Family History (FH) – Still Useful After All These Years

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Acknowledgements

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Learning Objectives

- Identify the utility of an evolving family history in the era of genomic medicine
- Establish the capacity to use genetic information to tier patient risk
- Formulate and utilize focused, problem-based family history questions and establish a system for collecting a comprehensive family history within a quality improvement context
- Apply various strategies in patient/family communication
I have funding from 1 JH and 2 federal grants and no private financial relationships to disclose. I will not discuss off-label or investigational use of “drugs.”

Every child deserves a good upbringing.

My 1° career goals are to:
Help make genetics work to help people improve scientific understanding, health, and well-being and assist communities to be more welcoming to all people.

Thanks for listening.
Bill Foege, IOM, 2005

“The challenge to public health genomics is to overcome inequitable allocation of benefits, the tragedy that would befall us if we made the promise of genetics only for those who could afford it and not for all society. ”
The Pediatrician’s Role

- Clinical Suspicion and Preventive System Approach
- First Response to Newborn Screen, Congenital Anomaly/Complex Conditions, Family History Risk

- Referral to Specialists
- Support

- Ongoing Management
- Medical Home
Dr. Barton Childs’ Questions

• Why this particular child?
• Why these findings? This disease?
• Why now?
• Is there something we could have done and can do going forward to prevent or lessen the problem?
• To do or not to do a genetic test – that is the question, but we have understood family history is important for a very long time.
Why in an era of genetic testing do we still need to do FH?

• Family is “home plate” for communication, care, health beliefs, change
• FH tells us about the genetic/environmental context in which the child’s illness and wellbeing unfolds
• FH is needed to interpret phenotype and genotype
• Doctor concern and recommendations can have impact on behaviors
Taking a good FH will be supplemented, not supplanted by genetic testing. Francis Collins, NCHPEG, 2006

10-20% of most common diseases related to +FH; accounting for majority of early adult disease. Yoon, 2006

FH may be the most effective public health tool to screen for familial cancer. Khoury, 2003

In cohort comparing DTC SNPS vs FH, (11.3%) were found to have additional potential genetic risks, including 5% whose FH were suggestive of hereditary cancer syndromes. Aiyar, 2012
Example direct-to-consumer report

Source: Genetics in Medicine, Volume 13, Number 2, February 2011
Outline

• Overview of FH
  – Talk it up – communication and information over time
  – Write it down – documentation in EHR from focused, problem-based hx to 3-generation pedigree
  – Pass it on – integrate in improved health

• What are our approaches in pediatrics?

• What instruments do you need in your FH toolkit?
What is FH?

• A communication and information tool with families across cultures
  – Foster rapport around family understanding
  – Recognize inheritance patterns
  – Demonstrate
    • Variation in disease expression
    • Reminder of those at risk
  – Emphasize medical documentation needs
  – Clarify misconceptions
  – Help with prevention, screening, case-finding and management
What are you doing about FH in your own family and pediatric work?

- Talking it up?
- Writing it down?
- Passing it on?
96% of Americans believe that family history is important to health. Yet, only about 30% have tried to collect and organize their family history information.
Lay of the Land

- Family trees important in most religions, legacies
- Genealogies - freedom, legal rights
- 2002 – CDC FH Initiative (HealtheCards, podcasts)
- 2004 – Surgeon General declares Thanksgiving FH Day
- 2006 – CDC Conference on pediatrics and FH
- 2008 – GINA signed
- 2009 – NIH conference on FH
- 2011 – Genetic Alliance FH project with FQHCs
- 2011 – AAP GPCI initiative
- 2012-13 – FH one of proposed menu (3/5) for stage 2 meaningful use (20% documented 1st relative)
ACCE Framework

• Analytic validity – Are FH reports accurate and reliable?

• Clinical validity – Are disease risk predictions that are derived from FH information accurate?

• Clinical utility
  – Does awareness of FH risk and targeted interventions affect disease outcome?
  – Was a follow-up plan/referral made and tracked in light of FH/clinical concerns?
FH in Primary Care – Does One Size Fit All? Wilson et al 2012

NO

Genetic case finding

• Target population
  – Clinical suspicion, pt. concern
• FH information
  – Depends on condition
• Other information
  – Generally less important
• Timing of use
  – Responsive to concerns, life stage
• Need for updating
• Linking with other tools
  – Clinical decision support
• Resources required
  – Valid risk criteria, time, confidence

Health promotion

– All, related to life course
– Can risk stratification be given?
– Important
– Periodic exam, opportunistic
– Effective behavior change interventions
– Emerging and variable
FH Tools Development and Evaluation Framework

• Broad and open-ended
• Checklists (EHR)
• Condition or guideline focused
• NOTE
  – General questions easy to answer “NO”
  – Systems review approach
  – Open-ended approach for family engagement
• Modular design – ask individuals re each family member, specific closed-ended items with systematic inquiries about conditions (Romitti 1997)
• Construct pedigree
• What is working or can work in your practice?
Goal: Tier risk
Who needs what?

