### Rethinking the Family Cancer History Questionnaire in the Era of Next Generation Sequencing Panels - Are We Asking the Right Questions?

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### Differential Diagnosis and Genetic Testing Strategy

**Background:** In primary care and medical/surgical oncology settings, the Family History Questionnaire is often used as a screening tool in identifying patients who may benefit from a genetics evaluation. Studies have shown however, that inherited cancer syndromes remain underdiagnosed, largely because clinicians often limit their investigation to immediate family members and do not document cancers in the extended family. Recent studies have also demonstrated that oncologists lack confidence in their ability to interpret risk from family history, particularly in cases where the patient presents with a rare cancer or has an unusual pattern of cancer in his or her family. Moreover, many providers focus only on collecting family history data for cancers associated with the more common conditions, such as hereditary breast and ovarian cancer syndrome (HBOC), and do not recognize overlapping features of other syndromes.

To address the problems clinicians face in interpreting complex family histories, we designed a cancer history questionnaire with embedded clinical decision support that assists clinicians with creating a differential diagnosis.

Specifically, we propose a two-step questionnaire (a simple, open-ended form for patients and a follow-up form for the clinician) that is designed to guide the patient and clinician to investigate family history by systematically reviewing major organ systems/tumor sites of affected relatives. This "check-list" format leads to a preliminary differential diagnosis and an associated condition/gene list. This approach allows for consideration of multiple conditions, and may be a time-saving way to collect more detailed family history data.

**Methods:** The PubMed database was searched for publications between 2007 to August 2014 for information regarding the following topics: 1) barriers to family history collection; 2) inaccurate or incomplete documentation of family history; 3) problems with interpretation of family history; 4) low rates of referral for eligible patients; 5) misdiagnosed cancer syndromes and incorrect ordering of a genetic test; 6) professional society practice guidelines for referral to genetic counseling/testing; and 7) professional education issues regarding the collection of cancer histories. The search was purposely broad and designed to capture information that described barriers to the accurate documentation of cancer family histories.

Information was also obtained by doing a web search for family history questionnaires and reviewing multiple cancer history forms used in oncology and primary care settings.

**References:**


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### Step 1: Patient-Facing Cancer History Form

**Background:** This form is intended for unaffected individuals with perceived or recognized familial cancer risk, and for affected individuals who have a diagnosis of cancer. It differs from other forms in that the first section is designed to educate the patient regarding the "red flags" of inherited cancer syndromes.

**A direct question about whether the patient is concerned about personal or family cancer history may prompt the clinician to ask about affected family members.**

An open-ended question about family cancer history is the starting point of the documentation process. Follow-up to these answers occurs in Step 2.

**Future Direction**

The primary aim of this project was to design a family history questionnaire with embedded clinical decision support. The next step is to evaluate this tool in a variety of clinical settings and determine whether it helps the practitioner to:

- Make a preliminary assessment of a patient’s inherited predisposition for cancer
- Prompt further investigation in complex cases
- Generate a differential and genetic testing strategy in high-risk patients

Other potential areas of research include an assessment of how effectively and efficiently the redesigned family history questionnaire helps clinicians capture and interpret cancer history compared to general health history forms. Additionally, the authors would like to assess whether targeted questions result in the clinician recognizing rare syndromes based on the "red flags" identified during the patient interview. Finally, we plan to evaluate the ease of use and the need for specialized training.

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### Step 2: To Be Filled Out By Clinician

**How to use the clinician form:** Starting with the cancers reported by the patient, the clinician circles the tumor site(s) in column I and documents the relationship of the family member to the proband as well as ages of onset.

Next, the clinician reviews the features of inherited cancer syndromes listed in column II. Unusual combinations of tumor types or histological features are listed as a prompt to ask further questions.

Column III contains a list of possible syndromes as well as the genes most commonly associated with the condition. The syndromes are in alphabetical order so that a clinician can quickly review whether the same syndrome shows up in different rows (i.e., common to different types of cancers).

Creating a broad differential: Column III also indicates whether a panel is a consideration for a specific cancer type.

**Referral to Genetics:** Many of these rarer cancer syndromes require a comprehensive genetics evaluation to establish a diagnosis. A key containing detailed information about each syndrome as well as criteria for testing is available for reference.


Pazdur et al, Cancer Management: A Multidisciplinary Approach, 12th ed., Oncology Group of CMPMedica, Print. Also see www.cancernetwork.com.

Website: www.GeneReviews.org