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Swiss Cancer Predisposition Cascade Screening Consortium for the use and impact of genetic testing in hereditary breast/ovarian cancer and Lynch syndromes: CASCADE Study

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on behalf of the *CASCADE Consortium*

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HEREDITARY BREAST-OVARIAN CANCER SYNDROME (HBOC)

Associated with increased risks for **breast, ovarian, prostate, and pancreatic cancers, and melanoma**

Involves mainly mutations to tumor suppressor genes

BRCA1 or *BRCA2*

Tumor suppressor genes

The *BRCA1* and *BRCA2* genes produce a protein that repairs damaged DNA. Mutations in these genes lead to the accumulation of genetic defects that can allow cells to grow and divide in uncontrollable ways.

COUCH FJ, NATHANSON KL, OFFIT K. SCIENCE.2014

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LYNCH SYNDROME (LS PREVIOUS HNPCC)

Inherited condition associated with high risks for **colorectal, endometrial** and other cancers

Genes belong to DNA mismatch repair (MMR) family, lead to microsatellite instability (MSI)

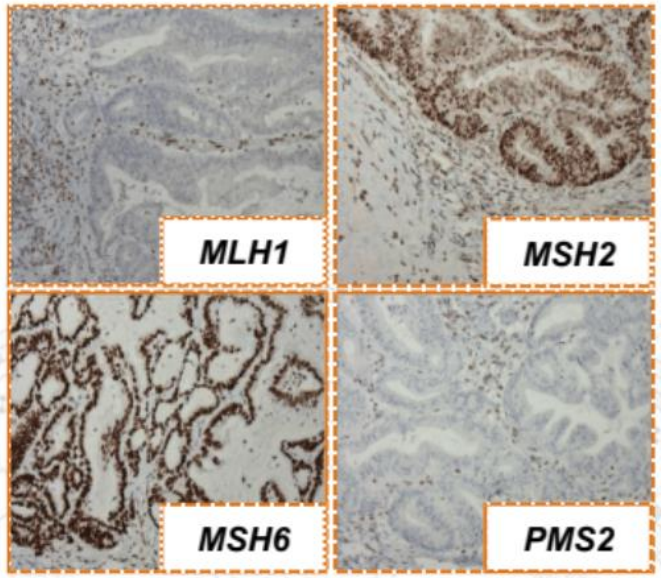
Test positive in 15% of colorectal and 24% of endometrial tumors

Sensitivity is 77-89% for Lynch Syndrome

MMR proteins missing in tumor tissue - Immunohistochemical (IHC) staining

Absent in 20% of colorectal and 25% of endometrial tumors

Sensitivity is 83% for LS



LE DT ET AL. N ENGL J MED. 2015

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HBOC AND LS "RED FLAGS"

