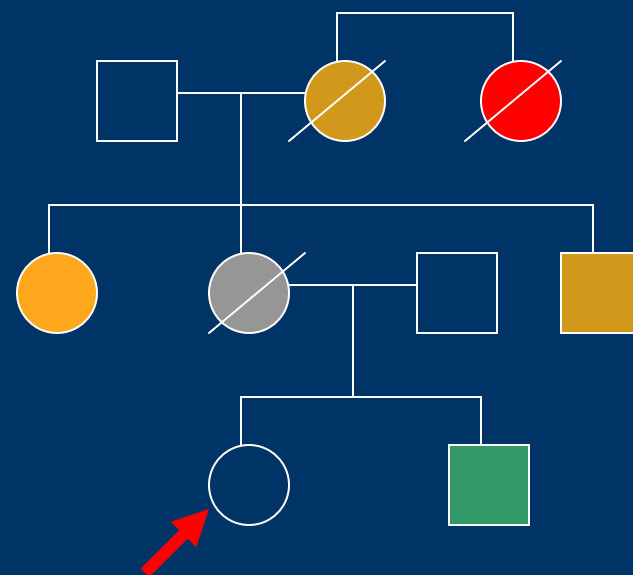# Family History: a Genomic Tool for Public Health and Preventive Medicine

Paula W. Yoon, ScD, MPH
CDC, Office of Genomics
& Disease Prevention

Pediatric Family History Meeting
February 24-25, 2006
Atlanta, GA
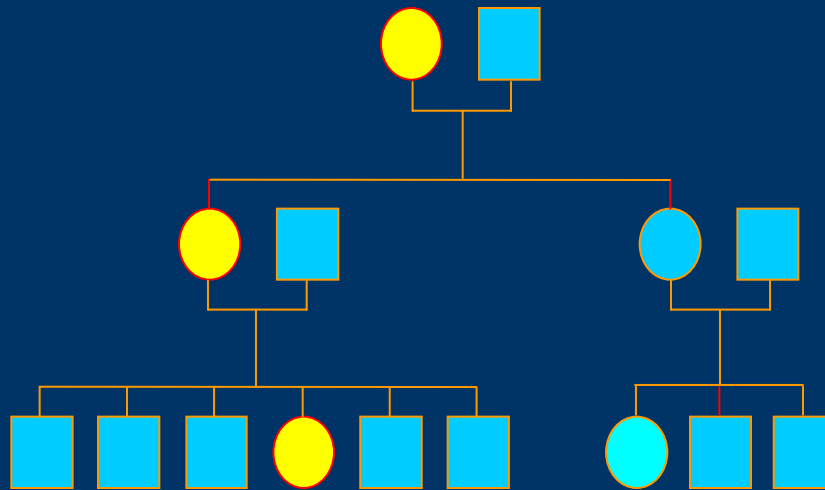
CDC Family History Public Health Initiative

Evaluate the use of family history for assessing risk of common diseases and influencing early detection and prevention strategies

Validity - Could disease information about a person's close relatives be used to predict their own risk for specific diseases?

