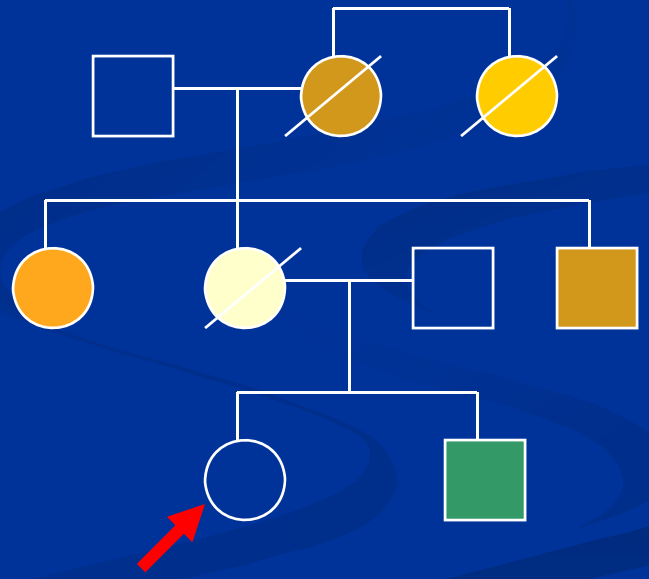
Family History: a Public Health Strategy to Prevent Cancer, Heart Disease and Diabetes

Paula W. Yoon, ScD, MPH
Centers for Disease Control and Prevention



SAFER • HEALTHIER • PEOPLE™

Outline of Presentation

- Potential role of family history for disease prevention and control
  - risk assessment
  - intervention
- What we know and what we don't know
  - heart disease
  - diabetes
  - cancer
- Research agenda

Family History as a Public Health Strategy

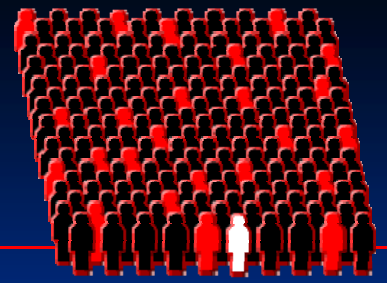
- Risk Assessment

  Using family history to identify individuals, families, and communities at increased risk for chronic diseases

- Intervention

  Using knowledge of family history to guide risk-specific interventions for prevention and early detection

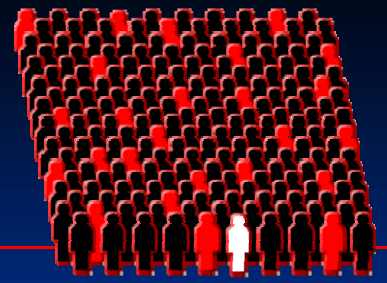
Familial Risk Assessment



- Population
  Study family history in populations (e.g., surveys) to not only establish disease associations, but identify populations most at risk and monitor preventive behaviors

- Individual
  Assess risk due to family history alone or in combination with other risk factors

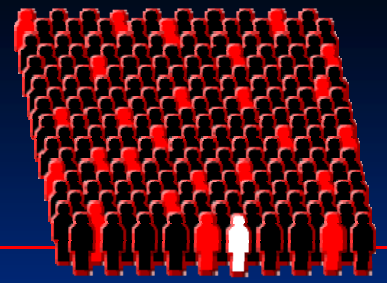
Intervention



Augment population approach with familial risk-based interventions such as ...

- targeted lifestyle changes
- screening at earlier ages, more frequently and with more intensive methods than used for average risk individuals
- chemoprevention
- for those at highest risk, prophylactic procedures and surgeries

Intervention

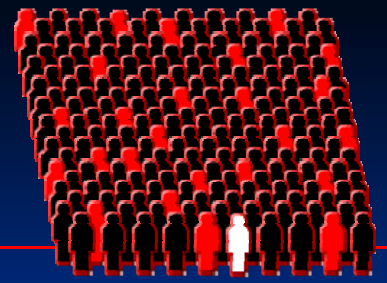


- Targeted lifestyle changes

E.g., diabetes

The USPSTF found good evidence that medium- to high intensity counseling interventions can produce medium to large changes in average daily intake of the core components of a healthy diet in adults patients at risk of diabetes.

Intervention

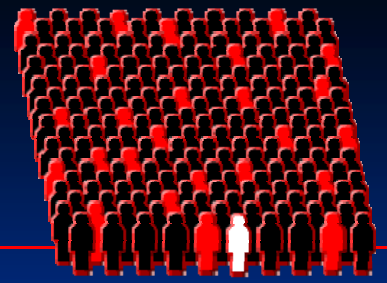


- Screening at earlier ages, more frequently and with more intensive methods than used for average risk individuals

E.g., colorectal cancer

The U.S. Multisociety Task Force on Colorectal Cancer and the American College of Gastroenterology recommend colonoscopy every 3-5 years, beginning at age 40, or 10 years younger than the youngest diagnosis in the family, whichever comes first.

Intervention

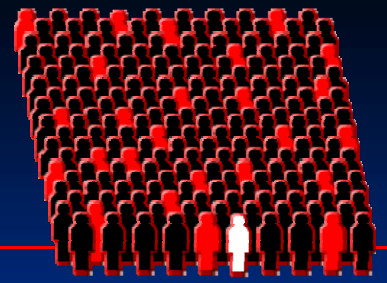


- Chemoprevention

E.g., Coronary Heart Disease

The USPSTF strongly recommends that clinicians discuss aspirin chemoprevention with adults who are at increased risk for CHD. Discussions with patients should address both the potential benefits and harms of aspirin therapy.

Intervention

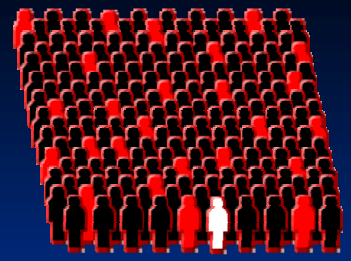


- For those at highest risk, prophylactic procedures and surgeries

E.g., Ovarian cancer

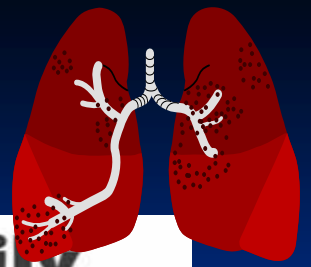
There may be surgical and chemopreventive options for patients at increased risk for developing ovarian cancer based on family history and/or genetic test results. The risks and benefits of these options vary depending on age, family history, and the presence or absence of a cancer susceptibility mutation.

