Medical Family History: Tools For Your Practice

National Coalition for Health Professional Education in Genetics

National Society of Genetic Counselors

Training Course in Sexual and Reproductive Health Research

Geneva 2011

Learning Objectives

After viewing this presentation, one should be able to:

- List three benefits of taking family history in medical practice
- Create a pedigree using standard symbols
- Identify five genetic red flags
- Know how to locate family history tools
- Know how to locate a genetics professional
- Use the core competencies to interpret family histories in case examples

Why Family History?

- **Single-gene disorders**:

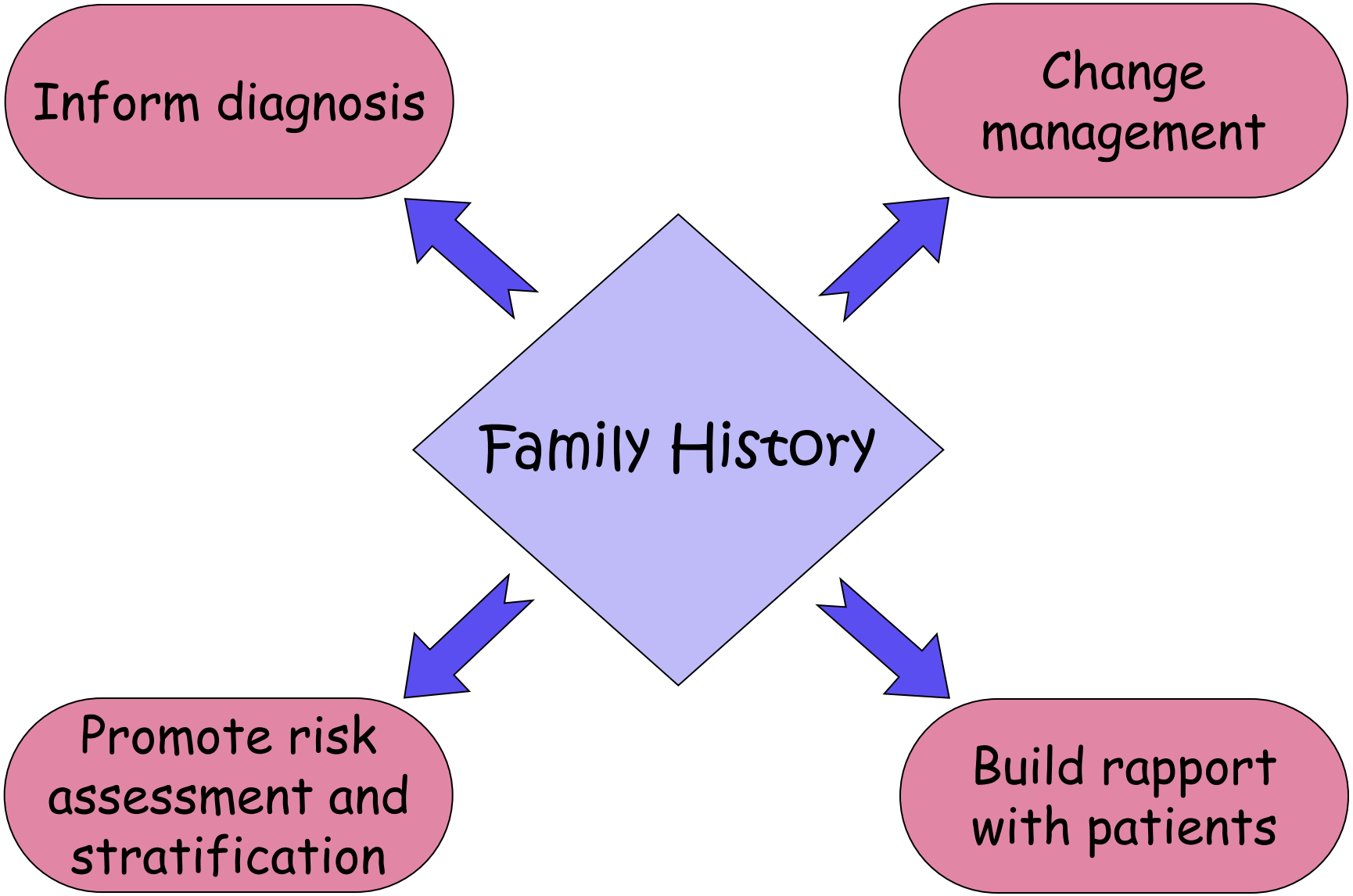
  Knowledge of family history can aid in the diagnosis and treatment of rare single-gene disorders such as cystic fibrosis, fragile X syndrome, Huntington disease, or familial hypercholesterolemia.

