

Historical Perspective

- 1960's and 1970's
Family history, sib correlations and adoption studies
- 1980's
 - Segregation analysis of pedigrees
- 1990's
 - Candidate genes
- 2000's
 - Genome-wide linkage and association analyses, population admixture studies
 - Gene function studies - microarrays

Family History as a Risk Factor

Independent predictor of disease - Why?

- Risk factors do not generally work in a linear fashion
- Interactions and modifiers are the rule in common disease
- Family history does not need to model these usually unknown interactions.
- Only the interactions that lead to disease expression will result in a +FHx

Family History - Key to Diagnosis and Treatment

- Finds a **subset** of the population at high risk
- Identifies **relatives** who need help
- **Treating families** is usually more effective than treating individuals

Can You Change Your Genes?

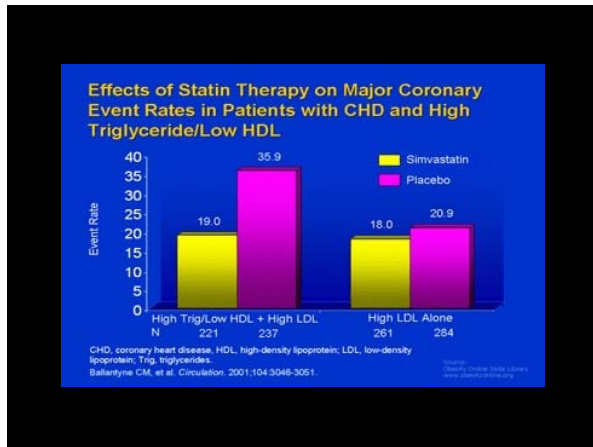
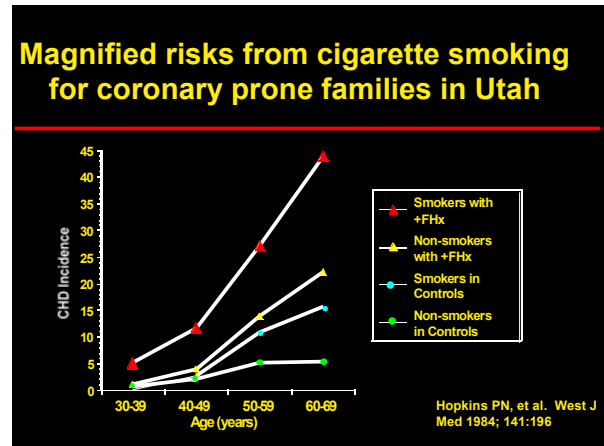
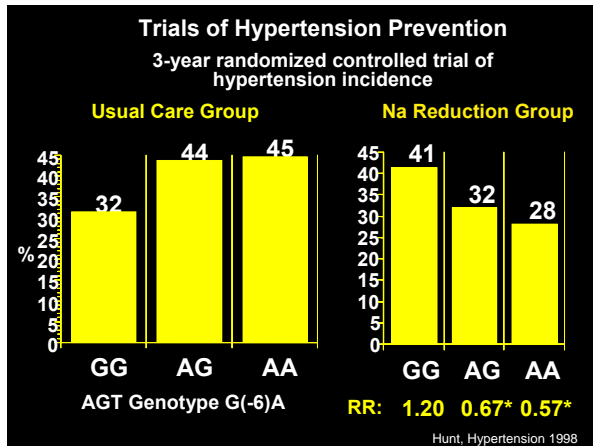
**Not at present
BUT
You can change gene
expression!**

Gene Expression

- **Calorie intake influences transcription rates of adipokine and insulin signaling genes**
- **Salt intake influences transcription rates of blood pressure regulation genes (e.g renin and the epithelial sodium channel in the kidney).**

Persons at greatest risk of disease can be helped the most by intervention

- Intervention on a genetic pathway is more successful in gene carriers than noncarriers
- Intervention on a single risk factor may remove an interaction resulting in greater than expected success



- ### Relative Risks of Common Risk Factors for CHD Mortality
- **6-year relative risk for mortality in MRFIT**
 - Chol 240 vs 200 = 1.7
 - Chol 240 vs 175 = 2.2
 - 41% of excess deaths are in the 203-244 range
 - **6-year mortality risk for HBP**
 - DBP ≥ 90 vs < 90 = 1.8
 - **Smoking**
 - RR = 2.4
- Stamler JAMA 1986;256:2823

Health Family Tree Project

**Utah High Schools
1983-1999**

Educate Population about FHx.
Identify High-risk Families.

Health Family Tree Program (Data collected 1983-1999)

Condition	N	Condition	N
Trees	75594	HBP	123844
Individuals	1138474	Diabetes	44250
MI	58648	High Chol	66663
Stroke	27398	Smokers	147298
BRCA	12957	Overweight	407749
Lung CA	7190	Alcohol	81862
Colon CA	9696	No exercise	557268

Relative Risk for CHD by Family History in 15,200 Utah Families

CHD FHx Definition	Prevalence	Relative Risk at Ages:		
		20-39	50-59	70+
1+ Affected	38%	2.9	1.3	1.3
1+ Age <55	13%	3.9	1.5	1.1
2+ Affected	8%	5.9	1.8	2.0
2+ Age <55	2%	12.7	2.9	0.7

Data for 94,292 persons. Hunt SC, et al. J Chron Dis 1986; 39:809

Family History of CHD in the Health Family Tree Study

Family History	% Families	% Early CHD	% All CHD
Mild	14.0	72.1	48.4
Moderate	3.2	34.7	17.6
Strong	1.0	16.8	6.3

Includes data from 122,155 families; 16,602 early CHD cases; 54,182 cases of CHD at any age