Family History is a Risk Factor for Common Diseases



	Relative Risk
Heart disease	2.0 – 5.4
Type II diabetes	2.4 – 4.0
Breast cancer	2.1 – 3.9
Colorectal cancer	1.7 – 4.9
Prostate cancer	3.2 – 11.0

Risk Assessment



Usefulness of Cardiovascular Family History Data for Population-Based Preventive Medicine and Medical Research (The Health Family Tree Study and the NHLBI Family Heart Study)

Roger R. Williams, MD*, Steven C. Hunt, PhD, Gerardo Heiss, MD, PhD, Michael A. Province, PhD, Jeannette T. Bensen, MS, Millicent Higgins, MD, Robert M. Chamberlain, PhD, Joan Ware, MSPH, and Paul N. Hopkins, MD, MSPH

Detailed medical family history data have been proposed to be effective in identifying high-risk families for targeted intervention. With use of a validated and standardized quantitative family risk score (FRS), the degree of familial aggregation of coronary heart disease (CHD), stroke, hypertension, and diabetes was obtained from 122,155 Utah families and 6,578 Texas families in the large, population-based Health Family Tree Study, and 1,442 families in the NHLBI Family Heart Study in Massachusetts, Minnesota, North Carolina, and Utah. Utah families with a positive family history of CHD (FRS ≥0.5) represented only 14% of the general population but accounted for 72% of persons with early CHD (men before age 55 years, women before age 65 years) and 48% of CHD at all ages. For strokes, 11% of families with FRS ≥0.5 accounted for 86% of early strokes (<75 years) and 68% of all strokes. Analyses of >5,000 families sampled each year in Utah for 14 years demonstrated a gradual decrease in the frequency of a strong positive family history of CHD (−26%/decade) and stroke (−15%/decade) that paralleled a decrease in incidence rates ($r = 0.86$, $p < 0.001$ for CHD; $r = 0.66$, $p < 0.01$ for stroke). Because of the collaboration of schools, health departments, and medical schools, the Health Family Tree Study proved to be a highly cost-efficient method for identifying 17,064 CHD-prone families and 13,106 stroke-prone families (at a cost of about $27 per high-risk family) in whom well-established preventive measures can be encouraged. We conclude that most early cardiovascular events in a population occur in families with a positive family history of cardiovascular disease. Family history collection is a validated and relatively inexpensive tool for family-based preventive medicine and medical research.

(Am J Cardiol 2001;87:129–135)

The Health Family Tree Study Utah, 1983-1996

- H.S. students completed forms at home
- Family history data collected on siblings, parents, aunts & uncles, grandparents
- Family history score calculated for each disease
- Report to each family with feedback and advice
- Public health nurses visited high risk families

CDC
SAFER·HEALTHIER·PEOPLE

Risk Assessment

Health Family Tree Study

Family history of coronary heart disease (CHD)

FHx Score	% Families	% Early CHD	% All CHD
≥0.5 (positive)	14	72.1	48.4
≥1.0 (str pos)	3.2	34.7	17.6
≥2.0 (v str pos)	1.0	16.8	6.3

Includes data from 122,155 families

Williams, et al. *Am J Cardiol* 2001; 87:129-135

CDC
SAFER·HEALTHIER·PEOPLE

Epi Studies of Family History and Cardiovascular Disease (CVD)

- Sibling CVD history assoc with greater risk than parental history
  - Framingham Offspring Study[1]

- Sisters of women with early CHD – 98% low risk by Framingham but 40% had coronary artery calcific.
  - Johns Hopkins Sibling Study[2]

- Assoc of early CHD with CAC - parent and sibling (2.7), sibling only (2.1), parent only (1.5)
  - Multi-Ethnic Study of Atherosclerosis[3]

[1]Murabito, JAMA 2005 [2]Michos, Am Heart J 2005 [3]Nasir, Circulat 2007

Development and Validation of Improved Algorithms for the Assessment of Global Cardiovascular Risk in Women

The Reynolds Risk Score

Paul M Ridker, MD, MPH
Julie E. Buring, ScD
Nader Rifai, PhD
Nancy R. Cook, ScD

IN THE DECADE BETWEEN 1956 AND 1966, investigators in Framingham, Mass, defined age, hypertension, smoking, diabetes, and hyperlipidemia as major determinants of coronary heart disease and coined the term *coronary risk factors*.[1-3] Over time, these markers were codified into global risk scores for assessment of cardiovascular risk.[5-8] However, for women, up to 20% of all coronary events occur in the absence of these major risk factors,[9] whereas many women with traditional risk factors do not experience coronary events.[10] Furthermore, over the past half

Context Despite improved understanding of atherothrombosis, cardiovascular prediction algorithms for women have largely relied on traditional risk factors.

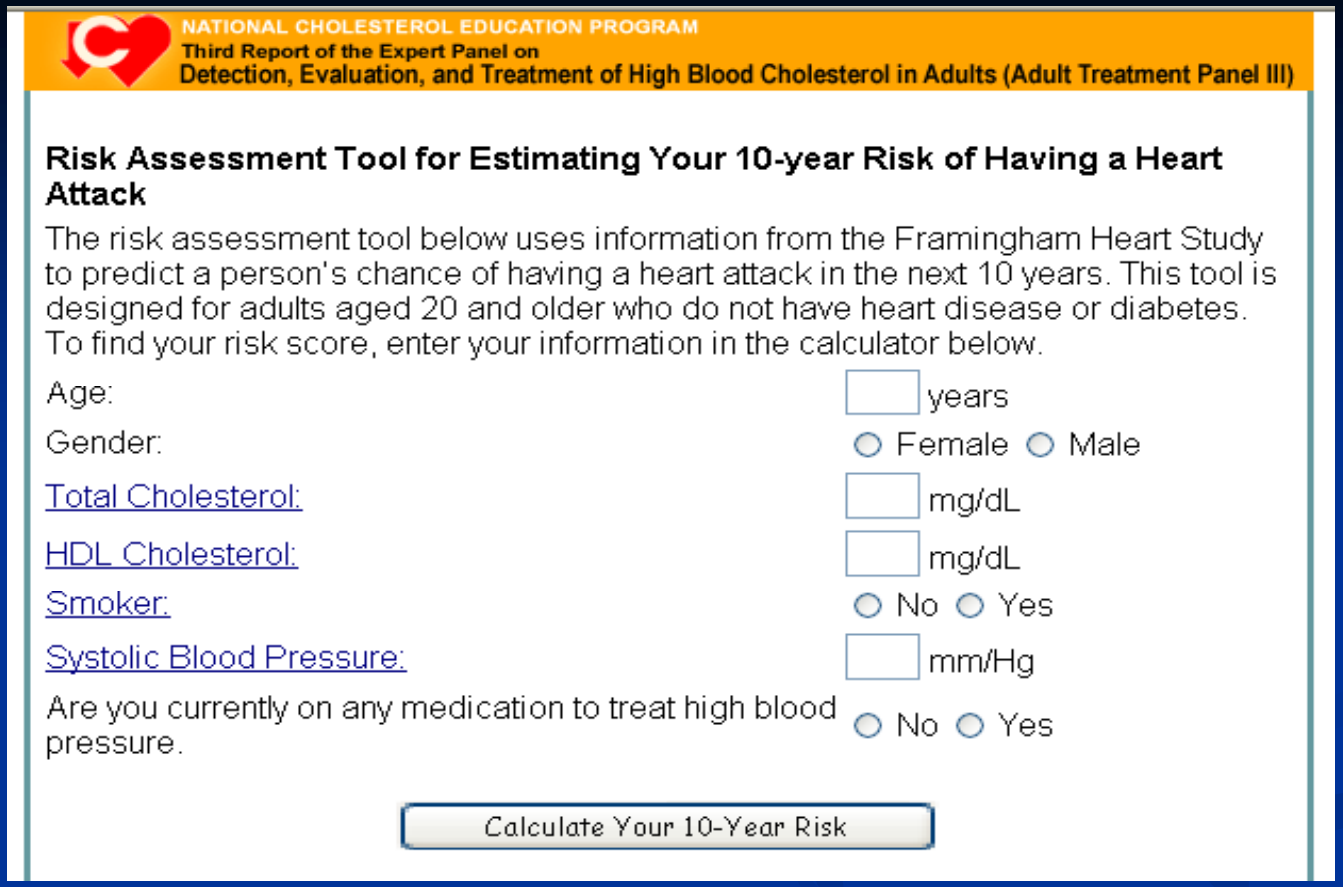
Objective To develop and validate cardiovascular risk algorithms for women based on a large panel of traditional and novel risk factors.