Utility - Would individuals at above average risk benefit from targeted interventions beyond what is recommended for the population at large ?
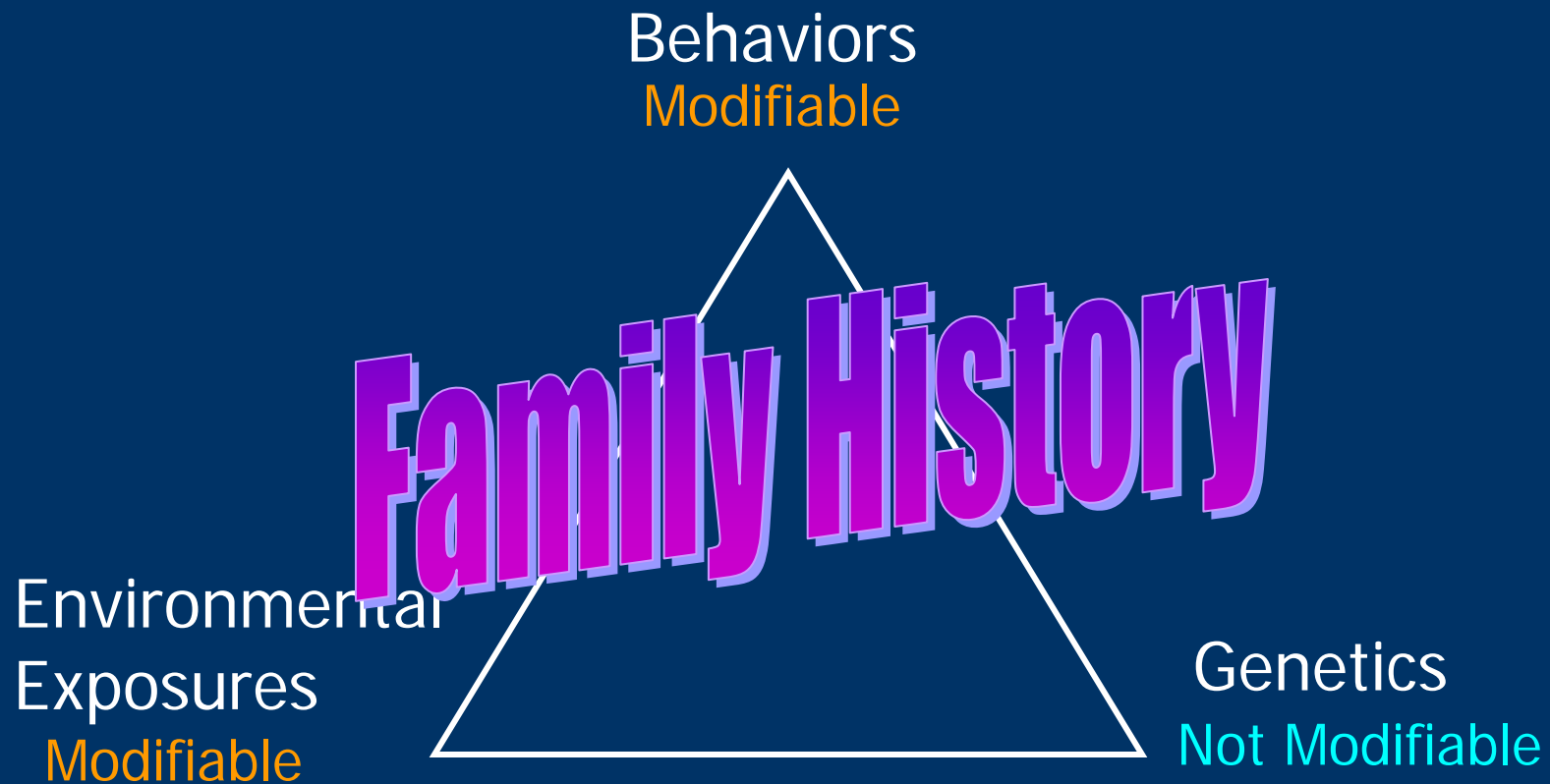
Added value of family history?

- One size fits all population approach to prevention has limits

- <u>Augment</u> with targeted and personalized prevention strategies focused on higher-risk families

- Awareness of familiar risk may be a motivating factor for behavior change and screening uptake

- Family-centered approaches to risk reduction may be more effective and have longer impact

- Earlier or more frequent screening based on familial risk may be cost effective

Family history is an independent risk factor for most chronic diseases of public health significance

