defect</td>
<td>Protein S deficient</td>
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<tr>
<td>Tissue factor pathway inhibitor</td>
<td>Protein S deficient</td>
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<td>Transient neonatal diabetes</td>
<td>Protein S deficient</td>
</tr>
<tr>
<td>Transthyretin</td>
<td>Protein S deficient</td>
</tr>
<tr>
<td>Tuberous sclerosis</td>
<td>Protein S deficient</td>
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<td>Type I hyperproteinaemia (apolipoprotein C-8 deficiency)</td>
<td>Protein S deficiency</td>
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<tr>
<td>Type IV hyperproteinaemia</td>
<td>Protein S deficient</td>
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<tr>
<td>Von Hippel-Lindau syndrome</td>
<td>Protein S deficient</td>
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<tr>
<td>Warden distal myopathy (SMAR)</td>
<td>Protein S deficient</td>
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<td>Werner syndrome</td>
<td>Protein S deficient</td>
</tr>
<tr>
<td>Williams syndrome</td>
<td>Protein S deficient</td>
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<tr>
<td>Wilson disease</td>
<td>Protein S deficient</td>
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<td>Wolf-Hirschprung syndrome</td>
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<td>Wolf syndrome</td>
<td>Protein S deficient</td>
</tr>
<tr>
<td>XL dilated cardiomyopathy</td>
<td>Protein S deficient</td>
</tr>
<tr>
<td>XL immunodeficiency, polyendocrinopathy, enteropathy</td>
<td>Protein S deficient</td>
</tr>
<tr>
<td>XL osteoelastic anemia</td>
<td>Protein S deficient</td>
</tr>
</tbody>
</table>

13 years of genetic testing

- BRCA1/2 mutation carriers in the US
  - ~1,000,000
- Number identified to date
  - ~20,000 to 30,000 (2 to 3%)

This is likely the best of any adult hereditary syndrome
Problems to solve

• Most high risk women are not being identified or referred for counseling

• Our Risk Clinics could not manage the volume if all high risk women were referred
Introduction and Concept

• In the age of the human genome project:
  – Our health care system must identify women at high risk of breast and ovarian cancer and manage them appropriately
  – This will decrease the morbidity and mortality of these diseases
Our solution

• We have developed a system that will
  – allow the patient to enter her own data into a database
  – decrease the labor intensive effort required of clinicians
    • Automatic analysis
    • Pedigree creation

• Thus
  – Decrease labor for staff
  – Decrease cost
  – Increase volume of patients cared for
  – Increase quality of care
Large scale methods

• More high risk women identified
  – Integration of FH into normal clinic workflow

• More women cared for by the Risk Clinic
  – Increased efficiency of risk counselor
Large scale methods

• More high risk women identified
  – Integration of effective FH into workflow
HughesRiskApps allows input to a central database from multiple sources

- Desktop in Mammo
- Tablet PC
- Website
Patient can enter her own data using a simple Tablet PC interface

- Requiring little or no help from the staff, patients enter their own data.
- 5th Grade Reading Level
- Available in English, Spanish and Italian

Sample screenshots follow
Patient can enter her own data using a simple Tablet PC interface

• Requiring little or no help from the staff, patients enter their own data.
• 5th Grade Reading Level
• Available in English, Spanish and Italian

Sample screenshots follow
Cancer Risk Assessment Survey

Do you have or have you ever had cancer?

- Yes
- No
- Not sure
- Clear

Back   Next
Do you have or have you ever had cancer?

- Yes
- No
- Not sure
- Clear

Back  Next
Which cancers do you have or have you had?

- Brain Cancer
- BREAST Cancer
- Cervical Cancer
- Colon or Rectal Cancer
- Hodgkins Lymphoma
- Kidney or Bladder Cancer
- Leukemia
- Liver Cancer
- Lung Cancer
- Lymphoma (Non-Hodgkins)
- Melanoma
- Ovarian Cancer
- Other
- Pancreatic Cancer
- Sarcoma
- Stomach Cancer
- Thyroid Cancer
- Uterine Cancer
How old were you when you were diagnosed with Breast Cancer?

45
1 2 3
4 5 6
7 8 9
0 Clear
Have any of your blood relatives had cancer?