Design, Setting, and Participants Thirty-five factors were assessed among 24 558 initially healthy US women 45 years or older who were followed up for a median of 10.2 years (through March 2004) for incident cardiovascular events (an adjudicated composite of myocardial infarction, ischemic stroke, coronary revascularization, and cardiovascular death). We used data among a random two thirds (derivation cohort, n=16 400) to develop new risk algorithms that were then tested to compare observed and predicted outcomes in the remaining one third of women (validation cohort, n=8158).

Main Outcome Measure Minimization of the Bayes Information Criterion was used in the derivation cohort to develop the best-fitting parsimonious prediction models. In the validation cohort, we compared predicted vs actual 10-year cardiovascular event rates when the new algorithms were compared with models based on covariates included in the Adult Treatment Panel III risk score.

Results In the derivation cohort, a best-fitting model (model A) and a clinically simplified model (model B, the Reynolds Risk Score) had lower Bayes Information Criterion scores than models based on covariates used in Adult Treatment Panel III. In the validation co-

Ridker, et al., JAMA 2007;297:611-619



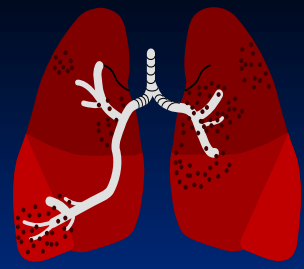
- 10 year risk: < 5% 5-10% 10-20% >20%
- Reynolds score adds - parental hx of MI before 60
  C-reactive protein
- 43% of women at 5 -20% reclassified into lower or higher
- Greatly improved accuracy

Ability of several risk assessment models to identify early-onset CHD (HealthStyles, 2003)

Risk assessment model	Area under the curve
Familial risk + demographics + related conditions	87.2
Familial risk + related conditions	84.6
Demographics + related conditions	84.6
Familial risk + demographics	82.3
Familial risk only	70.9

Scheuner, Genet Med, 2006

WISEWOMAN - Minnesota Sageplus Program



- Underinsured women aged 40-64 enrolled in the NBCCEDP
- Risk assessment and lifestyle intervention services for heart disease and stroke risk factors
- Risk assessment includes family history of early MI or sudden death in first degree relative
- Clinical assessment for all women previously diagnosed with heart disease or diabetes or with ATP III CHD risk score of >= 10%

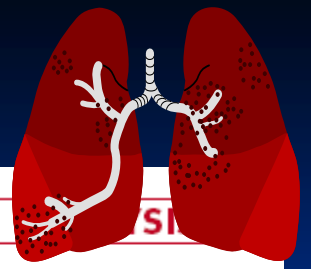
Risk Factors and Family History

Variable	*No FHx %*	*FHx %*	*Odds Ratio [95%CI]*
CHD	1.9	6.6	3.59 [1.60-8.05]
Hypertension	21.6	36.9	2.12 [1.48-3.03]
High cholesterol medication	5.3	14.7	3.10 [1.82-5.30]
Diabetes	3.7	6.5	1.78 [0.87-3.67]
Diabetes medication	2.4	3.6	1.52 [0.59-3.94]
Heart failure	0.3	1.8	6.55 [1.09-39.5]
Kidney failure	1.1	3.5	3.26 [1.12-9.53]

Sageplus Family History Screening: Follow-up

- Health counseling on significance of family health history and need for behavior changes
  - Brochure and family history collection tool
- Encouraged to discuss family history with family and healthcare provider
- Offer phone consultation with genetic counselor if concerns

Intervention



BMJ 2007;335:481-85.

Families of patients with premature coronary heart disease: an obvious but neglected target for primary prevention

Risk of premature coronary heart disease is increased in the families of affected patients. **C K Chow and colleagues** argue that targeting relatives for primary prevention would be an effective policy

First degree relatives of patients with premature coronary heart disease are at increased risk of the disease. Compared with the general population, siblings have at least double the risk, because of shared lifestyle risk factors and genetic predisposition. Offspring and partners are also at increased risk. Relatives have an increased prevalence of modifiable risk factors including hypertension, dyslipidaemia, and smoking. Some guidelines recommend screening of relatives, but surveys indicate that this does not occur in practice. We propose that first degree relatives of patients admitted for premature myocardial infarction should be identified and then offered screening and treatment for risk factors of coronary heart disease

C K Chow cardiology research fellow
A C H Pell consultant cardiologist, Monklands Hospital, Airdrie
A Walker health economist
C O'Dowd health economist, Robertson Centre for Biostatistics, University of Glasgow
A F Dominiczak professor of cardiovascular medicine
J P Pell professor of epidemiology, BHF Glasgow Cardiovascular Research Centre, University of Glasgow, Glasgow G12 8TA
Correspondence to: J Pell j.pell@clinmed.gla.ac.uk

Premature coronary heart disease—before 55 years in men and 60 in women—is more likely to reflect a genetic predisposition, so relatives of patients with premature onset are at greater risk than those of patients with late onset disease.[15 17] Among 45 317 health professionals, paternal history of myocardial infarction before 70 years conferred a relative risk of 1.7,[15] whereas a paternal history before 50 years carried a relative risk of 2.3. The corresponding figures for maternal history were 2.2 and 3.6. Increased risk is also due to shared lifestyle. Mothers exert a greater influence over the lifestyle of their offspring than fathers,[20] which accounts for the higher risk associated with maternal family history.[10 15] Risk is higher if more than one first degree relative is