Risk factors for common diseases

Behaviors
Modifiable

Family History

Environmental
Exposures
Modifiable

Genetics
Not Modifiable
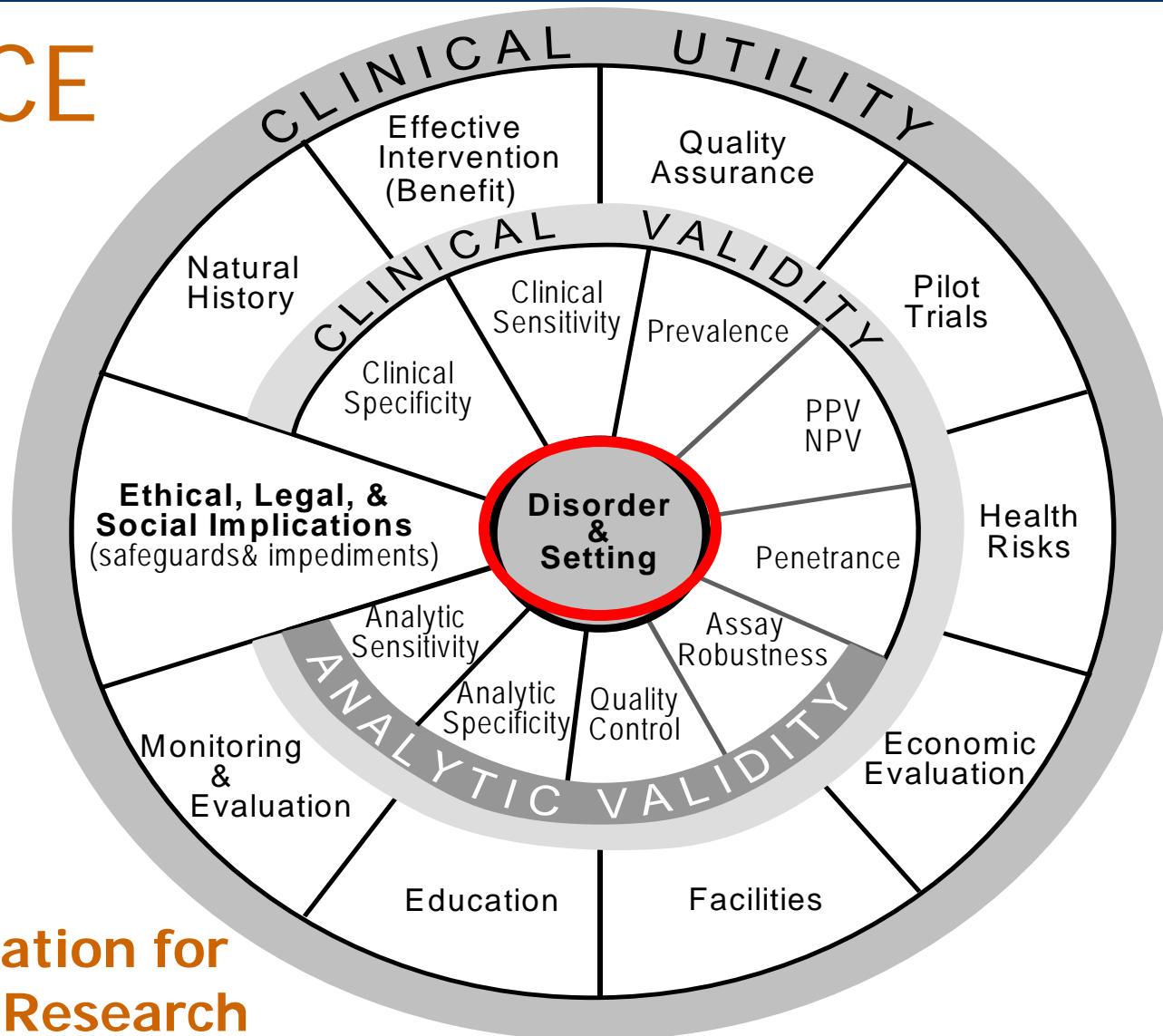
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Key Components of CDC's Family History Public Health Initiative

- Research – Define, measure, and assess family history in
  - populations
  - individuals

- Develop tools - for collecting and assessing family history, and guiding prevention efforts

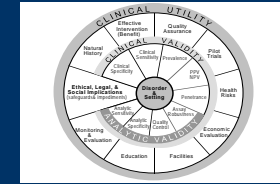- Evaluate - whether family history based strategies work

Research and evaluation framework

ACCE - Analytic validity

Accuracy and reliability of family history reporting

How accurate is the information - age of onset, type of relative, specific condition...?

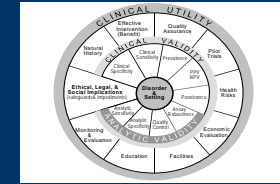What settings and formats yield valid information?

Assess the method

Sensitivity – identifies relatives who truly have the disease

Specificity - identifies relatives who truly do not have the disease

Gold standards – for validating the reports

ACCE - Analytic validity

NHLBI Family Heart Study   Bensen et al., 1999

- 3,020 probands
- 10,316 first degree relatives and spouses

Family history collected by mailed questionnaire
Gold Standard - relative's report of disease

	Diabetes	
	Sensitivity	Specificity
Proband vs. Spouse	0.83	0.98
Proband vs. Parent	0.87	0.98
Proband vs. Sibling	0.72	0.98

Age, gender, and disease status

ACCE - Clinical validity
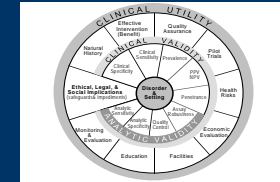
Accuracy of risk prediction

What information influences prediction – type of relative, age at onset, lineage, family size, number of affected...?

Population

- prevalence of family history
- family history – disease associations
- population attributable risk
- risk factor interactions
- validate risk stratification schemes

Individual

- assess and predict familial risk
- absolute risk for individuals

Measuring family history in population studies

Have any of your blood relatives ever been diagnosed with asthma?

Yes   No

Has your "relative" ever been diagnosed as having coronary heart disease?

At what age was "relative" diagnosed?

Is "relative" still alive?

What did "relative" die of?

Relative = parents, grandparents, aunts, uncles, siblings, children, nieces, nephews, cousins.....