- Yes
- No
- Not sure
- Clear
Cancer Risk Assessment Survey

Which of these relatives have had or currently have cancer?

- [ ] Sister
- [ ] Brother
- [ ] Nephew
- [ ] Niece

How many Sisters have had Cancer?

We will ask about other relatives on the next couple of screens.
Cancer Risk Assessment Survey

Which cancers does your Sister have or has she had?

- Brain Cancer
- BREAST Cancer
- Cervical Cancer
- Colon or Rectal Cancer
- Hodgkins Lymphoma
- Kidney or Bladder Cancer
- Leukemia
- Liver Cancer
- Lung Cancer
- Lymphoma (Non-Hodgkins)
- Melanoma
- Ovarian Cancer
- Other
- Pancreatic Cancer
- Sarcoma
- Stomach Cancer
- Thyroid Cancer
- Uterine Cancer

Back Next
Cancer Risk Assessment Survey

Which relatives on your MOTHER'S side have had or currently have cancer?

- [ ] Mother
- [ ] Maternal Grandmother
- [ ] Maternal Grandfather
- [ ] Maternal Aunt
- [X] Maternal Uncle

How many Maternal Uncles have had Cancer?

- [ ] 0
- [ ] 1
- [ ] More than 1

- [ ] Maternal Cousin (Female)
- [ ] Maternal Cousin (Male)

[Back] [Next]
Which cancers does your Uncle on your mother's side have or has he had?

- Brain Cancer
- BREAST Cancer
- Colon or Rectal Cancer
- Hodgkins Lymphoma
- Kidney or Bladder Cancer
- Leukemia
- Liver Cancer
- Lung Cancer
- Lymphoma (Non-Hodgkins)
- Melanoma
- Other
- Pancreatic Cancer
- Prostate Cancer
- Sarcoma
- Stomach Cancer
- Thyroid Cancer
How old was your Uncle on your mother's side when he was diagnosed with Prostate Cancer?
How many sisters do (did) YOU have?

2

1 2 3
4 5 6
7 8 9
0 Clear

Back  Next
Data Entry via Website
Surgeon General Data Entry

My Family Health Portrait
A tool from the Surgeon General

Using My Family Health Portrait you can:
- Enter your family health history
- Print your family health history to share with family or your health care worker
- Save your family health history so you can update it over time

Talking with your health care worker about your family health history can help you stay healthy!

Learn more about My Family Health Portrait

Create a Family Health History
Use a Saved History

En Español
Surgeon General Data Entry

• My Family Health Portrait allows patients to enter family history data
  – Data saved as an HL7 message
  – Data saved to HealthVault via HL7
Staff Data Entry Through Desktop Interface
The staff can enter or edit patient data using a simple Desktop interface.
Clinical Decision Support

• Immediate actions
  – BRCAPRO
    • Radiologist shown who is high risk
  – Patient receives written guidance
    • Letter suggesting they make an appointment
    • Information sheet

• Weekly
  – Letter sent to patient and PCP
Newton Wellesley Hospital Breast Center
4/1/2007 to 3/31/2008

25,763 Family histories analyzed

<table>
<thead>
<tr>
<th>Risk Calculations</th>
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</thead>
<tbody>
<tr>
<td><strong>Mutation Risk</strong></td>
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<tr>
<td><strong>BRCAPRO</strong></td>
</tr>
<tr>
<td><strong>Myriad Mutation Risk</strong></td>
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<tr>
<td>Probability of BRCA1/2 Mutation</td>
</tr>
<tr>
<td><strong>Cancer Risk</strong></td>
</tr>
<tr>
<td><strong>BRCAPRO</strong></td>
</tr>
<tr>
<td>Five Year Risk</td>
</tr>
<tr>
<td>Lifetime Risk</td>
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<tr>
<td><strong>Claus Model</strong></td>
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<tr>
<td>Five Year Risk</td>
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<td>Lifetime Risk</td>
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<td><strong>Gall Model</strong></td>
</tr>
<tr>
<td>Five Year Risk</td>
</tr>
<tr>
<td>Lifetime Risk</td>
</tr>
</tbody>
</table>

≥10% risk of mutation

915 Patients referred for counseling
Large scale methods

- More women cared for by the Risk Clinic
  - Increased efficiency of risk counselor
Next challenge:

Improve efficiency in the Risk Clinic to manage the influx of patients

- Minimize clinician work
- Minimize redundant data entry
- Minimize dictation and editing
Current Approach

<table>
<thead>
<tr>
<th>Patient provides family history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data into CAGENE</td>
</tr>
<tr>
<td>Data into Progeny</td>
</tr>
<tr>
<td>Assess risk level</td>
</tr>
<tr>
<td>Face to Face counseling</td>
</tr>
<tr>
<td>Letters/Notes generated</td>
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</tbody>
</table>
## Current Approach

<table>
<thead>
<tr>
<th>Step</th>
<th>Time</th>
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</thead>
<tbody>
<tr>
<td>Patient provides family history</td>
<td>0-10 minutes</td>
</tr>
<tr>
<td>Data into CAGENE</td>
<td>5-10 minutes</td>
</tr>
<tr>
<td>Data into Progeny</td>
<td>10-20 minutes</td>
</tr>
<tr>
<td>Assess risk level</td>
<td>5-10 minutes</td>
</tr>
<tr>
<td>Face to Face counseling</td>
<td>30-60 minutes</td>
</tr>
<tr>
<td>Letters/Notes generated</td>
<td>20-40 minutes</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>70-150 minutes</strong></td>
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<tr>
<td>RiskApps</td>
<td>Time</td>
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<td>----------------------------------------------</td>
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<tr>
<td>Patient provides family history</td>
<td>0 minutes</td>
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<tr>
<td>Data into CAGENE</td>
<td>0 minutes</td>
</tr>
<tr>
<td>Data into Progeny</td>
<td>0 minutes</td>
</tr>
<tr>
<td>Assess risk level</td>
<td>5 minutes</td>
</tr>
<tr>
<td>Face to Face counseling</td>
<td>30 to 60 minutes</td>
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<tr>
<td>Letters/Notes generated</td>
<td>10 minutes</td>
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</tbody>
</table>

45 to 75 minutes
Patient enters more detailed family history via a second level Tablet PC interface
Details about each family member are collected.
Cancer Risk Assessment Survey

Is MOM alive?

- Yes
- No
- Not sure
- Clear

Back  Next
Cancer Risk Assessment Survey

Does MOM have or has she ever had cancer?

- Yes
- Yes
- No
- Not sure
- Clear

Back  Next
Which cancers does MOM have or has she had?

- Brain Cancer
- BREAST Cancer
- Cervical Cancer
- Colon or Rectal Cancer
- Hodgkins Lymphoma
- Kidney or Bladder Cancer
- Leukemia
- Liver Cancer
- Lung Cancer
- Lymphoma (Non-Hodgkins)
- Melanoma
- Ovarian Cancer
- Other
- Pancreatic Cancer
- Sarcoma
- Stomach Cancer
- Thyroid Cancer
- Uterine Cancer

[Back] [Next]
<table>
<thead>
<tr>
<th>Cancer Type</th>
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<tbody>
<tr>
<td>Brain Cancer</td>
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<td>Colon or Rectal Cancer</td>
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<td>Lymphoma (Non-Hodgkins)</td>
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<td>Melanoma</td>
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<tr>
<td>Ovarian Cancer</td>
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<tr>
<td>Other</td>
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<tr>
<td>Pancreatic Cancer</td>
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<tr>
<td>Sarcoma</td>
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<td>Stomach Cancer</td>
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<tr>
<td>Thyroid Cancer</td>
<td></td>
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<tr>
<td>Uterine Cancer</td>
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</tr>
</tbody>
</table>
Did MOM have breast cancer in both breasts?