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

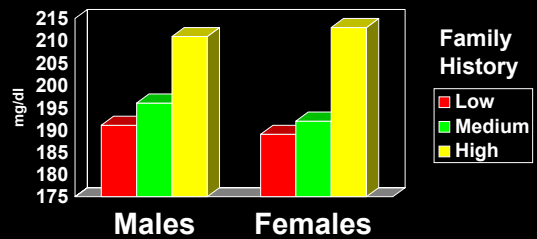
Family History of Stroke in the Health Family Tree Study

Family History	% Families	% Early Stroke	% All Stroke
Mild	11.0	86	68
Moderate	1.4	22	16
Strong	1.0	19	12

Includes data from 122,155 families; 4,600 early stroke cases; 22,425 cases of stroke at any age

Williams, Am J Cardiol 2001;87:129

Mean Cholesterol Levels by Family History in Utah Families



Jorde, et al. Am J Cardiol 1988;62:708

Population Assessment of Family History

- Every family should know their family history for each of the common chronic diseases
 - For the last 20 years, the Health Family Tree project has been run in Utah high schools
 - Educates students AND their families
 - By report, families are encouraged to getting screening and medical advice to reduce their risk.

Triage at MASH 4077



Population vs High-Risk Strategy: Do we need to choose?

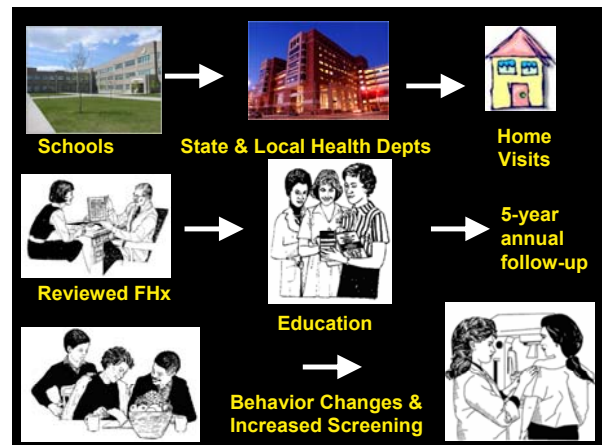
- Triage families according to greatest need based upon disease expression
 - Not according to risk factor distributions
- Aggressively target prevention to the high-risk families
- Continue to encourage population risk factor reduction for the rest

High-risk Strategy using FHx is a Population Strategy

- Family histories of an entire population are collected and analyzed
 - Families become aware of diseases in relatives as they collect the information
- A family history report will put their family history into perspective
- Lifestyle modification and further assessment by medical personnel can be encouraged

National Family History Screening

- Can easily be expanded from a school-based approach for use by:
 - Public health agencies
 - Medical personnel (clinics, physicians, etc)
 - General public



High Risk Family Intervention

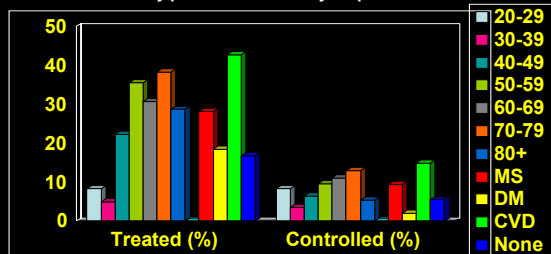
- At baseline:
 - High-risk families knew less about risks, had worse health habits, and utilized resources less
- At 5-year follow-up:
 - High-risk families improved to match average risk families for nearly all variables

Five year % Increase from Baseline in Health Indicators in 400 High Risk and 400 Average Risk Families for CHD

Health Indicator	High Risk Families	Control Families
Had annual medical exam	149	17
Had annual BP check	135	18
Lost weight	45	18
Reduced salt	2	29
Added exercise	48	11
Reduced fats	48	34
Lower cholesterol	43	55
More fruits, grains, vegetables	62	40

Need for Risk Factor Control

Treatment and Control of Combined Hypertension/Dyslipidemia



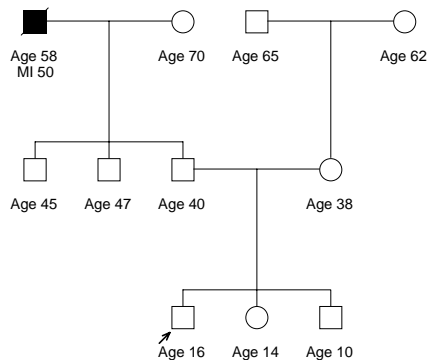
Wong et al. Am J Cardiol 2006;98:204

Risk Factor Control

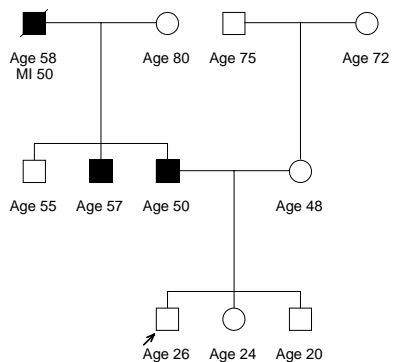
- Is lack of control the patient's or physician's fault? My opinion:
MD doesn't emphasize enough to patient the need to continue on medications
Patients don't realize the risks of noncompliance
- A positive family history is a great tool to overcome both problems if used correctly

A Positive Family History is VERY Age-related

Moderate Risk Pedigree?



10 Years Later



Summary

- Family history independently predicts disease incidence
- Population-based screening identifies the subset at greatest risk
- Those at highest risk need greater help, but also respond the best
- Helps achieve education and public health goals using both a population and high-risk approach