Family history data collection

Family history of CHD example:

1. Have you ever been diagnosed by your doctor as having coronary heart disease (e.g., myocardial infarction, coronary bypass graft surgery or angioplasty)

2. Has your mother ever been diagnosed as having coronary heart disease?

3. Has your father ever been diagnosed as having coronary heart disease?

Yes, at or before aged 60   Yes, after age 60   NO   DK

4. How many of your brothers and sisters have been diagnosed with coronary heart disease <u>at or before age 60?</u>

5. How many of your brothers and sisters have been diagnosed with coronary heart disease <u>after age 60?</u>

6. How many of your mother's relatives (her sisters, brothers and parents) were diagnosed with coronary heart disease <u>at or before age 60?</u>

7. How many of your mother's relatives (her sisters, brothers and parents) were diagnosed with coronary heart disease <u>after age 60?</u>

8. How many of your father's relatives (his sisters, brothers and parents) were diagnosed with coronary heart disease <u>at or before age 60?</u>

9. How many of your father's relatives (his sisters, brothers and parents) were diagnosed with coronary heart disease <u>after age 60?</u>
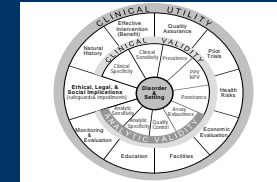
<div align="center">
None   One   Two or more   DK
</div>

ACCE - Clinical validity

Sensitivity – identifies individuals who will develop the disease

Specificity – identifies individuals who will not develop the disease

Positive Predictive Value – probability that individuals will develop disease given a positive family history

** Trade off between keeping it simple and collecting enough information to make prediction possible**

Preliminary data - Healthstyles 2003: risk of cardiovascular disease associated with familial CHD

Familial CHD:	Early CHD n=178	Late CHD n=79	Early Stroke n=121	Late Stroke n=50
Strong (n=1273) OR[a] (95% CI)	4.9 (3.3-7.2)	2.6 (1.5-4.7)	3.0 (1.9-4.7)	1.5 (0.8-2.8)
Moderate (n=471) OR[a] (95% CI)	2.0 (1.1-3.6)	2.3 (1.1-5.0)	2.5 (1.4-4.7)	0.3 (0.1-1.5)
AUC[a] (%)	82.3	80.5	75.7	73.0

Referent group = weak familial CHD (n=2291). Early = at or before age 60; Late = after age 60; CHD = coronary heart disease
[a]Adjusted for age, gender, ethnicity/race, educational level, income, and marital status.

Scheuner et al. Healthstyles 2003

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Preliminary data - NHANES '99-02: predictive value of family history in screening for undiagnosed diabetes

Risk Factor	Sensitivity (%)	Specificity (%)	PVP (%)	PVN (%)
Increased familial risk	47.6	73.2	5.3	97.8
High familial risk	19.4	94.4	9.9	97.4
BMI ≥ 25	88.1	38.4	4.2	99.1
Increased familial risk and BMI ≥ 25	45.2	81.4	6.9	98.0
High familial risk and BMI ≥ 25	17.6	96.5	13.4	97.5

Hariri et al. NHANES 99-02

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ACCE - Clinical utility
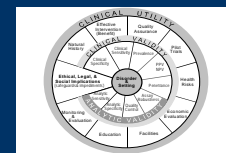
**Effectiveness of family history assessment
for disease detection and prevention**

- Will individuals at increased risk due to family history be more motivated to make lifestyle changes?

- Will targeted interventions based on family history have an impact on disease prevention?

- Are there health risks associated with family history assessment and intervention?

- Is the approach cost-effective?

ACCE - Clinical utility
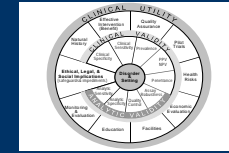
Risk-reducing and risk-aware behaviors by family history category