[Yes, Yes, No, Not sure, Clear]
And so on for each family member
Desktop Application for the Risk Counselor
Data from Tablet available for review, editing and enhancement by the risk counselor:

Table interface
Pedigree Interface
Additional risk factors are edited/enhanced
BRCA and other genetic test results can be easily recorded

<table>
<thead>
<tr>
<th>Gene</th>
<th>DNA Change</th>
<th>AA Change</th>
<th>Significance</th>
<th>Allelic State</th>
<th>Comments</th>
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<td>BRCA1</td>
<td></td>
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<td>Deleterious</td>
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<td>BRCA2</td>
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<td>Group</td>
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<td>Breast/Ovarian</td>
<td>Familial Known Mutation Test</td>
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<td>BRCA1 full sequencing</td>
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<td></td>
<td></td>
<td>BRCA2 full sequencing</td>
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<td>BRCA1 and BRCA2 full sequencing</td>
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<td></td>
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<td>BRCA1 and BRCA2 with 5 site rearrangement</td>
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<td></td>
<td></td>
<td>Ashkenazi (BRCA1 and BRCA2)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Other</td>
<td></td>
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<td></td>
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<td>BART</td>
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<td>Ashkenazi (BRCA 1 and 2) plus full gene sequencing</td>
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<tr>
<td></td>
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<td>Ashkenazi (BRCA 1 and 2) plus full gene sequencing + 5 site rearrangement</td>
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<tr>
<td></td>
<td></td>
<td>p53 Full Gene Sequencing</td>
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<td>PTEN Full Gene Sequencing</td>
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<td>ATM Full Gene Sequencing</td>
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<td></td>
<td></td>
<td>CHECK2 Full Gene Sequencing</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Name: Harriet
Age: 50
Bloodline: 
Relationship: Mother
Status: Dead
<table>
<thead>
<tr>
<th>Gene</th>
<th>DNA Change</th>
<th>AA Change</th>
<th>Significance</th>
<th>Allelic State</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRCA1</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**BRCA1 and BRCA2 with 5 site rearrangement**

**Name:** Harriet  
**Bloodline:**  
**Relationship:** Mother  
**Age:** 50  
**Status:** Dead
Testing of other genes (Cardiac shown here) by groups makes useful for any genetics clinic.
Counselor can link families seen before to the current patient.
Risk algorithms run

- Graphs show BRCAPRO run multiple times for the same family using different parameters
BRCAPRO has been run for each relevant family member, with the risk of mutation shown for each.
Genetic Testing recommendations are made
Genetic Testing recommendations are made
Myriad and BRCAPRO results are shown with the ability to use the slider to set the clinician’s decision as to the risk of mutation.
Right bottom side of the screen, family members are listed in order of likelihood of mutation. The willingness of each to be tested can be recorded.
Lifetime risk of breast cancer and the management suggestions are shown for multiple scenarios: without testing (Current synthesis), as if the patient tested positive, as if the patient tested negative and the population risk.
Lifetime risk of ovarian cancer and the management suggestions are shown for multiple scenarios: without testing (Current synthesis), as if the patient tested positive, as if the patient tested negative and the population risk.
Switch perspective to consider the BRCA2 case
Gail model results are displayed
Claus model results are displayed
Myriad model results are displayed
Colorectal tab
PREMM Model

Mutation Risk = 28%

- Presence of CRC in the proband: 0%
- 2 or more CRC in the proband: 0%
- Endometrial cancer in the proband: 0%
- Other HNPCC cancer in the proband: 0%
- Adenoma in the proband: 0%
- 1.5 for presence of 1 CRC in first-degree relative + 0.5 for presence of CRC in second-degree relatives: 1.5
- 0 for 2 or more first-degree relatives with CRC: 0
- 0.5 if a 1 first-degree relative has endometrial cancer + 0.5 for presence of any second-degree relatives also affected: 1
- 0 for 2 or more first-degree relatives with endometrial cancer: 0
- 1 for first- or second-degree relatives with other HNPCC cancer: 1
- -25 for sum of ages at diagnosis - 45 of CRC/adenoma: -25
- -5 for sum of ages at diagnosis - 45 of endometrial cancer: -5

Synthesis of Mutation Risk:

- PREMMPRO: 44%
- PREMM: 28%
Clinical Decision support suggests alternative syndromes in order of likelihood.
Clinical Decision support shows manifestations of selected syndrome.
Patient Name: Test Patient

Unit Number: 99903291001
Date Of Birth: 06/23/1958

Breast/Ovarian Colorectal OMIM Syndromes

Syndrome
- Cowden
- Peutz-Jeghers
- Muir-Torre
- Nonpoly colon
- Ovarian Germ Cell
- BRCA1
- BRCA2
- Desmoid