Personal health history

Age of cancer onset ≤50 years

Two primary cancers in the same person

Family health history

3+ cases of HBOC- or LS – associated cancers in the same side of the family

Male breast cancer

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CURRENT FLOW OF GENETIC INFORMATION FOR HBOC AND LS

Proband is given total responsibility for disseminating results

General lack of knowledge about genetics and cancer

Not an urgent issue

Not everyone lives in area

Lack of communication in the family

No follow-up as to whether relatives pursued genetic counseling and/or testing

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USE OF CANCER GENETIC SERVICES FOR HBOC AND LS IN SWITZERLAND

11% of all Swiss breast cancer patients have genetic testing

25% of breast cancer patients with a strong family history have genetic testing

Lower numbers for LS – 95% of affected individuals do not know they have LS

AYME A, ET AL.. BREAST CANCER RES TREAT. 2014
FEDEWA SA, ET AL., PLOS ONE. 2015

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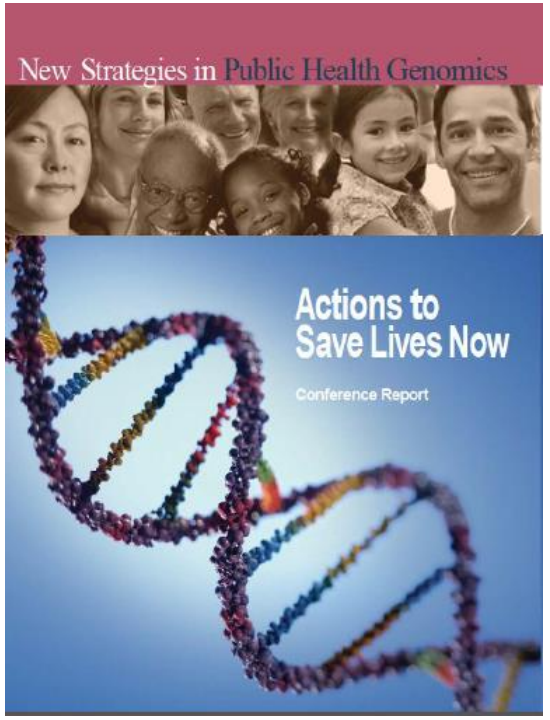
CENTER DISEASE CONTROL & PREVENTION (CDC) OFFICE PUBLIC HEALTH GENOMICS

Tier-1 genetic conditions suitable to promote translational research, linking genetics to public health and epidemiology

- Breast/ovarian or other *BRCA*-related cancers
- Colorectal cancer associated with Lynch Syndrome (LS)
- Familial hypercholesterolemia

Cascade genetic screening is a public health intervention: Interface of Clinical and Public Health Genomics

Identify relatives of individuals with known mutations and promote systematic familial genetic testing



KHOURY MJ, EVANS JP. JAMA. 2015

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CANCER PREDISPOSITION CASCADE GENETIC SCREENING CONSORTIUM

Multidisciplinary team

Epidemiology, Medicine, Nursing, Psychology, Public Health, Sociology

Multiple clinical sites in three linguistic regions of Switzerland

Basel, Bellinzona, Bern, Geneva, Jura, Lugano, Zurich

Specific Aim 1: Identify HBOC and LS mutation carriers and their close blood relatives and promote cascade genetic screening

Specific Aim 2: Develop web-based interventions designed to increase coping, family communication and support, and decrease decisional conflict

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PILOT PHASE OF CASCADE STUDY

1. Feasibility of cancer predisposition cascade genetic screening for HBOC and LS
   - ✓ Identify and recruit mutation carriers (HBOC and LS) from clinic-based genetic testing records
   - ✓ Identify and recruit close blood relatives (first- and second-degree, and first cousins)
   - ✓ Assess willingness to participate in family-based cohort
   - ✓ Assess willingness to participate in focus groups (communication barriers, acceptability of web-based and family-based intervention)
2. Design a survey that assesses
   - ✓ Barriers and facilitators to using cancer genetic services
   - ✓ Gaps in the long-term coordination of cancer surveillance and management of cancer risk
   - ✓ Need for interventions that enhance family communication, coping, and quality of life of mutation carriers and relatives

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Progress in Recruitment of Mutation Carriers

N=56 MC identified from clinic records

	Not contacted
Ineligible	6

N=

% in

N=5 MC accepted participation

	Not contacted
Declined	**1**
Did not give any reason	1
Pending	**13**

3d invitation letter …

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Progress in Recruitment of Mutation Carriers

Characteristics	Mean and Frequencies
Age	48.0±10.4
Willing to invite % relatives	75% (16% - 100%)

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PROGRESS IN RECRUITMENT OF RELATIVES

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Characteristics	Frequencies
Not living in Switzerland	36

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CHALLENGES

Survey and recruitment material in three languages – culturally appropriate

Ethics Committees – various cantons

Consent form vs. survey of mutation carriers for inviting relatives

Families with uneven size – analytical problems when running data analyses

Identifying relatives when they return a survey

Referring physician

Resources and manpower – keeping tract recruitment process, surveys, reminders

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THANK YOU FOR YOUR ATTENTION