Assessment: Family Hx
Risk Classification:
- Average
- Moderate (“Familial”)
- High/Genetic

Intervention:
- Standard prevention recommendations
- Personalized prevention recommendations
- Referral for genetic evaluation with personalized prevention recommendations
FH Needs of Pediatricians

- Family-centered communication
- Just-in-time (e.g. with acute/major problem) +/- prevention/health maintenance focus – with something serious, directly ask if anyone else in family has it
- Effective case finding and referral
- Safety and quality
- Risk tiering and reduction – What in your child’s family health history is a concern to you?
- Important for certain billing – pertinent FH for level 4, complete FH for level 5
So what? A 3 yo girl with neck “nodes”

- Erratic behavior
- Staying thin
- Thyroid nodule discovered
- + FH for thyroid/parathyroid cancer
- MEN2B -ret-oncogene (tyrosinase-kinase receptor) on 10q11.2 with >95% mutation at codon 918
- Current clinical trial of oral Vandetanib, a RET kinase, vEGFR and EGFR inhibitor
Diagnosis

• Remember many “severe” conditions are “rare”, but collectively common
  ~ 1 in 500 prevalence – neonatal sepsis, familial hypercholesterolemia, hypertrophic cardiomyopathy
  ~ For every 2 cases of SIDS, one case each of CF and NF
Index of Suspicion

• With negative FH, esp in small families, think AR conditions
  - Alpha 1-antitrypsin deficiency (1 in 484 Caucasians, 1 in 324 Hispanics)
  - Cystic fibrosis (1 in 17,000 African-Americans)

• Is consanguinity present?
  – Closer relatedness of ancestors > amount of shared genetic information
  – 1st cousins ~2X risk
FH Providing Value

• Health promotion programs
  – Healthy Eating and Activity Together (HEAT) obesity prevention

• Risk assessment tools
  – FIRM (1/2 page family index of risk for mood disorders) gave clinically meaningful discrimination of pediatric bipolar disorder (Algorta et al 2012)

• Testing algorithms
  – FH of hypertrophic cardiomyopathy - a key clinical predictor of a genetic diagnosis with direct clinical relevance, particularly in the pretest genetic counseling setting (Ingles et al 2013)
Does it make a difference?

- +FH of croup strongest risk factor for croup and its recurrence *Pruikkonen et al, Paed Peri Epi, 2009*

- +FH of ≥2 family members having asthma, atopy, or smoking ~3X risk for perioperative adverse broncho/laryngospasm events (p<0.0001) *von Ungern-Sternberg et al, 2008*

- Yes, after newborn screening – fewer instances of subsequent children dying/morbidity from screened conditions
Screening/prevention guidelines that include FH

• Challenges in pharmacogenomics – FH vs testing
• Spina bifida
  – Prevent recurrence with maternal folic acid
• Athletes
  – Sudden cardiac death, AHA
  – Serum lipids, NHLBI
Pediatric Care Goals

• Have an effective system to pay attention, sort, address

• Like Harry Potter
  – Get out from under the stairs, know FH
  – Study the chemistry, know some genetics
  – Sort, tier risk
  – Avoid toxic forces, don’t overpromise tests
  – Use power for good
Think of family history in quality improvement context

• What are you currently doing?
  – Which tool – EHR, paper, portal, other?
  – Who is doing – process?
• What is working well? Not?
• Time for a change, pilot?
• Can you create prompts? Family feedback?
  Team feedback?
Not easy yet, but what is?