Hariri et al. Healthstyles 2004
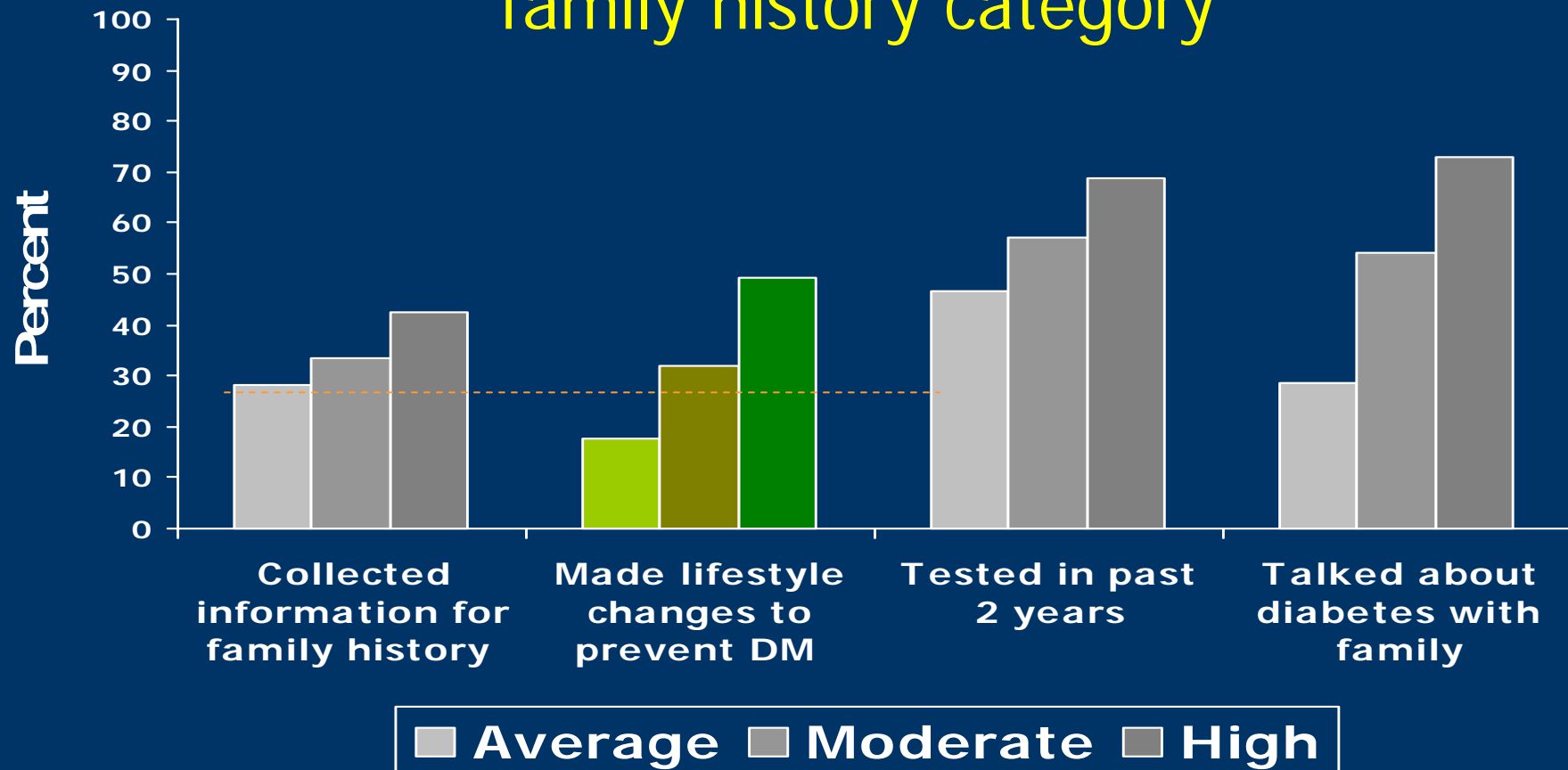
Evaluation of Family Healthware

Univ of Michigan
Case Western Reserve
Evanston Northwestern HRI

Purpose – assess impact of personalized prevention messages on behavior and screening uptake

Study Population ~ 8000 patients age 35-65

Methods

Arms	Enrollment	6 months later
Group 1	Pre Test + FHx tool (personal messages)	Post Test
Group 2	Pre Test (standard messages)	Post Test + FHx tool

Effects of a Controlled Family-based Health Education/Counseling Intervention

Marika Salminen, MSc; Tero Vahlberg, MSc; Ansa Ojanlatva, PhD, CHES, CSE
Sirkka-Liisa Kivelä, MD, PhD

Objective: To describe the effects of a controlled family-based health education/counseling intervention on health behaviors of children with a familial history of cardiovascular diseases (FH-CVDs). **Methods:** The intervention group (IG, n=432) received 5 counseling sessions. The control groups 1 (CG1, n=200) and 2 (CG2, n=423) received no counseling. Outcome measures comprised changes in diet, exercise, and cigarette smoking. **Results:** The changes in the use of fats and salt, and in exercise, were more favorable in IG than in CG1 and/or CG2. **Conclusion:** Health education/counseling produced positive effects on diet and nutrition in particular and in part in exercise.

Key words: adolescent, child, early intervention, health behaviors, primary prevention

Ethical, Legal, and Social Implications
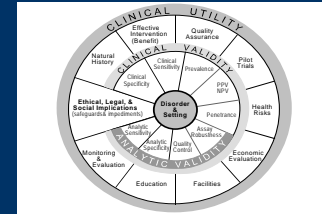
Are there issues affecting data collection and interpretation that might negatively impact individuals, families, and society ?

- Are there legal issues regarding informed consent, ownership of the data, or obligation to disclose?

- What is known about stigmatization, discrimination, privacy/confidentiality, and personal, family, and social issues associated with family history assessment and risk labeling?

Ethics

Just a family medical history?