Show NCBI Entry  Show Gene Test

Related Diseases
- Bone Sarcoma
- Brain Cancer
- Breast Cancer
- Colon or Rectal Cancer
- Kidney or Bladder Cancer
- Lymph Node Cancer
- Melanoma
- Small Intestine Cancer
- Thyroid Cancer
- abnormal adrenal steroid production
- acidosis
DoubleClick on syndrome opens specific OMIM Website and
RightClick on syndrome opens specific Genetests Website
RightClick on syndrome opens both OMIM Website and Genetests Website
Generates multiple documents, saving time on dictation and cost of transcription

• Letter to referring doctor
• Letter to the patient
• Progress note for chart
• Letter to relatives who need testing
• Letter of Medical Necessity for insurance company
  – Justify genetic testing
  – Justify MRI
Letter to the patient

Avon Foundation Comprehensive Breast Care Center
Dr. Kevin S. Hughes, M.D.
Massachusetts General Hospital
55 Fruit Street, Yawkey
Boston, Massachusetts 022114
Fax (617) 724-3895
Phone (617) 724-0048

09/27/2008

10 Main Street
Boston, MA 02115

Dear Mary Test,

You were seen at the Avon Foundation Comprehensive Breast Care Center on 09/27/2008.

You provided the following information regarding your personal and family history:

<table>
<thead>
<tr>
<th>Relationship</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Self</td>
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<tr>
<td>Sister</td>
<td>Breast Cancer age 37</td>
</tr>
<tr>
<td>Paternal Aunt</td>
<td>Breast Cancer age 35</td>
</tr>
<tr>
<td></td>
<td>Breast Cancer age 36</td>
</tr>
<tr>
<td>Paternal Aunt</td>
<td>Ovarian Cancer age 45</td>
</tr>
</tbody>
</table>

Our discussion included, but was not limited to: family history/pedigree review, genetic principles (explanation of genes, gene mutations, and how gene mutations lead to cancer), features of a hereditary and sporadic cancer, risk of carrying a mutation and risk of passing on a mutation (autosomal dominant inheritance), risk of developing breast/ovarian/other cancer with a mutation, risk management/cancer prevention options for a mutation carrier, benefits, limitations and implications of genetic testing, description of the testing process, possible test results (positive, negative, true negative, uncertain test result), clinical implications of results for patient and family members, medical and other insurance discrimination based on genetic testing results, and genetic test cost, possible medical insurance coverage, and the process of pre-authorization.
The pattern of cancers in your family raises the possibility of a mutation in the BRCA1 or BRCA2 genes (which are associated with inherited breast and ovarian cancer). Typically, in a hereditary breast and ovarian cancer family, there are several women affected over more than one generation, diagnosis is more likely at a young age, there are often cases of bilateral breast cancer, or breast plus ovarian cancer, in a single relative and there can be male breast cancer in a relative. Your family seems to follow this pattern. We discussed what is known about the characteristics of inherited breast and ovarian cancer, cancer susceptibility genes, the likely pattern of inheritance with a mutation in the BRCA1 or BRCA2 gene, and the probability of inheriting the gene from a carrier. Testing for these genes is now available for families with a likelihood of having hereditary cancer. A woman who inherits the mutation has a very high risk of developing breast cancer and/or ovarian cancer while a woman who does not inherit the mutation has a risk equivalent to that of the average woman her age.

The patient was counseled extensively with regard to the benefits, limitations, and implications of genetic testing. Our discussion included, but was not limited to: family history/pedigree review; genetic principles (explanation of genes, gene mutation, and how gene mutations lead to cancer); features of hereditary and sporadic cancer; risk of carrying a mutation and risk of passing on a mutation (autosomal dominant inheritance); risk of developing breast/ovarian cancer with and without a mutation; risk management/cancer prevention options, including the strengths and limitations of each; benefits/limitations of genetic testing; description of the testing process; possible test results (positive, negative, true negative, uncertain test results); clinical implications of results for patient and family members; potential medical and other insurance discrimination based on genetic testing results; genetic test cost, possible medical insurance coverage, and the process of preauthorization.