- **Common, complex diseases**:

  Family history has been shown to be a major risk factor for many chronic diseases such as cardiovascular disease, cancer, mental illness, and asthma.

  ⇨ Family history may be the primary risk factor!

Why Family History?



Prioritizing Information

Comprehensive vs. targeted family history

Comprehensive

- General healthcare setting
- Elicit general health information about relatives
  1) Major medical concerns
  2) Chronic medical conditions
  3) Hospitalizations, surgeries
  4) Birth defects
  5) Mental retardation, learning disabilities, developmental delay

Targeted

- Specialized clinical setting or evaluation for specific concerns
- Specific information about the condition of concern

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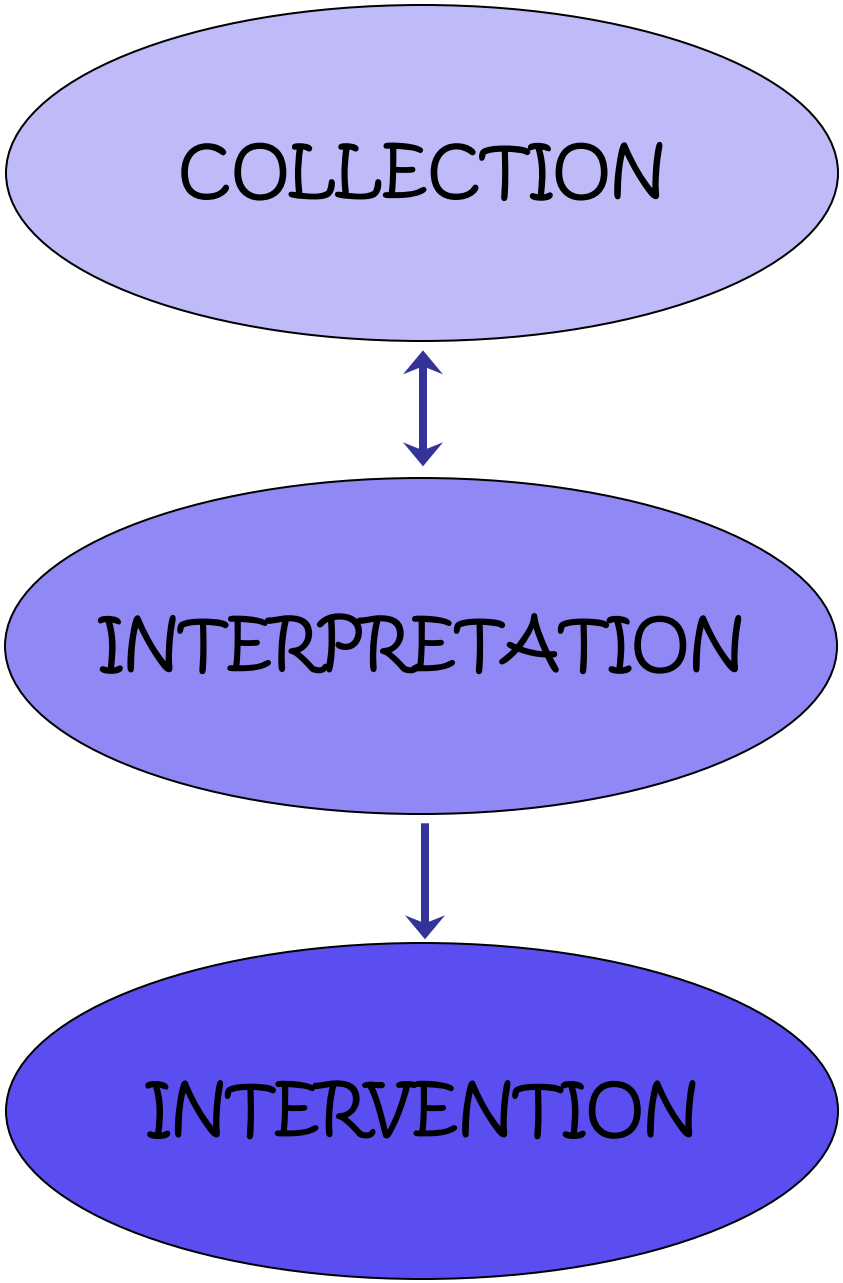
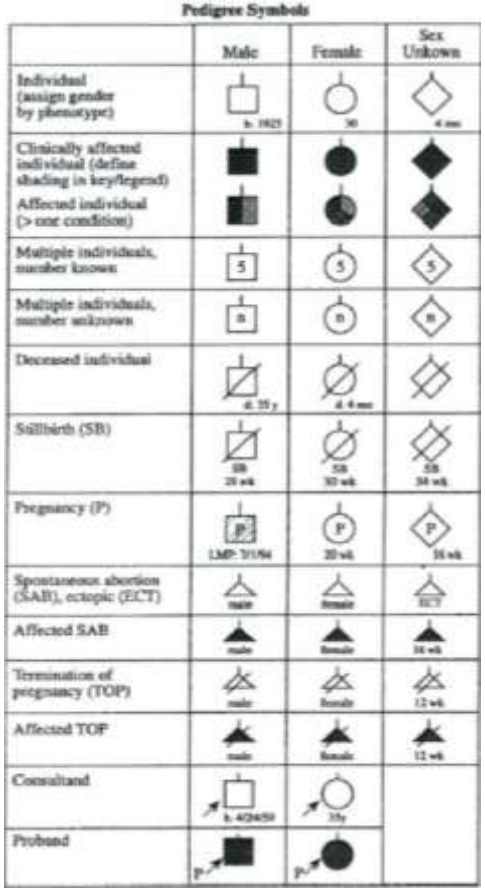
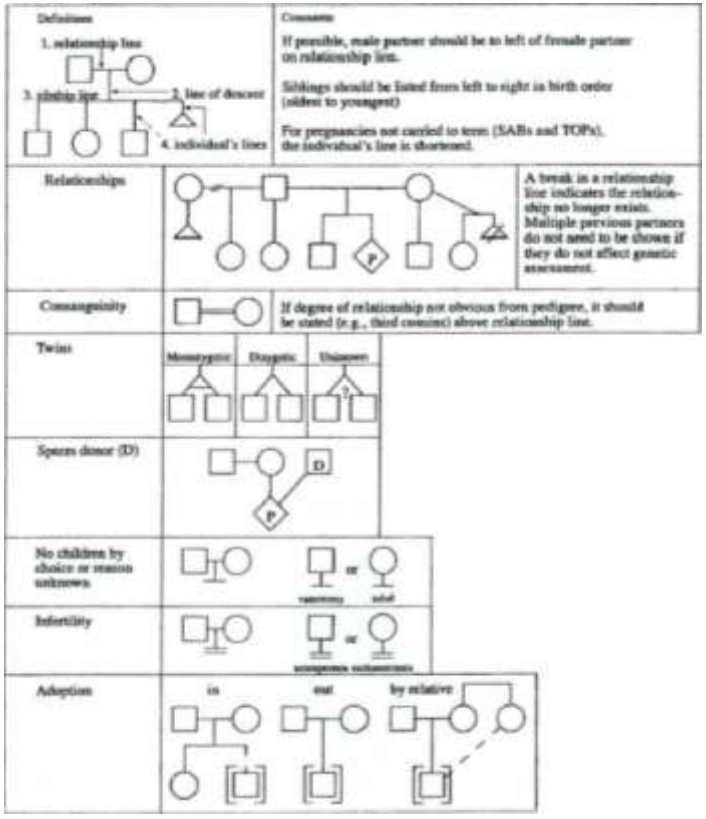