Dagmar Schmitz, Urban Wiesing

If you have a family history of inherited disease, giving details could lead to discrimination

A recent case in Germany has highlighted the use of genetic information obtained from family medical histories in employment decisions. Although laboratory genetic testing is rarely used in occupational health medicine, prospective employees are often asked about family medical history and may be unaware of the potential consequences. We argue that information

Institute of Ethics and History in Medicine, University of Tuebingen, 72076 Tuebingen,

- Family medical history can yield predictive genetic information

- Secure free and informed consent before taking family history

- If not possible (workplace settings), FHx should not be used

- Discrimination based on genetic info should be prohibited irrespective of the origin of the info

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Ethics

Implications of data protection legislation for family history

Anneke Lucassen, Michael Parker, Robert Wheeler

Clinical geneticists currently collect and store information on family history without explicit consent. Are they flouting the Data Protection Act?

- Family medical history is important for medical management

- Relatives not routinely consented or told such records exist

- Data Protection Act – fair process requires family members consent to inclusion in medical record

- Public interest in high standards of confidentiality outweighs argument of fair processing of familial information

- Clinical geneticists should not be obliged to contact all people mentioned in family history

Welcome to Family Healthware

Family Healthware is a free tool that collects information on your:

- lifestyle behaviors
- use of screening tests
- family history of six major diseases

and produces a personalized report that:

- analyzes your family history as a risk factor for disease
- recommends screening, lifestyle and other changes to improve your health.

Click to learn about:

Family Healthware

Family History & Health

Returning Users

Username:

Password:

[Go]

Forgot your username or password?

New Users

Begin your Family Healthware assessment today...

[Create My Account]

Family Healthware is not designed to replace medical advice and discussions with a health professional. You should talk to your health professional before making a decision about your medical care.

Desirable features of a public health screening tool to collect family history and influence prevention

- Self-administered

- Easily applied and adaptable to different settings

- Simple but collects enough information to assess risk

- Tied to algorithms that interpret risk

- Useful in combination with other risk factors

- Tied to risk-appropriate and evidence-based prevention strategies

- Integrated approach to disease prevention

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Family Healthware
Using Family History to Promote Health

My Profile
Username/Password
Personal Information
Health Behaviors
Screening Tests

My Family Profile
Family Profile Introduction
Create Family Tree
Add Family Member

My Report

My Profile – Personal Information

Please enter your personal information.

Today's Date: 1/30/2006

First Name: [   ]

Last Name: [   ]

Email (*optional*):   [   ]

What is your current height?   ☐ feet [0] inches

What is your current weight?   [   ] lbs.
(pregnant women should indicate weight prior to pregnancy)

Date of Birth: Month [month ▼] Day [day ▼] Year [   ]

Gender: ○ Male ○ Female

Are you adopted?   ○ No/Don't know   ○ Yes

Race/Ethnic Group (*optional*):   [PLEASE SELECT: ▼]

Having a Jewish heritage may affect your risk for breast cancer. Do you have any ancestors who are Ashkenazi Jews? (Jewish families from Eastern or Central Europe)? (*optional*)

○ No/Don't know   ○ Yes

[Previous Screen]   [Save & Continue]

![Family Healthware - Using Family History to Promote Health]

Glossary **Logout**

[CDC logos]

My Profile
- Username/Password
- Personal Information
- **Health Behaviors**
- Screening Tests

My Family Profile
- Family Profile Introduction
- Create Family Tree
- Add Family Member

My Report

My Profile – My Health Behaviors

Question 1 of 5

Tobacco

Do you smoke tobacco, including cigarettes, a pipe, or cigars?

○ Yes, I currently smoke cigarettes, a pipe, or cigars

○ No, I used to smoke

○ No, I have never smoked (or smoked less than 100 cigarettes, pipes, or cigars in my lifetime)

Previous Screen | **Save & Continue**

Tobacco
Physical activity
Fruits/vegetables
Alcohol
Aspirin

Family Healthware
Using Family History to Promote Health

Glossary Logout

My Profile
Username/Password
Personal Information
Health Behaviors
Screening Tests

My Family Profile
Family Profile Introduction
Create Family Tree
Add Family Member

My Report

My Profile – My Screening Tests
Question 1 of 8

Cholesterol

Blood cholesterol is a fatty substance found in the blood. Have you had your blood cholesterol checked by a health professional?

