“This is great information, but how do I use it?:”

Information needs of genetic counselors related to reclassification of Variants of Uncertain Significance

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Conflicts of Interest

• I, or an immediate family member, including my spouse or partner, have NO financial relationship(s) relevant to the content of this educational activity.
Learning Objectives

• Identify challenges in communicating uncertain complex scientific information from the bench to the bedside.

• Describe a method for creating effective communication between scientists and providers.

Mavaddat, N. et al. (2013) Journal of the National Cancer Institute
Genetic Counseling and Testing

- Makes an appointment and attends pre-test genetic counseling
- The patient decides to have genetic testing
- The genetic counselor receives the results
- The genetic counselor discloses the result to the patient in a post-test genetic counseling session

Genetic Test Results

- Positive (+)
- Negative (-)
- Unknown (?)

Images of DNA and a genetic counselor are included in the diagrams.
We knew patients struggled with VUS results, but we didn’t know how Genetic Counselor’s dealt with them...

<table>
<thead>
<tr>
<th>IARC Classification</th>
<th>Definition</th>
<th>Posterior Probability Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Definitely Pathogenic (Harmful)</td>
<td>&gt; 0.99</td>
</tr>
<tr>
<td>4</td>
<td>Likely Pathogenic</td>
<td>0.95-0.99</td>
</tr>
<tr>
<td>3</td>
<td>Uncertain</td>
<td>0.05-0.949</td>
</tr>
<tr>
<td>2</td>
<td>Likely Not Pathogenic</td>
<td>0.001-0.049</td>
</tr>
<tr>
<td>1</td>
<td>Not Pathogenic (Not Harmful)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
A Review of a Multifactorial Probability-Based Model for Classification of BRCA1 and BRCA2 Variants of Uncertain Significance (VUS)

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Specific Aims

• Specific Aim 1: To classify BRCA1 and BRCA2 VUS using a multifactorial model.

• Specific Aim 2: To establish the utility of functional analysis for classifying BRCA2 VUS as deleterious or neutral.

• Specific Aim 3: Translation of VUS reclassification to clinical practice

Human Mutation paper – academic paper – not highly accessible

Specific Aim 3: Translation of VUS reclassification to clinical practice
Translation of VUS Reclassification to Clinical Practice

YEARS 1/2
- Baseline survey mailing
- Analyze data

YEARS 2/3
- Develop and refine VUS Genetic counseling aid
- Conduct Interviews with Genetic Counselors
- Disseminate to GC’s in study sample

YEARS 3/4
- Second Survey Mailing
- Analyze data and compare results to baseline survey

YEAR 5
- Refine VUS genetic counseling Aid
- Disseminate final VUS aid to ALL GC’s

Patient Template Letter

- Directed to the patient
- Lower reading level
- Encouraged to share with family and other healthcare providers

Suggested template letter for sending results of VUS to a patient after counseling on results in person or by phone:

Dear [Patient’s last name],

This letter provides you with a written record of your recent genetic test. For you, the result of your test included a variant of uncertain significance (VUS). This type of result can be confusing to explain to your other health care providers or to your family, so sharing this letter may be a way to help those discussions.

Genetic counseling includes a process known as discussion of results that you share with your health care providers, including your family. If you have a VUS, it is important to discuss the implications with any other family members who may be equally at risk.

The VUS found in your test was in the gene [insert gene name].

The VUS found in your test was in the gene [insert gene name].

This VUS was not found to be associated with any known genetic disorders. However, if you have a family history of cancer, it may be helpful for you to have your clinical genetic counselor discuss the implications of the VUS found in your test.

We recommend discussing the implications of the VUS with your genetic counselor. If you have any questions, please feel free to contact them.

This letter includes a description of the VUS and how it was identified. It is not intended to be a substitute for medical advice or counseling.

If you have any questions or concerns, please contact your genetic counselor.

Sincerely,

[Your Name]
Provider Focused Factsheet

Sections included:
• What is the purpose of this guide?
• What information is contained in this guide?
• What is the best way to use this guide in my clinical practice?
• A word of caution.

Pilot Interviews

• Genetic counselors identified through personal channels
• Geographically diverse sample
• 10 phone interviews
• Semi-structured interview guide
• 30 minutes
• Informal feedback mechanism
Patient Template Letter

**Liked**

- Appropriate for their patients
- Would use at least part of it in their practice

**Constructive Feedback**

- Could it be adapted?
- Emphasis on testing family members for **research only**.
- Clarification about maintaining contact – patient or provider?
- Letter condensed to a single page.
- Reduce reading level.

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**Revised layout to be reduced to a single page.**

**Used red font to indicate modifiable aspects of the letter**

**Modified the text to say family members should not be tested for VUS to find out their cancer risk**

**Revised wording to include bi-directional communication.**
Fact Sheet

**Liked**
- Appreciated direct information sharing
- Liked the table format
- Liked “word of caution” section

**Constructive Feedback**
- Who conducted the reclassification and how?
- How is this different from laboratory reports?
- How can the tables be used?
- What is the clinical utility of this information?
- What is the technical note?

The following sections were added for additional clarification:

- How is a VUS classified using the IARC multifactorial likelihood model?
- Can functional studies be used to reclassify VUS?
- What is the best way to use this guide in clinical practice?
Take-Home Messages

• Communicating scientific information is challenging even to healthcare professionals
  – It is important to consider the channel, message, tone, etc.

• Surveys can be useful...but...

Piloting intervention materials with the target population is invaluable
  – Iterative & longitudinal process
  – Should be considered when writing grants
Acknowledgements

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Additional References

• Vos J, Gómez-Garcia E, Oosterwijk JC, et al. Opening the psychological black box in genetic counseling. The psychological impact of DNA testing is predicted by the counselee’s perception, the medical impact by the pathogenic or uninformative BRCA1/2-result. Psycho-Oncology. 2012;21(1):29-42.