While over 1000 mutations have been identified in the BRCA1 and BRCA2 genes, each family has only a single family specific mutation (With rare exceptions). Therefore, the best approach is to undertake full gene sequencing of both the BRCA1 and BRCA2 genes in an affected family member first, to identify the family specific mutation. Once the family specific mutation is identified, we can test the patient, and other family members, for that single mutation. On the other hand, if her relative tests negative, it markedly decreases the risk of hereditary breast/ovarian cancer syndrome in the family, but does not totally remove that risk. It is still possible that the family harbors an undetectable mutation, or a mutation in a different gene that can also cause hereditary cancer. In that case, we will manage the patient based on her family history, with some amelioration of risk provided by this negative test. We might also consider testing other family members to see if they carry mutations, if there is a substantial chance that that will clarify the situation.

You can find additional information about hereditary breast or ovarian cancer on the following websites:

http://www.inheritedrisk.com
http://www.facingourrisk.org
You can find additional information about hereditary breast or ovarian cancer on the following websites:

http://www.inheritedrisk.com
http://www.facingourrisk.org

Sincerely,

Dr. Kevin S. Hughes, M.D.
09/27/2008

Dear Linda,

Your niece, Mary Test, was seen at the Avon Foundation Breast Care Center, on 09/27/2008 to discuss the risk of hereditary cancer in your family.

The pattern of cancers in your family raises the possibility of a mutation in the BRCA1 or BRCA2 genes, which are associated with inherited breast and ovarian cancer. Typically, in a hereditary breast and ovarian cancer family, there are several women affected over more than one generation, diagnosis is more likely at a young age, there are often cases of bilateral breast cancer, or breast plus ovarian cancer, in a single relative and there can be male breast cancer in a relative. Your family history seems to follow this pattern. Testing for these genes is now available for families with a likelihood of having hereditary cancer. A woman who inherits the mutation has a very high risk of developing breast cancer and an increased risk of ovarian cancer while a woman who does not inherit the mutation has a risk equivalent to that of the average woman her age.

While over 1000 mutations have been identified in the BRCA1 and BRCA2 genes, each family has only a single family specific mutation (With rare exceptions). Therefore, our approach is to undertake genetic testing of a family member with cancer first, to identify the family specific mutation. Once this mutation is identified, we can test other family members, for that single mutation.

You would be the best person to test initially in your family.

We would suggest that you make an appointment to be seen at a center in your area where genetic testing and consultation is available to discuss this further. You can ask your doctor to suggest a center, or you can contact one of the centers listed here:

Ryan Bisson, M.S.
MD Anderson Cancer Center Orlando
Letter to relative includes list of testing centers in her area.

MP 710
1400 South Orange Avenue
Orlando, FL 32806
321-841-7299
ryan.bisson@orhs.org

Elizabeth P Capp, M.S.N., A.R.N.P., A.O.C.N.
Coastal Oncology, PL
Suite 450
325 Clyde Morris Boulevard
Ormond Beach, FL 32174
386-673-2442
ecapp@coastaloncology.net

Jenny P Wey, M.S., C.G.C.
H. Lee Moffitt Cancer Center Research Institute
Lifetime Cancer Screening Prevention Center
4117 East Fowler Avenue
Tampa, FL 33617
813-979-6770
permutjm@moffitt.usf.edu

Lisa Brown, M.S.
University of Florida Shands Cancer Center
Department of Hematology/Oncology
2000 Southwest Archer Road
Gainesville, FL 32610
352-265-0111
librown@ufacc.ufl.edu

We have given this letter to your niece to give to you, as we are not allowed to contact you directly. However, you have the right to contact us, if you wish. If you need additional information, please feel free to contact us.
You can find additional information about hereditary breast or ovarian cancer on the following websites:

http://www.inheritedrisk.com
http://www.facingourrisk.org

Sincerely,

Dr. Kevin S. Hughes, M.D.
Letter to the referring doctor

Avon Foundation Comprehensive Breast Care Center
Dr. Kevin S. Hughes, M.D.
Massachusetts General Hospital
55 Fruit Street, Yawkey 7
Boston, Massachusetts 02114
Fax (617) 724-3895
Phone (617) 724-0048

09/27/2008

Dr. John R Smith, M.D.
101 Oak St
Suite 434
Anytown, MA 02099

Re: Mary Test DOB: 01/02/1966 MRN: 09240801

Dear Dr. Smith,

Your patient, Mary Test, was seen at the Avon Foundation Comprehensive Breast Care Center on 09/27/2008.