Source: UT Southwestern Medical Center
Date: September 11, 2007

More on: Heart Disease, Stroke Prevention, Cholesterol, Vioxx, Chronic Illness, Diseases and Conditions

Women Less Likely Than Men To Change Habits That Increase Heart Disease Risk

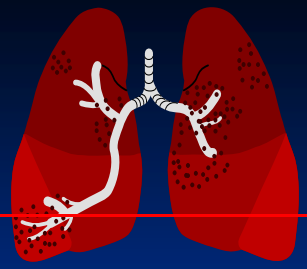
Science Daily — Smoking, eating fattening foods and not getting enough exercise are all lifestyle habits that can lead to poor health and cardiovascular disease – more so if you have a family history. But researchers at UT Southwestern Medical Center have found that women don't change these habits as often as men, even when they have relatives with heart disease.

The scientists found that women with a family history of heart disease are less likely than men to change habits such as smoking and infrequent physical activity. They also are more likely to engage in lifestyle choices that increase their risk of heart disease than are women who did not report a history of heart disease.

Dr. Amit Khera led research showing that women - even those with a history of cardiovascular disease in their families are less likely than men to change unhealthy habits such as smoking and infrequent physical activity. (Credit: Image courtesy of UT Southwestern Medical Center)

"A family history of heart disease is as important an indicator of future cardiovascular health in women as it is in men – perhaps more important," said Dr. Amit Khera, assistant professor of internal medicine and senior author of the study. "And yet there is an underappreciation of cardiovascular-

Intervention



- Dallas Heart Study[1] –
  - subjects with FHx early MI, compared to no FHx perceived lifetime risk of MI > average
  - among FHx+ MI, women less aware of risk and had worse lifestyle choices compared to men

- HARVEST study[2] - never treated stage 1 hypertension
  - at baseline FHx+ assoc with higher prevalence of undesirable lifestyle
  - over 6 years, FHx+ individuals improved lifestyle
  - FHx- individuals had increasingly poor lifestyle
  - FHx- had significantly higher initiation of drug therapy

[1] Patel, Am Heart J 2007 [2] Winnicki J Hyperten 2006

CDC
SAFER·HEALTHIER·PEOPLE

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

Am J Health Behav. 2005;29(5):395-406

Salminen, Am J Health Behav, 2005

SUPPLEMENT ARTICLE

Is Family History a Useful Tool for Detecting Children at Risk for Diabetes and Cardiovascular Diseases? A Public Health Perspective

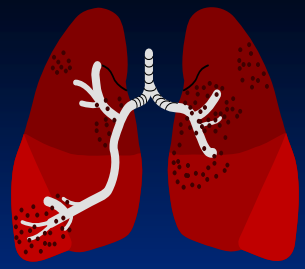
Rodolfo Valdez, PhD, MSc[a], Kurt J. Greenlund, PhD[b], Muin J. Khoury, MD, PhD[a], Paula W. Yoon, ScD, MPH[a]

[a]National Office of Public Health Genomics and [b]Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

The authors have indicated they have no financial relationships relevant to this article to disclose.

Valdez, Pediatrics, Sept supplement, 2007

Family History and Heart Disease



- Risk Assessment
  - Increasing evidence that FHx is important risk factor
  - Risk prediction tools are limited when RR low (Levine & Levine, Preven Medic 2007)

- Intervention
  - Targeting lifestyle (motivation): little evidence
  - Disease screening: need cost benefit studies and more specific clinical guidelines about FHx
  - Chemoprevention: aspirin, statins? antihypertensives?
  - Prophylactic procedures/surgeries: NA

CDC
SAFER • HEALTHIER • PEOPLE

Family History of Diabetes

- Prevalence of diabetes - 8% and increasing
- More than 1/3 have not been diagnosed
- The association between diabetes and familial risk for the disease is graded and independent of other major risk factors
- What role can family history play in risk assessment, identification of undiagnosed diabetes, and intervention?

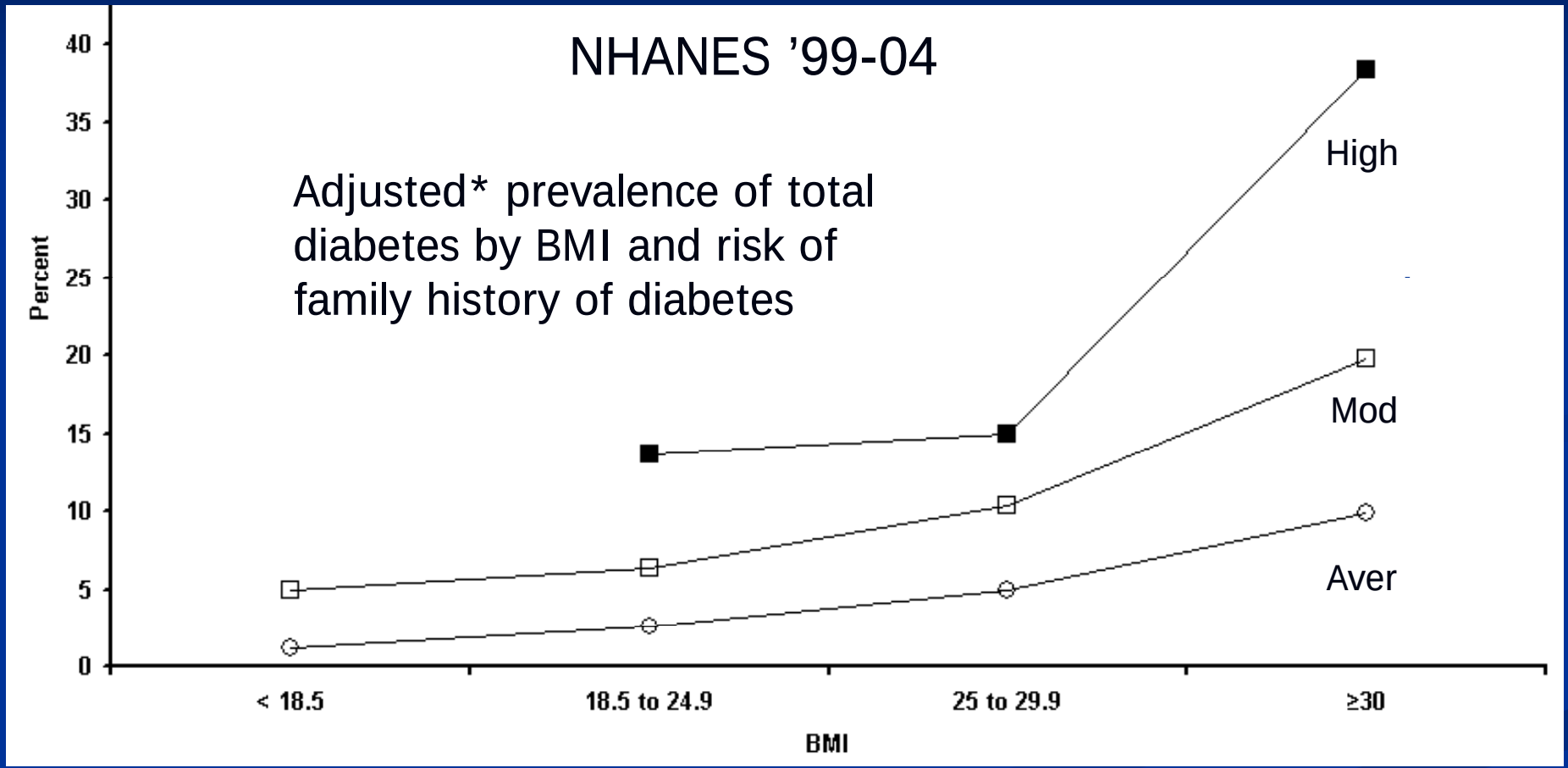
Familial risk strata and adj* prevalence of diabetes: NHANES '99-04