Challenges

• Unknown relatives, adoptions
• Accuracy
• Takes time
• Fatalism
• Family communication
• Discrimination/stigmatization
• Duty to recontact

Responses

• Have to start somewhere, genetic testing may address, cultural awareness
• Specificities>sensitivities
• Family starts, update at visits, point of care tools (6/3 min:new/old by MD Acheson 2000; 15+ min Surgeon General tool Owens 2011)
• Genetic variation more typical
• Need to listen, share tools
• GINA, state laws
• Define responsibilities
Time for FH

• Tips for efficiency
  – Family completes at home or in waiting room
  – Use checklist or other tools
  – Add to problem list, other tracking system
  – Have a plan for updates
  – Referral/testing processes in place
<table>
<thead>
<tr>
<th>Conditions</th>
<th>Allergies 1</th>
<th>Congenital hip dislocation</th>
<th>Intellectual disability 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergies, food 1</td>
<td>Depression 4</td>
<td>Migraines, headaches 5</td>
<td></td>
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<tr>
<td>Alzheimer disease or other form of dementia 6</td>
<td>Developmental Delay 3</td>
<td>Neural tube defects 7</td>
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<tr>
<td>Anxiety 4</td>
<td>Eczema 1.8</td>
<td>Obesity 4</td>
<td></td>
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<tr>
<td>Asthma 1</td>
<td>Fragile X syndrome 9</td>
<td>Spina bifida 7</td>
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<tr>
<td>Autism spectrum disorder 10</td>
<td>Intellectual disability 3</td>
<td>Thyroid disease 11</td>
<td></td>
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<tr>
<td>Congenital deafness/hearing loss 12</td>
<td>Kidney disease 4</td>
<td></td>
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</tbody>
</table>
Life course – Bright Futures

• Prenatal
  – Choose a FH tool and review
  – If mother with strong FH allergies, emphasize breastfeeding

• Newborn
  – FH hearing loss, congenital cataracts, retinoblastoma, metabolic-genetic diseases

• Infancy
  – Review high cholesterol, obesity early CV disease, type 2 diabetes
Life course – Bright Futures

• Childhood
  – With anxiety and depression/suicide, ask FH
  – With FH congenital renal disease, do BP <3yrs
  – With FH permanent hearing loss, continue hearing screening
  – With FH CAD ≤55 y, MI, angina, vascular disease, sudden cardiac death, chol ≥240, screen for dyslipidemia (newer recommendations available)
GPCI Quality Improvement Project

• Who?
  – 13 primary care practice teams across the U.S.

• What?
  – Testing tools and strategies for delivery of genetics in primary care

• Goals:
  – Collect multigenerational FH for all patients aged 0-21 as part of the health supervision visit
  – Improve care and management of patients with genetic conditions
AAP – GPCI-QIP General FH Elements

• Include parents, brothers, sisters, aunts, uncles, first cousins, grandparents, (nephews, nieces)
• Medical conditions running in family (>2 relatives)
• Ethnicity
• Consanguinity
• Parental (patient) concerns re FH
• Incomplete FH knowledge (egg adoption, estrangement)
AAP – GPCI-QIP General FH Elements

Any relative told they have (indicate who, what):
• Structural or sensory birth defects
• Cancer (<50 yrs, specify type)
• Carrier of genetic condition
• Clotting, bleeding, or blood disorder
• DD, ID, ASD, LD, received special education services
• Early, sudden, unexplained, or unexpected death (< 50 yrs, give details)
• Heart attack (<55 yrs in men, <65 yrs in women)
• Known genetic condition
• Multiple miscarriages/stillbirths
• Seizures
GPCI FH Tools

Comprehensive FH Tools for New Patients

- Pediatric Genetic Screening Questionnaire
- GPCI Family History Grid
- GPCI Family History Checklist
Stay Tuned for New FH Tools!

• Final product – paper FH tool from GPCI-QIP
  – Released in December 2013
  – Use questions to modify patient portal questionnaire and EHR screens

• Electronic Pediatric FH Tool
  – Developed by NCHPEG, March of Dimes, and Partners Healthcare
  – Available for use fall 2013
  – Tablet-based with patient-entered FH questionnaire
  – Also embeds Clinical Decision Support and pedigree
### GPCI FH Grid

<table>
<thead>
<tr>
<th>Mother’s Side</th>
<th>Child’s Grandmother</th>
<th>Child’s Grandfather</th>
<th>Child’s Aunts</th>
<th>Child’s Uncles</th>
<th>Child’s Cousins</th>
</tr>
</thead>
<tbody>
<tr>
<td>☑️ If living</td>
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<tr>
<td>Structural birth defects (ex: congenital heart disease, spina bifida, extra or missing fingers, clubfeet)</td>
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<tr>
<td>Sensory birth defects (ex: congenital deafness, congenital blindness)</td>
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</tbody>
</table>

Grid examines the Child’s Immediate Family – Parents and siblings, and Mother’s side and Father’s side, respectively, in three separate grids per the conditions included in the Family History Checklist on slide 41.
### Biological Family History

*DK = don’t know*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Yes</th>
<th>No</th>
<th>DK</th>
<th>Who</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Childhood hearing loss</td>
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<td>Nasal allergies</td>
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<td>Asthma</td>
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<td>Tuberculosis</td>
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<td>Heart disease (before 55 years old)</td>
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<td>High cholesterol/related cholesterol medication</td>
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<td>Anemia</td>
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<td>Bleeding disorder</td>
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<td>Dental decay</td>
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<tr>
<td>Cancer (before 55 years old)</td>
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</tbody>
</table>

(Biological Family History continued on back side.)