She provided the following information regarding her personal and family history:

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Our discussion included, but was not limited to: family history/pedigree review, genetic principles (explanation of genes, gene mutations, and how gene mutations lead to cancer), features of a hereditary and sporadic cancer, risk of carrying a mutation and risk of passing on a mutation (autosomal dominant inheritance), risk of developing breast/ovarian/other cancer with a mutation, risk management/cancer prevention options for a mutation carrier, benefits, limitations and implications of genetic testing, description of the testing process, possible test results (positive, negative, true negative, uncertain test result), clinical implications of results for patient and family members, medical and other insurance discrimination based on genetic testing results, and genetic test cost, possible medical insurance coverage, and the process of pre-authorization.

The pattern of cancers in the patient’s family raises the possibility of a mutation in the BRCA1 or BRCA2 genes (which are associated with inherited breast and ovarian cancer). Typically, in a hereditary breast and ovarian cancer family, there are several women affected over more than one generation, diagnosis is more likely at a young age, there are often cases of bilateral breast cancer, or breast plus ovarian cancer, in a single
relative and there can be male breast cancer in a relative. Her family history seems to follow this pattern. We discussed what is known about the characteristics of inherited breast and ovarian cancer, cancer susceptibility genes, the likely pattern of inheritance with a mutation in the BRCA1 or BRCA2 gene, and the probability of inheriting the gene from a carrier. Testing for these genes is now available for families with a likelihood of having hereditary cancer. A woman who inherits the mutation has a very high risk of developing breast cancer and/or ovarian cancer while a woman who does not inherit the mutation has a risk equivalent to that of the average woman her age.

The patient was counseled extensively with regard to the benefits, limitations, and implications of genetic testing. Our discussion included, but was not limited to: family history/pedigree review; genetic principles (explanation of genes, gene mutation, and how gene mutations lead to cancer); features of hereditary and sporadic cancer; risk of carrying a mutation and risk of passing on a mutation (autosomal dominant inheritance); risk of developing breast/ovarian cancer with and without a mutation; risk management/cancer prevention options, including the strengths and limitations of each; benefits/limitations of genetic testing; description of the testing process; possible test results (positive, negative, true negative, uncertain test results); clinical implications of results for patient and family members; potential medical and other insurance discrimination based on genetic testing results; genetic test cost, possible medical insurance coverage, and the process of pre-authorization.

While over 1000 mutations have been identified in the BRCA1 and BRCA2 genes, each family has only a single family specific mutation (With rare exceptions). Therefore, the best approach is to undertake full gene sequencing of both the BRCA1 and BRCA2 genes in an affected family member first, to identify the family specific mutation. Once the family specific mutation is identified, we can test the patient, and other family members, for that single mutation. On the other hand, if her relative tests negative, it markedly decreases the risk of hereditary breast/ovarian cancer syndrome in the family, but does not totally remove that risk. It is still possible that the family harbors an undetectable mutation, or a mutation in a different gene that can also cause hereditary cancer. In that case, we will manage the patient based on her family history, with some amelioration of risk provided by this negative test. We might also consider testing other family members to see if they carry mutations, if there is a substantial chance that that will clarify the situation. The patient agrees with recommendation.

You can find additional information about hereditary breast or ovarian cancer on the following websites:

http://www.inheritedrisk.com
http://www.facingourrisk.org

Thank you for letting us share in the care of your patient.

Sincerely,
Report generated at the click of a button
HughesRiskApps complies with the HL7 standard

• Data can be shared with any HL7 compliant software
• Data can be uploaded or downloaded to any EHR that has a complete family history section and that is HL7 compliant
  – None currently exist but EHR vendors are likely to improve their product to this level soon
HughesRiskApps can help move us into the Genomic Age on a population level

• More high risk women identified
  – Integration of FH into normal clinic workflow

• More women cared for by the Risk Clinic
  – Increased efficiency of risk counselor
References

• Scheuner 2004 AmJMEdGenSeminars Contribution Of Mendelian Disorders To Common Chronic Disease


• Shabo A and Hughes, KS. Family History Information Exchange Services Using HL7 Clinical Genomics Standards. Intl Journal on Semantic Web & Information Systems 1(4): 42-65