Collection

1) Recognize, understand, and use standard pedigree symbols





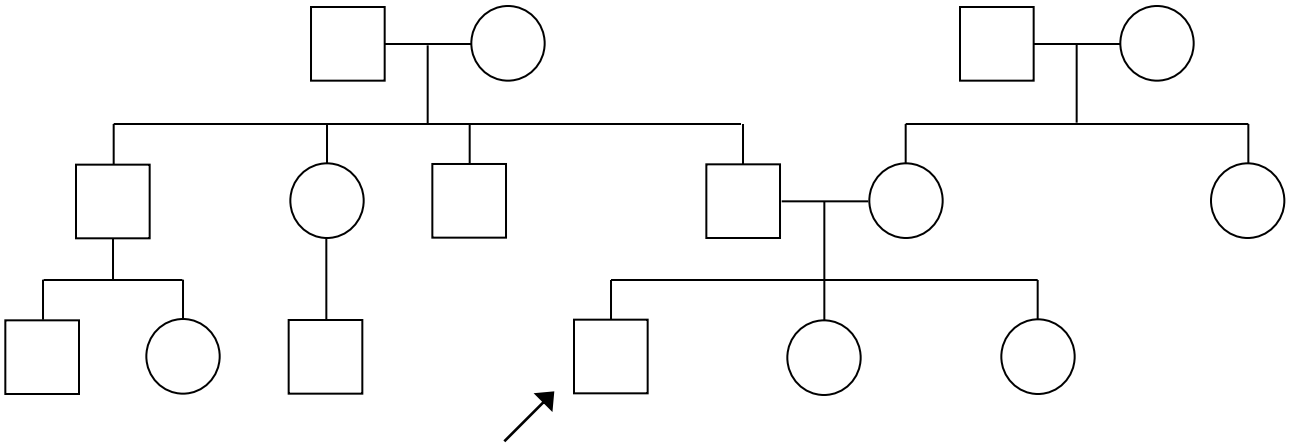
Bennett, et al. (1995). Recommendations for standardized human pedigree nomenclature. *Am J Hum Genet, 56*(3), 745-52.

Collection

2) Produce at least a three-generation pedigree that includes:

- Identification of the patient

  Identify the patient, or **consultand**, with an arrow

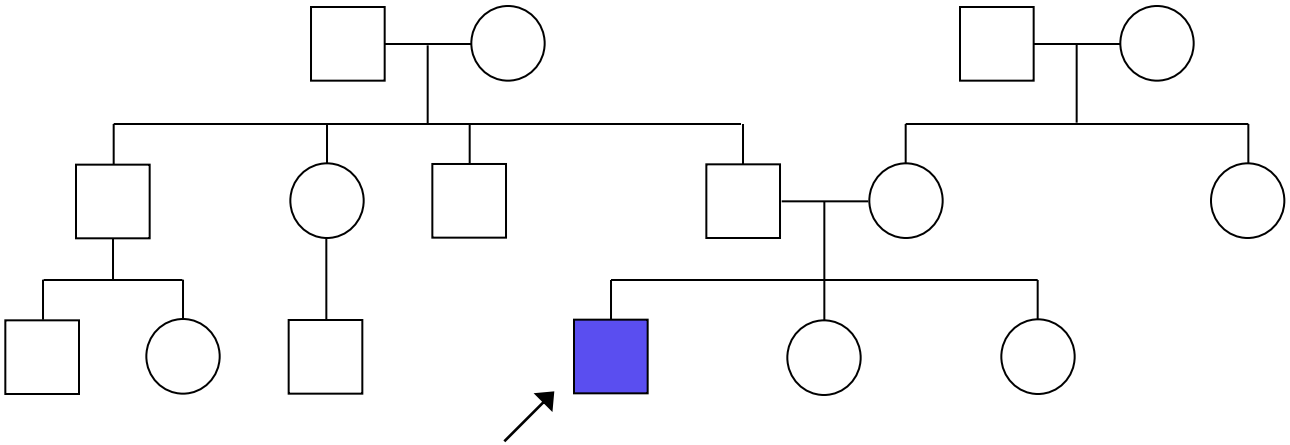


Collection

- Identification of the **proband**:

The **proband** is the affected individual who brings the family to medical attention

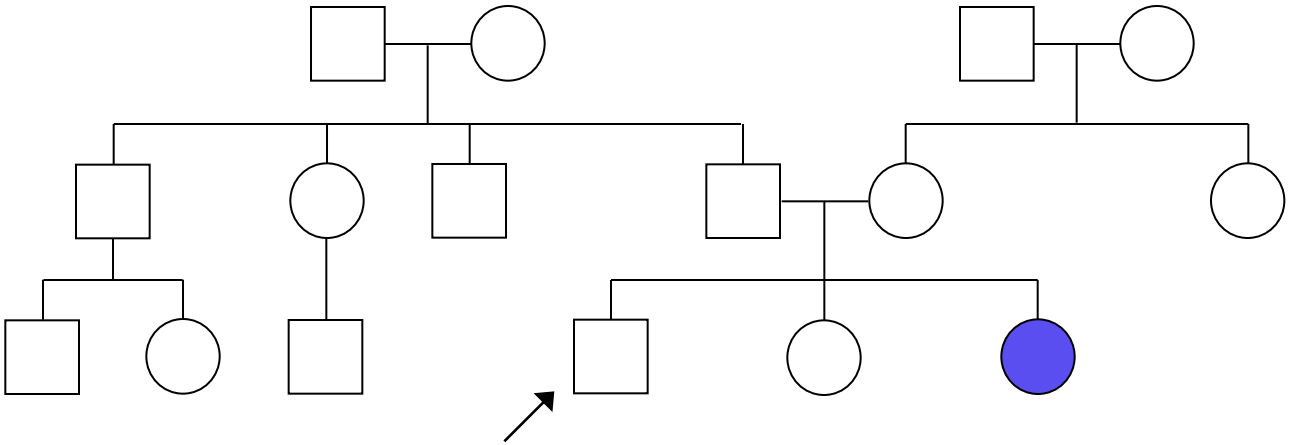
(A **consultand** is often also a **proband**)



Collection

- When the **proband** is not the **consultand**:

In this case, the patient's sister is the first person to bring the family to medical attention.



Collection

2) Produce at least a three-generation pedigree that includes:

- Patient's first-, second-, and third-degree relatives
- Information on maternal and paternal relatives
- Representation of "full" from "half" relationships
  example: children with same or different partner
- Affected and unaffected relatives