PLEASE SELECT:
- PLEASE SELECT:
- Never
- Yes, within the past year
- Yes, 1 to 2 years ago
- Yes, 3 to 5 years ago
- Yes, 6 to 10 years ago
- Yes, more than 10 years ago
- Don't know/Not sure

Previous Screen   Save & Continue

Cholesterol	Fecal occult blood test	Clinical breast exam
Blood pressure	Colonoscopy	Mammogram
Blood glucose	Sigmoidoscopy	

Family Healthware
Using Family History to Promote Health

My Profile

My Family Profile

Family Profile Introduction

Create Family Tree

Add Family Member

My Report

My Family Profile - Create Family Tree

Family Members	Please enter number of family members (living or deceased)
Mother	1
Father	1
GrandParents	4
Daughter	0
Son	0
Sister (including half-sisters)	0
Brother (including half-brothers)	0
Mother's Sister	0
Mother's Brother	0
Father's Sister	0
Father's Brother	0

Previous Screen   **Save & Continue**

Family Healthware
Using Family History to Promote Health

CDC

My Profile

My Family Profile

Family Profile Introduction

Create Family Tree

Add Family Member

Mother

Mother's Mother

Mother's Father

Father

Father's Mother

Father's Father

My Report

My Family Profile

Delete Member

Health History of My Mother

Please enter a name for your **Mother :** Paula

☐ Check if you don't know if this relative had any of these diseases.

Did your mother ever have...?

	Yes	No	Don't Know	Age at first diagnosis (estimate if not sure)
Coronary Heart Disease	●	○	○	Please select one: ▼
Stroke	○	●	○	Please select one: ▲
Diabetes	○	●	○	less than 20
				20 to 24
Colon Cancer	○	●	○	25 to 29
				30 to 34
Breast Cancer	○	●	○	35 to 39
				40 to 44
Ovarian Cancer	○	●	○	45 to 49
				50 to 54
				55 to 59
				60 to 64 ▼

Previous Screen   Save & Continue

![Family Healthware logo — Using Family History to Promote Health](logo) **Family Healthware**
Using Family History to Promote Health