Familial risk stratum	Proportion of population (%)	Prevalence of diagnosed diabetes (%)	Prevalence of undiagnosed diabetes (%)
High	6.8	19.1	8.4
Moderate	23.0	8.9	3.0
Average	70.2	3.6	2.3

*By Age, Sex, race/ethnicity, and BMI

Valdez, Diabetes Care 2007

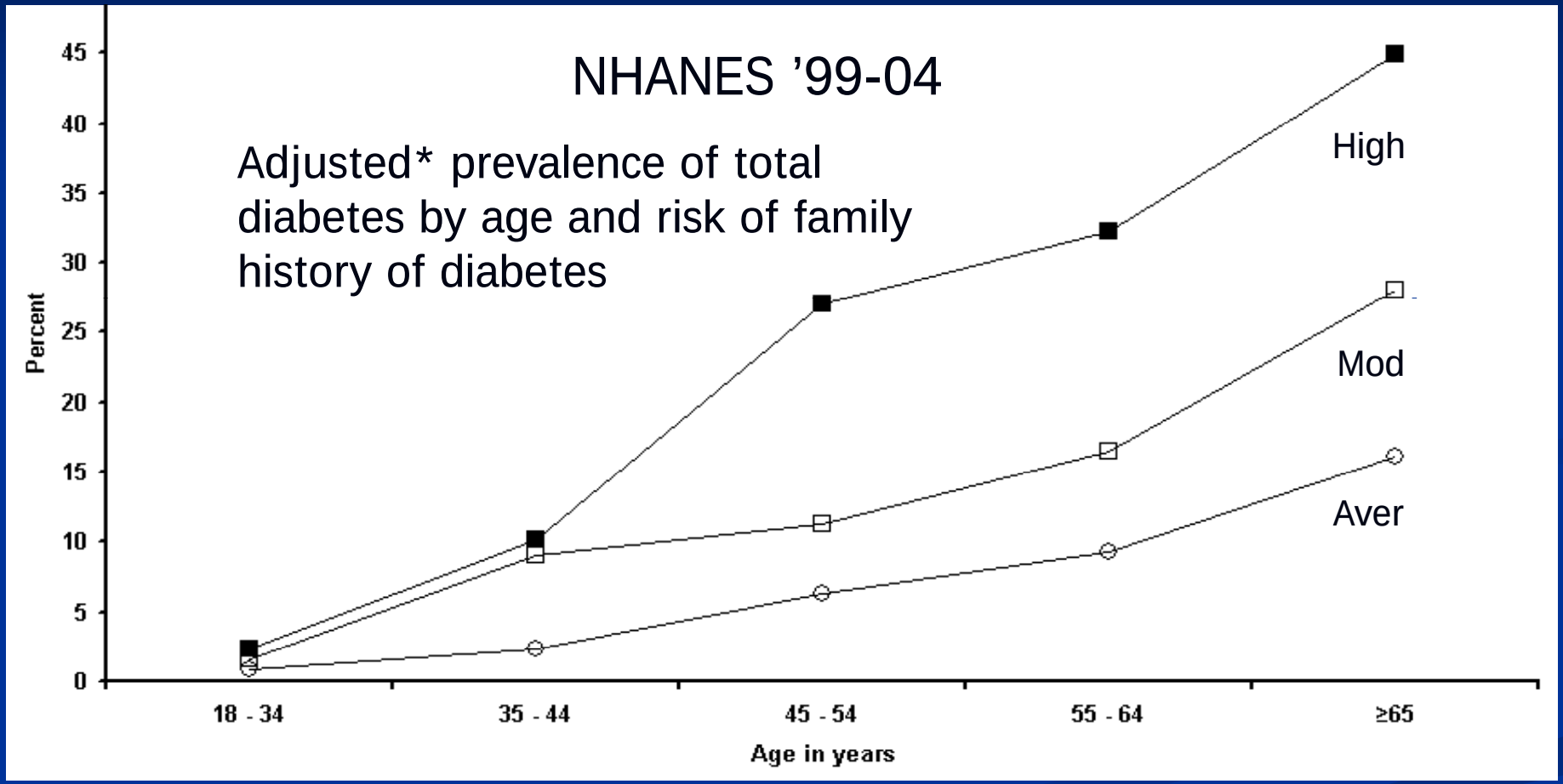
Family History of Diabetes



*Adj for age, sex, race/ethnicity, educ

Valdez, Diabetes Care 2007

Family History of Diabetes



*Adj for BMI, sex, race/ethnicity, educ

Valdez, Diabetes Care 2007

Risk Assessment

- What non-invasive factors predict risk or help identify undiagnosed diabetes?
- Does family history improve the predictive value of the tool?
- What is the evidence for existing risk prediction tools?

Risk assessment tools for diabetes

The Atherosclerosis Risk in Communities

- Clinical - AUC = 0.71

waist circumference	ethnicity
height	age
blood pressure	family history (parents)

- Fasting glucose only: AUC = 0.74
- Clinical + glucose: AUC = 0.78
- Clinical + glucose + lipids: AUC = 0.80

Assessments based on clinical info only may be of value as a first step in serial diagnostic strategies for prevention in community settings.

