Models of genetic Counselling

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Disclosure conflicts of interest speaker

<table>
<thead>
<tr>
<th>(potential) conflicts of interest</th>
<th>No</th>
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<tbody>
<tr>
<td>Relationships with companies</td>
<td>AstraZeneca</td>
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<tr>
<td>Research funding</td>
<td>MLDS; Dutch cancer society; KIKA; Horizon2020</td>
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Treatment options are changing e.g. in BRCA testing process

- More patients referred for BRCA testing
- Quicker results needed
- Testing at diagnosis or during early treatment phase (Role/timing of counselling changes as a consequence)
- Identification of somatic (tumour) mutations
- Testing multiple genes involved in breast or ovarian cancer or risk will generate a more complex output in the lab
Barriers for \textit{BRCA} testing and counselling

Consequences \textit{BRCA}-testing for patient and relatives:

- Difficult interpretation
  - VUS
  - Tumour vs germline
  - Other hereditary cause than \textit{BRCA}
- Communication by team of professionals
- Timing of test results

\textbf{Florence Nightingale}
Common current practice

Ovarian or Breast cancer with pos. family history at least 10% risk of \textit{BRCA} mutation

Clinical geneticist counselling

Germline \textit{BRCA} mutation analysis

Clinical geneticist counselling

Germline test consequences for treatment and hereditary cancer risks in family

All Ovarian cancer patients: approximately 10–15% germline \textit{BRCA1/2} mutations

Women with positive family history for breast/ovarian cancer*

Usual care
n=334

Randomisation

Telephone counselling
n=335

Clinical geneticist counselling

Germline BRCA mutation analysis

Clinical geneticist counselling

Germline BRCA mutation analysis

Telephone-based genetic counselling

Telephone-based genetic counselling

*≥10% risk for BRCA1/2 mutation
Telephone-based counselling (USA)

Telephone counselling was non-inferior to in-person counselling for:

- Post-counselling knowledge score
- Decisional conflict
- Cancer distress and Perceived stress
- Satisfaction with counselling (assessed only at 2 weeks)

Schwartz MD et al. J Clin Oncol 2014;32:618–626
East Scotland model

All Patients with ovarian cancer (high grade serous histology)

Oncologist (med/gyn)

Uptake ~95%

Germline BRCA mutation analysis

13% (19/146) Mutation positive

No mutation

No genetic counselling

Clinical geneticist counselling
All patients with epithelial ovarian cancer

Ovarian tumour BRCA mutation analysis

Clinical geneticist counselling

Germline BRCA mutation analysis

18% somatic BRCA ½ mutation

57% germline mutation (of those with a somatic mutation)

Test consequences for treatment

Test consequences for treatment and hereditary cancer risks in family

Personal communication
Summary Models for BRCA-testing

All patients with epithelial ovarian cancer

Breast cancer with positive family history for breast/ovarian cancer

Test consequences for treatment

Oncologist (med/gyn)

Ovarian tumour BRCA mutation analysis

Clinical geneticist counselling

Germline BRCA mutation analysis

Both the patient and her relatives well informed on consequences

More digital information and/or telephone counselling before testing.

Personal communication from presenter
Barriers for *BRCA* testing and counselling

Consequences *BRCA*-testing for patient and relatives:

- Difficult interpretation
  - VUS
- Tumour vs germline
- Other hereditary cause than *BRCA*
- Communication by team of professionals
- Timing of test results

*Personal communication from presenter*
The VUS Problem

VUS, variant of uncertain significance; UV, unclassified variants

In ~8% of BRCA screens a VUS is identified
Interpretation and Clinical Reporting

- Essential to establish causal role of mutation and whether it is deleterious
- Report should be generated based on classification of mutation
- IARC 5 Class system commonly used

<table>
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<tr>
<th>Class</th>
<th>Description</th>
<th>Likelihood</th>
<th>Clinical management</th>
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<tr>
<td>5</td>
<td>Definitely pathogenic</td>
<td>&gt;0.99</td>
<td>Test at-risk relatives for variant</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Full high-risk surveillance guidelines</td>
</tr>
<tr>
<td>4</td>
<td>Likely pathogenic</td>
<td>0.95–0.99</td>
<td>Test at-risk relatives for variant*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Full high-risk surveillance guidelines</td>
</tr>
<tr>
<td>3</td>
<td>Uncertain</td>
<td>0.05–0.949</td>
<td>Do not use for predictive testing in at-risk relatives*</td>
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<tr>
<td>2</td>
<td>Likely not pathogenic or of little clinical significance</td>
<td>0.001–0.049</td>
<td>Do not use for predictive testing in at-risk relatives*</td>
</tr>
<tr>
<td>1</td>
<td>Not pathogenic or of no clinical significance</td>
<td>&lt;0.001</td>
<td>Do not use for predictive testing in at-risk relatives*</td>
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*Recommend continuing to test proband for any additional testing modalities available for the disorder in question, e.g. rearrangement testing

IARC, International Agency for Research on Cancer
Professional barriers

Teamwork by Oncologists and Clinical Geneticists

1. Interpretation of *BRCA*-test result (tumor vs germline & mutation vs VUS)
2. Interpretation of Family history for
   - Other hereditary causes than *BRCA*
   - Familial cancer risk in non-*BRCA* families
3. Communication of test result and of familial cancer risk

After *BRCA*-germline testing face-to-face clinical geneticist in case of:
- Positive *BRCA*-test result
- Positive family history (Other hereditary or familial causes of cancer)
- Complex test results (VUS, germline vs tumour, multiple genes)
Professional barriers

Teamwork by Oncologists and Clinical Geneticists

1. Interpretation of *BRCA*-test result (tumor vs germline & mutation vs VUS)
2. Interpretation of Family history for
   • Other hereditary causes than *BRCA*
   • Familial cancer risk in non-*BRCA* families
3. Communication of test result and of familial cancer risk

After *BRCA*-germline testing face-to-face clinical geneticist in case of:

- positive *BRCA*-test result
- positive family history (Other hereditary or familial causes of cancer
- Complex test results (VUS, germline vs tumour, multiple genes)
Communication on implications

- **Patients** (consequences for treatment, consequences for relatives, unclear test result, other hereditary causes than BRCA, familial instead of hereditary cause)

- **Relatives** (They need to know)
Patient preferences

• Adequate information
  • *BRCA*, other genetic causes, familial, sporadic
• Multidisciplinary team work
  − (same information by all members of the team)
• Information for relatives (children!)
Summary

Professionals:
1. Interpretation of BRCA-test result (tumor vs germline & mutation vs VUS)
2. Interpretation of Family history for:
   • Other hereditary causes than BRCA
   • High Familial cancer risk in non-BRCA families
3. Communication of BRCA-test result and of familial cancer risk

Patients:
1. Consequences for treatment
2. Consequences for relatives:
   • Positive BRCA-test
   • High familial cancer risk without BRCA-mutation
   • Other cancer syndromes