My Profile

My Family Profile

My Report

Introduction

Family Tree

Assessment Summary

Coronary Heart Disease

Stroke

Diabetes

Colon Cancer

Breast Cancer

Ovarian Cancer

Screening Tests

Lifestyle Changes

Print My Report

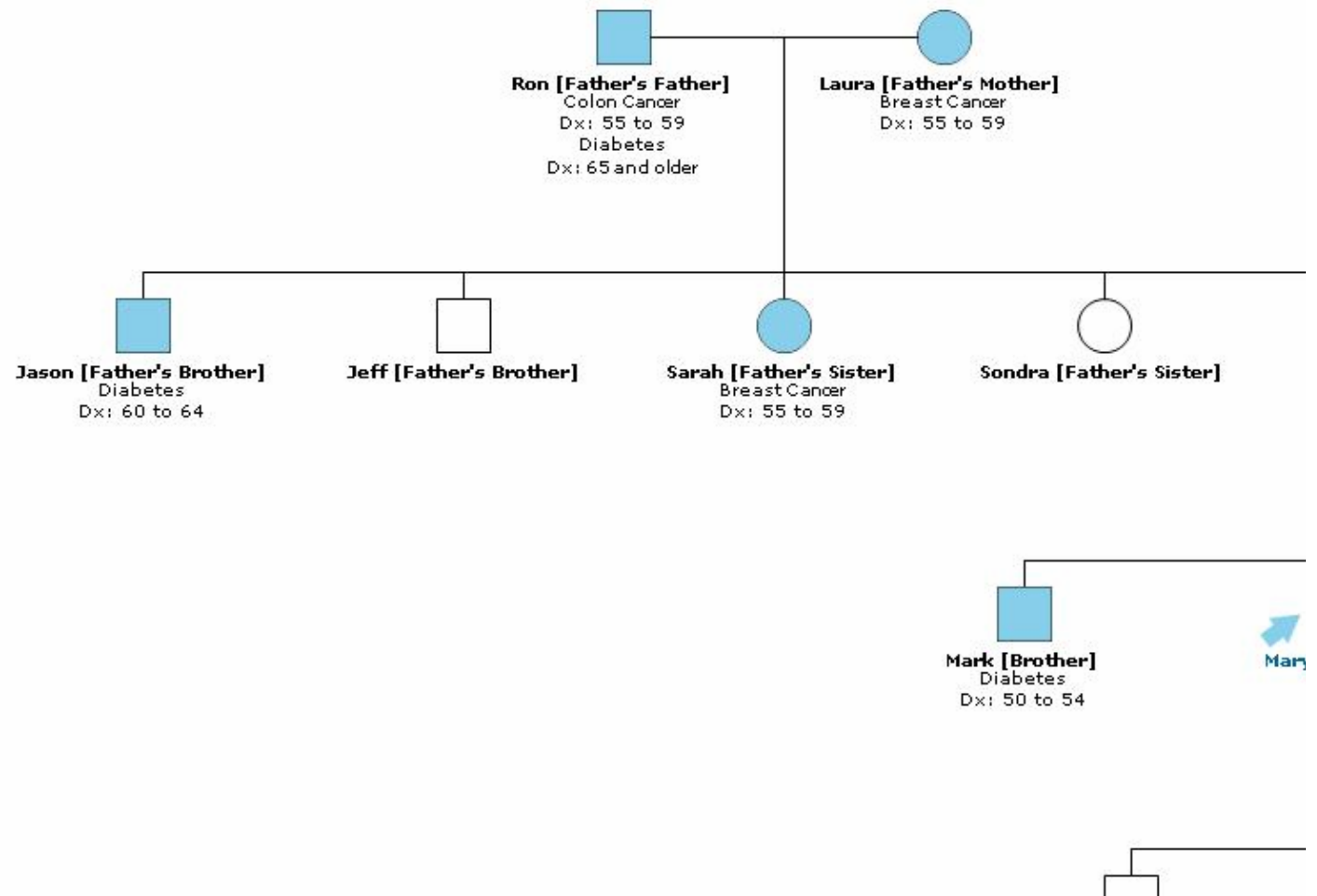Disease Resources

Lifestyle Resources

Family History Resources

My Report – Family Tree

My Report - Family Tree
Mary Smith - January 20, 2005

☐ Male   ○ Female   ■ ● Family Members with a History of Disease   Dx: Age at first diagnosis

Ron [Father's Father]
Colon Cancer
Dx: 55 to 59
Diabetes
Dx: 65 and older

Laura [Father's Mother]
Breast Cancer
Dx: 55 to 59

Jason [Father's Brother]
Diabetes
Dx: 60 to 64

Jeff [Father's Brother]

Sarah [Father's Sister]
Breast Cancer
Dx: 55 to 59

Sondra [Father's Sister]

Mark [Brother]
Diabetes
Dx: 50 to 54

Mary

Family Healthware
Using Family History to Promote Health

- ⊞ **My Profile**
- ⊞ **My Family Profile**
- ⊟ **My Report**
  - Introduction
  - Family Tree
  - **Assessment Summary**
  - Coronary Heart Disease
  - Stroke
  - Diabetes
  - Colon Cancer
  - Breast Cancer
  - Ovarian Cancer
  - Screening Tests
  - Lifestyle Changes
  - Print My Report

  - Disease Resources
  - Lifestyle Resources
  - Family History Resources

My Report - Assessment Summary

Disease:	Family history's impact on risk:
Coronary Heart Disease	WEAK
Stroke	WEAK
Diabetes	STRONG
Colon Cancer	WEAK
Breast Cancer	MODERATE
Ovarian Cancer	WEAK

Learn more about family history as a risk factor for disease.

You should print your full report and discuss it with your health care professional. However, you can also view the entire report online by selecting Continue.

[Print My Report]   [Previous Screen]   [Continue]

Glossary Logout

My Report - Breast Cancer

My Profile
My Family Profile
My Report
- Introduction
- Family Tree
- Assessment Summary
- Coronary Heart Disease
- Stroke
- Diabetes
- Colon Cancer
- **Breast Cancer**
- Ovarian Cancer
- Screening Tests
- Lifestyle Changes
- Print My Report

- Disease Resources
- Lifestyle Resources
- Family History Resources

The impact of your family history on Breast Cancer risk is :   **MODERATE**

Why your family history is a risk factor:
- Two or more closely related family members with breast cancer.

What you can do to reduce your risk:

Screening Tests

- Schedule breast cancer screening today

Mammograms and clinical breast exams are screening tests that can help detect breast cancer early, when it is most treatable. Due to your family history, other screening tests or prevention options may be helpful. Talk to your health professional about your risk of breast cancer, the best tests for you, and how often you should be screened.

Clicking on hyperlink will pop up a text box with the detailed messages

Lifestyle Changes

- Lose weight

- Increase your intake of fruits and vegetables

- Increase your physical activity

Additional Risk Assessment

Other factors can influence your risk of breast cancer such as the age when you began menstruation, a full-term pregnancy before age 30, or use of hormone replacement therapy.

Talk to your health professional about these factors and how they might influence your risk.

Resource Guide:

Family Healthware
Using Family History to Promote Health

Evaluating Family History Tools
for Health Promotion and Disease Prevention

October 2005

Breast Cancer
Colorectal Cancer
Coronary Heart Disease
Diabetes
Ovarian Cancer
Stroke

U.S. Surgeon General's Family History Initiative

- Thanksgiving Day, 2004
  - First Annual National Family History Day

- Family history tool for the public

  My Family Health Portrait
  A tool from the U.S. Surgeon General

- Resource packet for health professionals

  http://www.hhs.gov/familyhistory/

http://www.hhs.gov/familyhistory/

Family history is a risk factor for diseases throughout all stages of life

birth defects
blood disorders

diabetes
depression

Alzheimer's disease
osteoporosis

infants

children

adolescents

adults

older adults

asthma
autism

cancer
heart disease

For more information

Paula Yoon

Contact: pyoon@cdc.gov

Office of Genomics and Disease Prevention

Website: http://www.cdc.gov/genomics