Schmidt, Diabetes Care 2005

Risk assessment tools for diabetes

German Diabetes Risk Score

- To estimate 5-year probability of developing diabetes

waist circumference	physical activity
height	smoking
hx of hypertension	red meat
whole-grain bread	coffee
alcohol	age

- AUC = 0.82 – 0.84 0.75 - 0.83 for undiagnosed
- Accurate screening tool to identify high risk individuals who would benefit from diet and lifestyle changes

Schulze, Diabetes Care, 2007

CDC
SAFER · HEALTHIER · PEOPLE

Intervention Diabetes

The Impact of Family History of Diabetes on Glucose Testing and Counseling Behavior in Primary Care

HARVEY J. MURFF, MD, MPH[1,2]
RUSSELL L. ROTHMAN, MD, MPP[1,3]
DANIEL W. BYRNE, MS[1]
SAPNA SYNGAL, MD, MPH[4,5]

Epidemiological evidence has revealed increasing prevalence rates of type 2 diabetes (1,2), with an estimated 6.3% of the U.S. adult population having either diagnosed or undiagnosed diabetes (3). Individuals with a family history of diabetes are at increased risk of developing diabetes, and lifestyle modification can help reduce this risk (4–6). Several studies have demonstrated that lifestyle choices, such as regular exercise or healthy dietary choices, are associated with a reduced risk of developing diabetes (7–10). The purpose of this study was to determine whether a family history of diabetes was associated with a provider's decision to screen for diabetes or with a provider's counseling about lifestyle modifications.

RESEARCH DESIGN AND METHODS — The study was con-

99386, and 99387) (12) were included within our study sample. We excluded patients with a personal history of diabetes. This study was approved by the Brigham and Women's Institutional Review Board.

We abstracted information from patient charts regarding demographics, personal medical history, and family history. A family history was considered positive in cases where a first-degree relative had been identified. First-degree relatives included mother, father, sibling, or child. Information was obtained from chart review regarding the ordering of laboratory tests. We conservatively overestimated potential screening for diabetes by including all plasma glucose testing as possible screening for diabetes, regardless of whether the sample was fasting or random. We also reviewed the visit note for any documentation by the provider of inquiring about and counseling with re-

individuals with their weight recorded and those without weight recorded. Models constructed using imputed weight data (based on sex and age matching) and nonimputed weight data were not significantly different, and the results shown do not include imputed data.

We constructed hierarchal regression models to determine patient and provider factors associated with a family history of diabetes documented within the medical record and used generalized estimating equations to account for physician-level clustering (13). All analyses were performed using SAS software version 8.2 (SAS Institute, Cary, NC).

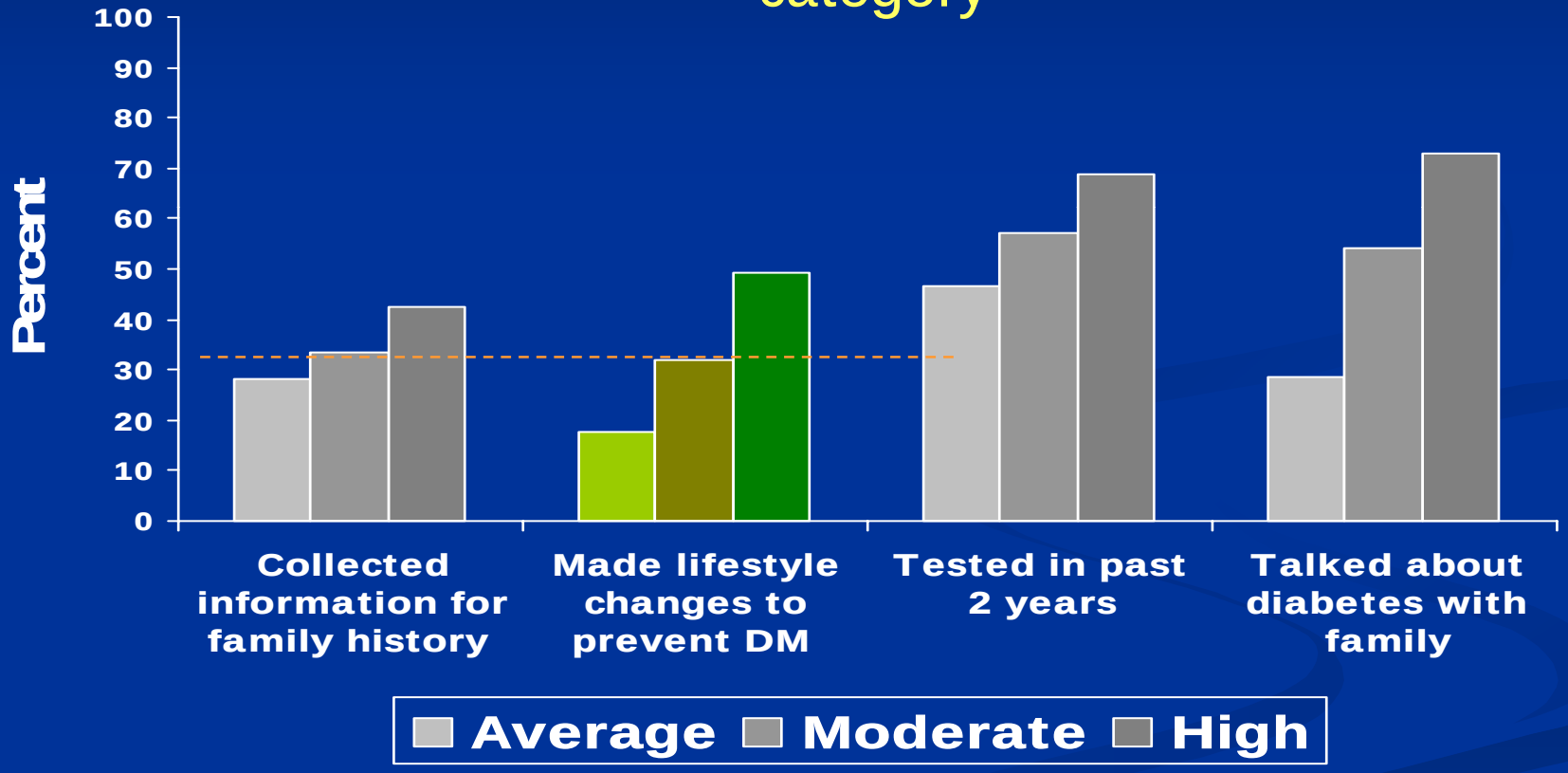
RESULTS — A total of 516 new patient annual preventative visits were included in our analysis. Patient characteristics and rates of glucose testing and lifestyle counseling are presented in Table 1.