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### Biological Family History (Continued from front side)

*DK = don’t know*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Yes</th>
<th>No</th>
<th>DK</th>
<th>Who</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver disease</td>
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<td>Kidney disease</td>
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<tr>
<td>Diabetes (before 55 years old)</td>
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<td>Bed-wetting (after 10 years old)</td>
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<td>Obesity</td>
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<td>Epilepsy or convulsions</td>
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<tr>
<td>Alcohol abuse</td>
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<tr>
<td>Drug abuse</td>
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<tr>
<td>Mental illness/depression</td>
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<tr>
<td>Developmental disability</td>
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<tr>
<td>Immune problems, HIV, or AIDS</td>
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<tr>
<td>Tobacco use</td>
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<tr>
<td>Additional family history</td>
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</tr>
</tbody>
</table>

*Initial History Questionnaire*
Tips to Improve Patients’ Understanding

• Improve patient health literacy and define family relationships
  – Use “brothers and sisters” instead of siblings
  – “Mom’s/Dad’s side” instead of maternal and paternal
  – Define relationships in terms of relation to child and parent – aunt is the “mom’s sister”
  – First cousins once removed are 2 people for whom a first cousin relationship is one generation removed. The child of ones’ first cousin; also the first cousin of one’s parents
  – Tool development is an iterative process! Collect feedback on your tool from your patients
Patient Communication Strategies

• Notice clues to potentially inaccurate or missing health information. For example, there are no reported cases of cancer in the family

• If the patient seems doubtful of recalling the exact condition, recommend they communicate with their family to obtain accurate information

• Exercise compassion when discussing the FH
  – Avoid the terms, "positive", "negative", and "uneventful"
  – Use the term "condition" instead of "disease"
  – Soften your questions with phrases such as, "Is there a possibility of...?"
I’ve Collected it, Now What?

• Discuss FH with patient/families
  – Did they have any questions when completing the form?

• Ask follow-up questions for positives

• Review red flags in the FH, decide what to do

• Update FH annually
  – Parent/family reviews information previously provided
  – Any new diagnoses or deaths?
Follow-up questions on cancer FH

- Type
- Age at diagnosis
- Age at death (esp. if dx. Age not known)
  - !<50 years
- Others with same/related cancers
SCREEN Mnemonic

• Some Concerns – about conditions running in the family?
• Reproduction – any problems with pregnancy, infertility, or birth defects in the family?
• Early disease, death, or disability?
• Ethnicity – How would you describe or where were your parents born?
• Nongenetic – Any other risk factors/nonmedical conditions running in the family?
SIDE questions - focused

Mother’s side

Any Similar problems?
Any Inherited conditions in family?
Any unexplained Deaths < 50 yoa?
Any Extraordinary lab tests/reactions?

Father’s side
Risk stratification

High Risk:
1. Premature disease in a 1\textsuperscript{st}o relatives, (sibling, parent or child)
2. Premature disease in a 2\textsuperscript{nd}o relative (CAD only)
3. Two affected 1\textsuperscript{st}o relatives
4. One 1\textsuperscript{st}o relative with late or unknown disease onset and an affected 2\textsuperscript{nd}o relative with premature disease from the same lineage
5. Two 2\textsuperscript{nd}o maternal or paternal relatives with at least one having premature onset of disease
6. \( \geq 3 \) affected maternal or paternal relatives
7. Presence of a “moderate risk” family history on both sides of the pedigree
Risk stratification

Moderate risk:
1. One 1\textsuperscript{st} relative with late or unknown onset of disease
2. Two 2\textsuperscript{nd} relatives from the same lineage with late or unknown disease onset

Average risk:
1. No affected relatives
2. Only one affected 2\textsuperscript{nd} relative from one or both sides of the pedigree
3. No known family history
4. Adopted person with unknown family history

Scheuner et al., Am J Med Genet 1997; 71:315-324
Recognizing family risk

- Family history of known genetic disorder
- Multiple affected family members with same or related disorders
- Earlier age at onset of disease than expected
  - Breast, ovarian, endometrial cancer < 50 yrs (premenopausal)
  - Colon and prostate cancer < 50 yrs
  - Stroke and noninsulin-dependent diabetes < 50 yrs
  - Dementia < 60 yrs
  - Coronary artery disease < 55 yrs males, < 65 yrs in females
- Sudden cardiac death in a person who seemed healthy
- Multifocal or bilateral occurrence in paired organs
- Ethnic predisposition to certain genetic disorders
Asking the Right Questions

“The Rule of Two/Too”  Chen, Saul 2013

• TOO tall
• TOO short
• TOO early
• TOO many
• TOO young
• TOO different

• TWO tumors
• TWO generations
• TWO in the family
• TWO birth defects
# Examples of Genetic Disorders Seen in Specific Ethnic and Racial Groups

Chen, Saul 2013

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Genetic Disorder</th>
<th>Inheritance Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>Sickle cell disease, G6PD</td>
<td>AR, XLR</td>
</tr>
<tr>
<td>Amish/Mennonite</td>
<td>MSUD, EVC, CHH, GA1</td>
<td>All AR</td>
</tr>
<tr>
<td>Ashkenazi Jewish</td>
<td>TSS, Canavan, Gaucher Type 1, BRCA1/2, FD, NP</td>
<td>AR and AD (BRCA1/2)</td>
</tr>
<tr>
<td>Finnish</td>
<td>Hered nephrosis, CHH, infantile neuronal CL</td>
<td>AR</td>
</tr>
<tr>
<td>French Canadian</td>
<td>Tyrosinemia, TSS, cystinosis</td>
<td>AR</td>
</tr>
<tr>
<td>Mediterranean</td>
<td>Beta thal, G6PD, sickle cell</td>
<td>AR and XLR (G6PD)</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>Beta thal, FMF</td>
<td>AR</td>
</tr>
<tr>
<td>Puerto Rican</td>
<td>Hermansky-Pudlak syndrome</td>
<td>AR</td>
</tr>
<tr>
<td>Southeast Asian</td>
<td>Alpha and Beta thal</td>
<td>AR</td>
</tr>
<tr>
<td>Portuguese</td>
<td>MJD</td>
<td>AR</td>
</tr>
</tbody>
</table>
Electronic FH Tools

• My Family Health Portrait
• Family Health History Record Keeper
• Genetic Alliance - Does it Run in the Family?
• Family Tree, National Society of Genetic Counselors
• NCHPEG Prenatal and Pediatric (coming soon) tools
• Use the patient portal of your EMR
Electronic Tools

My Family Health Portrait
A tool from the Surgeon General

Using My Family Health Portrait you can:
- Enter your family health history.
- Print your family health history to share with family or your health care worker.
- Save your family health history so you can update it over time.

Talking with your health care worker about your family health history can help you stay healthy!

Learn more about My Family Health Portrait

Create a Family Health History

En Español

Use a Saved History

Em Português

In Italiano

Image courtesy of https://familyhistory.hhs.gov/fhh-web/home.action
Genetic Red Flags

• Multiple affected members
• Earlier than expected age at onset of disease
• Condition in the less-often-affected sex
• Disease in the absence of known risk factors
• Ethnic predisposition to certain genetic disorders
• Close biological relationship between parents (consanguinity)
Indications When to Consider Referral

- Significant neurological/developmental problem
- Congenital anomaly – heart, diaphragmatic hernia, renal agenesis, TE fistula, limb-bone malformation, dysmorphic features
- Growth problems
- Strong positive FH for risk stratification & recurrence
- Other – abnormal skin findings, nonviral cardiomyopathy, clotting abnormalities, bilateral-multifocal malignancies, multiple miscarriages, infertility
Bottom line

• Talk it up, write it down, pass it on
• Improve forms/processes you have in place
• Discuss FH with other preventive health topics
• Incorporate other family members in discussion
• Do near birth or get from ob, update annually
To more healthy birthdays!

KEEP CALM AND RESEARCH YOUR FAMILY HISTORY : )
Questions
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Thank you for your participation!

For more information, please contact
Lindsay Wilson
lwilson@aap.org
847/434-7612

www.GeneticsinPrimaryCare.org
Join Us for Our Next Webinar!

Overview of Genetic Testing and Screening

Date: Tuesday, October 8, 2013 12pm Eastern
Faculty: Leah Burke, MD, FAAP, FACMG

Registration is now open!
https://www3.gotomeeting.com/register/989190834