Seventy-nine patients (15%) had identified one or more first-degree relative with a history of diabetes. Fifty-two percent of patients with a first-degree relative with diabetes had a plasma glucose

Murff, Diabetes Care, 2004

Intervention Diabetes

Risk-reducing and risk-aware behaviors by family history category



Hariri, Genet Med, 2006

Intervention Diabetes

Family History of Diabetes, Awareness of Risk Factors, and Health Behaviors Among African Americans

Kesha Baptiste-Roberts, MPH, Tiffany L. Gary, PhD, Gloria L.A. Beckles, MD, MSc, Edward W. Gregg, PhD, Michelle Owens, PhD, Deborah Porterfield, MD, and Michael M. Engelgau, MD, MS

Diabetes is a major contributor to morbidity and mortality and generates large direct as well as indirect costs.[1–3] The prevalence of diabetes among US adults[4] has increased substantially over the past several decades and stood at 8.7% in 2002.[2,5] The burden of type 2 diabetes disproportionately affects African Americans. For example, data from nationally representative samples show that White men are one half to one fifth as likely than African American men to have or develop diabetes, and African American women are approximately 100% more likely than White women to have or develop the disease.[6,7] It is estimated that 33% to 50% of people with type 2 diabetes are

Objectives. We examined the role of family history of diabetes in awareness of diabetes risk factors and engaging in health behaviors.

Methods. We conducted a cross-sectional analysis of 1122 African American adults without diabetes who were participants in Project DIRECT (Diabetes Interventions Reaching and Educating Communities Together).

Results. After adjustment for age, gender, income, education, body mass index, and perceived health status, African Americans with a family history of diabetes were more aware than those without such a history of several diabetes risk factors: having a family member with the disease (relative risk [RR] = 1.09; 95% confidence interval [CI] = 1.03, 1.15), being overweight (RR = 1.12; 95% CI = 1.05, 1.18), not exercising (RR = 1.17; 95% CI = 1.07, 1.27), and consuming a high-calorie diet (RR = 1.10; 95% CI = 1.00, 1.17). Also, they were more likely to consume 5 or more servings of fruits and vegetables per day (RR = 1.31; 95% CI = 1.02, 1.66) and to have been screened for diabetes (RR = 1.21; 95% CI = 1.12, 1.29).

Conclusions. African Americans with a family history of diabetes were more aware of diabetes risk factors and more likely to engage in certain health behaviors than were African Americans without a family history of the disease. (*Am J*

Baptiste-Roberts, AJPH, 2007

Intervention Diabetes

- Project Direct – 1122 AA adults without diabetes in NC
  62% women; 35% over 50 years; 65% overweight
- 36% FHx of diabetes – 20% mother; 11% father; 18% sibling
- Compared to FHx-, those with FHx+ were more:
  - aware of diabetes risk factors
  - likely to consume 5+ fruits and vegetables per day
  - likely to have been screened
- Health Belief Model
  FHx diabetes ---→ perceived susceptibility --→ likelihood of behavior change

Baptiste-Roberts, AJPH, 2007

CDC
SAFER·HEALTHIER·PEOPLE

Family History and Diabetes

- Much validation work needs to be done for risk assessment tools

- Intervention options are mainly lifestyle changes
  - studies are limited: cross sectional & self reports
  - behaviors are very difficult to change
  - population vs high risk approach

- Screening guidelines
  - USPSTF – only for adults with hypertension or hyperlipidemia
  - ADA – begin age 45 every 3 years for normal risk high risk (FHx) – younger and more frequently

CDC
SAFER·HEALTHIER·PEOPLE

Family History and Cancer

- 5-10% of cancers strong hereditary basis
- 10 -30% familial
- Family history is key to risk assessment
- Identification of high risk is important for disease detection (screening)
- Role of family history in guiding other prevention strategies is less clear

Family History and Cancer

- 5-10% of cancers strong hereditary basis
- 10 -30% familial
- * Family history is key to risk assessment
- * Identification of high risk is important for disease detection (screening)
- Role of family history in guiding other prevention strategies is less clear

Risk Assessment and Cancer

- Cancer family history should be routine part of patient care
- Barriers to collecting FHx in clinical setting
- New tools being developed - computerized, self-administered, automated assessment

Examples –
Your Disease Risk
Family Healthware

GREAT
*James*Link
MyGenerations

Issues with Risk Assessment Tools

- What is the purpose and setting for the risk assessment?
- What family history data should be collected?

relatives	age at onset
age at death	cause of death
co-morbidities	race/ethnicity

- Should other risk factors be included in the assessment?
- What criteria will be used to assess risk?

Annals of Internal Medicine | CLINICAL GUIDELINES

Genetic Risk Assessment and *BRCA* Mutation Testing for Breast and Ovarian Cancer Susceptibility: Recommendation Statement

U.S. Preventive Services Task Force*

This statement summarizes the U.S. Preventive Services Task Force (USPSTF) recommendations on genetic risk assessment and *BRCA* mutation testing for breast and ovarian cancer susceptibility, along with the supporting scientific evidence. The complete information on which this statement is based, including evidence tables and references, is included in the evidence synthesis available through the USPSTF Web site (www.preventiveservices.ahrq.gov). The recommendation is also posted on the Web site of the National Guideline Clearinghouse (www.guideline.gov).

Ann Intern Med. 2005;143:355-361. www.annals.org

For author affiliation, see end of text.

Individuals who wish to cite this recommendation statement should use the following format: U.S. Preventive Services Task Force. Genetic risk assessment and *BRCA* mutation testing for breast and ovarian cancer susceptibility. Ann Intern Med. 2005;143:355-61.

*For a list of the members of the U.S. Preventive Services Task Force, see the Appendix.

Summary of Recommendations

The U.S. Preventive Services Task Force (USPSTF) recommends against routine referral for genetic counseling or routine breast cancer susceptibility gene (*BRCA*) testing for women whose family history is not associated with an increased risk for deleterious mutations in breast cancer susceptibility gene 1 (*BRCA1*) or breast cancer susceptibility gene 2 (*BRCA2*).

This is a **grade D recommendation**. (See **Appendix Table 1** for a description of the USPSTF classification of recommendations.)

The USPSTF found fair evidence that women without certain specific family history patterns, termed here "increased-risk family history" (see Clinical Considerations for a definition), *have a low risk for developing breast or ovarian cancer associated with* BRCA1 *or* BRCA2 *mutations. Thus, any*

rious mutations in *BRCA1* or *BRCA2* genes be referred for genetic counseling and evaluation for *BRCA* testing.

This is a **grade B recommendation.**

The USPSTF found fair evidence that women with certain specific family history patterns (increased-risk family history) have an increased risk for developing breast or ovarian cancer associated with BRCA1 *or* BRCA2 *mutations. The USPSTF determined that these women would benefit from genetic counseling that allows informed decision making about testing and further prophylactic treatment. This counseling should be done by suitably trained health care providers. There is insufficient evidence to determine the benefits of chemoprevention or intensive screening in improving health outcomes in these women if they test positive for deleterious* BRCA1 *or* BRCA2 *mutations. However, there is fair evidence that prophylactic surgery for these women significantly decreases breast*

USPSTF, Ann Intern Med, 2005

Family history screening protocols for mutation testing

Table 3

Level of agreement (kappa statistic) between each pair of the six family history screening protocols estimated using the 118 women with any personal or family history of breast/ovarian cancer

	NBCC	WCGS	NICE	NCCN	USPSTF
NYS/ACMG	Low (0.39)	Fair (0.50)	Fair (0.47)	Low (0.33)	Good (0.80)
NBCC	—	Fair (0.52)	Low (0.57)	Fair (0.75)	Low (0.37)
WCGS	—	—	Low (0.47)	Fair (0.62)	Fair (0.52)
NICE	—	—	—	Fair (0.49)	Fair (0.44)
NCCN	—	—	—	—	Low (0.36)

NYS/ACMG, New York State/American College of Medical Genetics; NBCC, National Breast Cancer Centre, Australia; WCGS, Wales Cancer Genetic Services; NICE, National Institute for Clinical Excellence (tertiary referral); NCCN, National Comprehensive Cancer Network; USPSTF, United States Preventive Services Task Force.

Palomaki, Genet Medic, 2006

Cancer Risk Assessment

- Lack of agreement between protocols
- Most algorithms were developed from clinical data (e.g., registries and some case-control studies)
- Need to validate assessment criteria using population level data
- However, for most cancers, family history is the strongest predictor of future risk

Clinical Guidelines for Cancer Screening - USPSTF

- Colorectal – Persons at higher risk (e.g., 1st-degree relative < 60 years) screening at an earlier age is reasonable
- Breast - Women at increased risk (e.g., family history in a mother or sister) more likely to benefit from regular mammography beginning in the 40s
- Prostate – If early detection improves outcomes, men > 45 at increased risk (AA men and men with family history of 1st-degree relative) may benefit

Risk Assessment – Economic Analysis

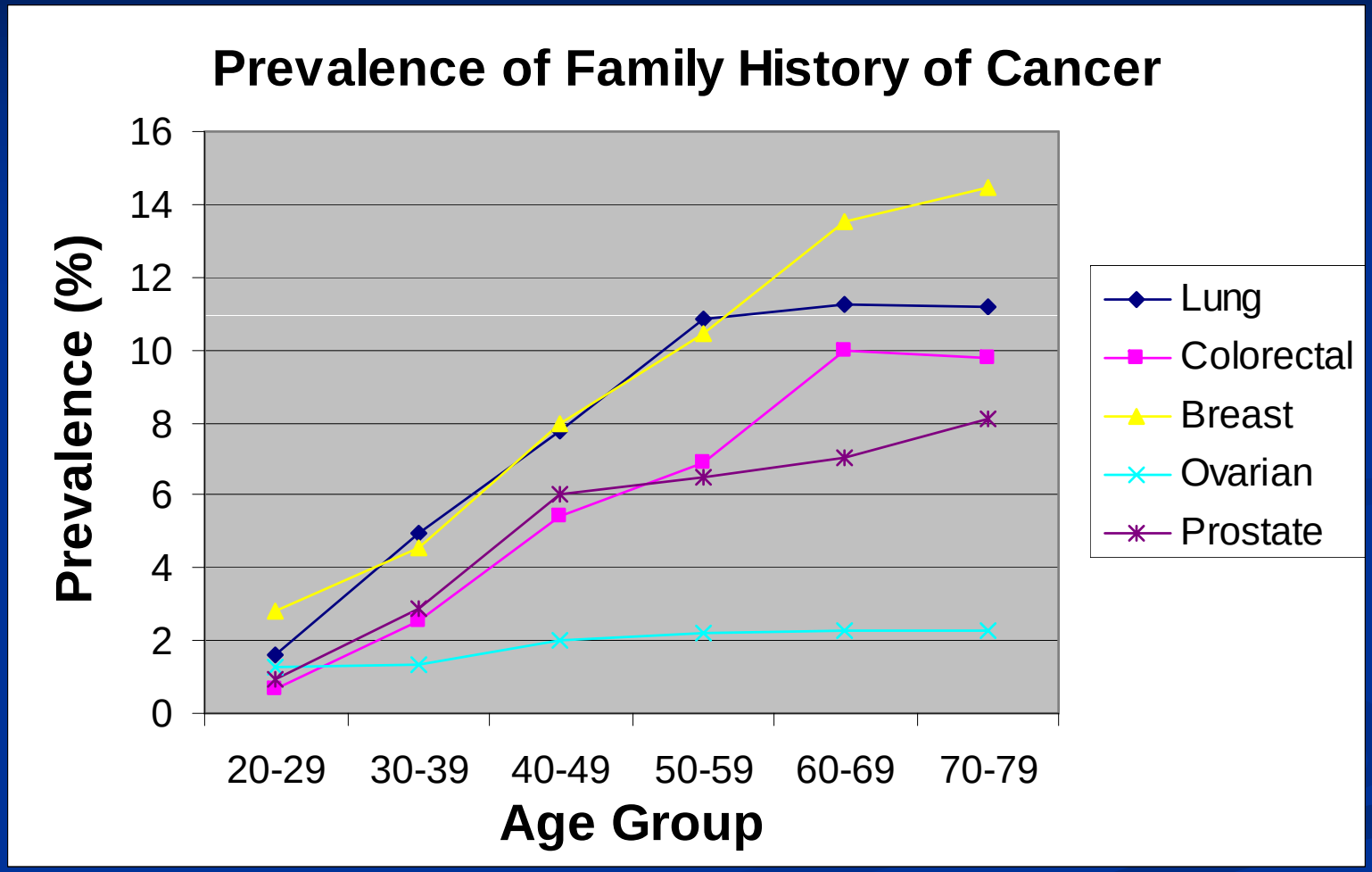
- Estimate clinical and economic effect of using FHx to identify persons for CC screening before age 50

- Population estimates
  - 22 mill eligible for FHx assessment (40-44 years)
  - 1 mill eligible for early colonoscopy
  - 2,834 invasive cancers detected
  - 29,331 life years gained
  - program cost - $900 million
  - discounted cost per life year gained - $58,228.

- Costly but potentially beneficial; need more data

Ramsey, Cancer Epidemiol Biomarkers Prev, 2005

Risk Assessment – Economic Analysis



Ramsey, Genet Med, 2006

Family History for Public Health

- High risk approach can augment population approach
  - Increase screening rates
  - Motivate families to eat healthier and exercise
- Research agenda
  - Validate risk assessment algorithms
  - Develop decisions support tools
  - Study impact of family history on interventions
  - Study cost-effectiveness for detection and prevention programs
  - Review clinical preventive services guidelines and identify gaps

For more information

Paula W. Yoon

Contact: pyoon@cdc.gov

Division for Heart Disease and Stroke Prevention

CDC