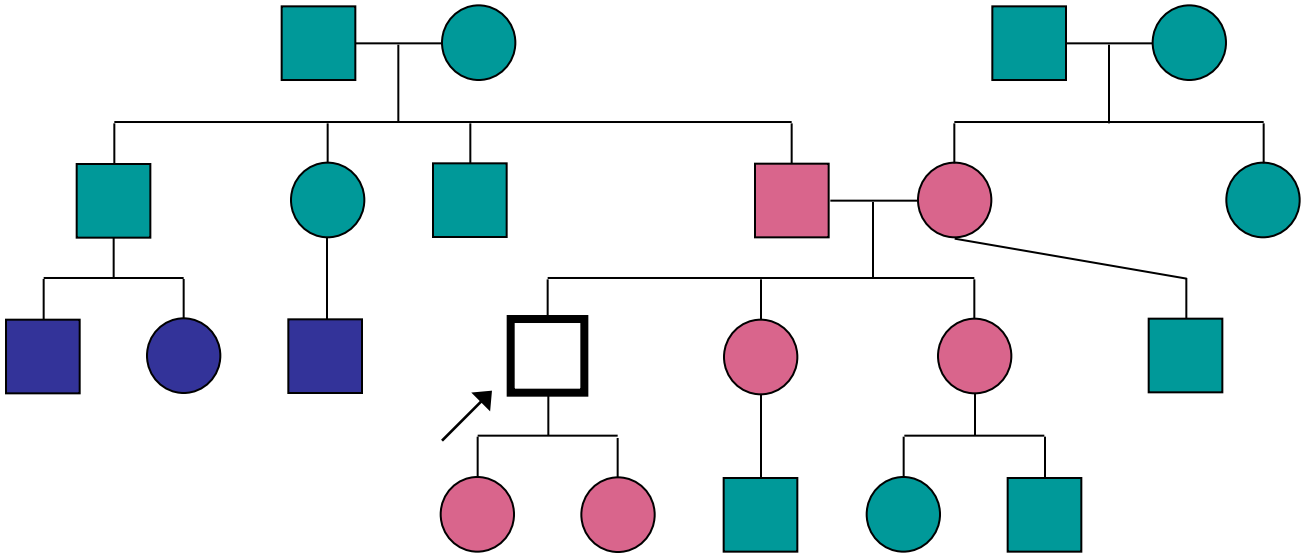
Collection

2) Produce at least a three-generation pedigree that includes:

- Identification of the historian, or person providing the information
  - May be the patient or someone else, such as a parent
- Date of collection (or date of update), and name of collector (or updater)
- Legend or key, if symbols are used to designate disease

Collection

Degrees of Relationship



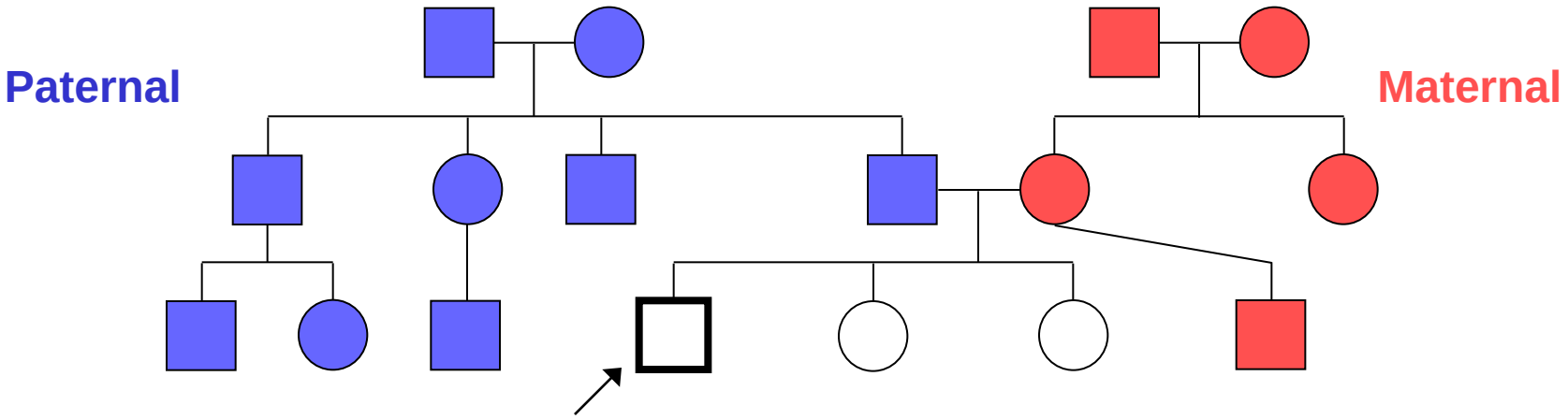
First-degree relatives: parents, siblings, children

Second-degree relatives: half-siblings, aunts, uncles, grandparents, nieces & nephews

Third-degree relatives: first cousins

Collection

Maternal and paternal relatives



Collection

3) Elicit the following information for individuals represented in pedigree as required for clinical indications:

- Age, birth date, or year of birth
- Relevant health information
- Diagnosis, age at diagnosis
- Age at death, or years of birth/death
- Cause of death
- Ethnic background for each biological grandparent

Adapted from: Bennett, R.L. (1999). *The Practical Guide to the Genetic Family History*. New York: Wiley-Liss.

Collection

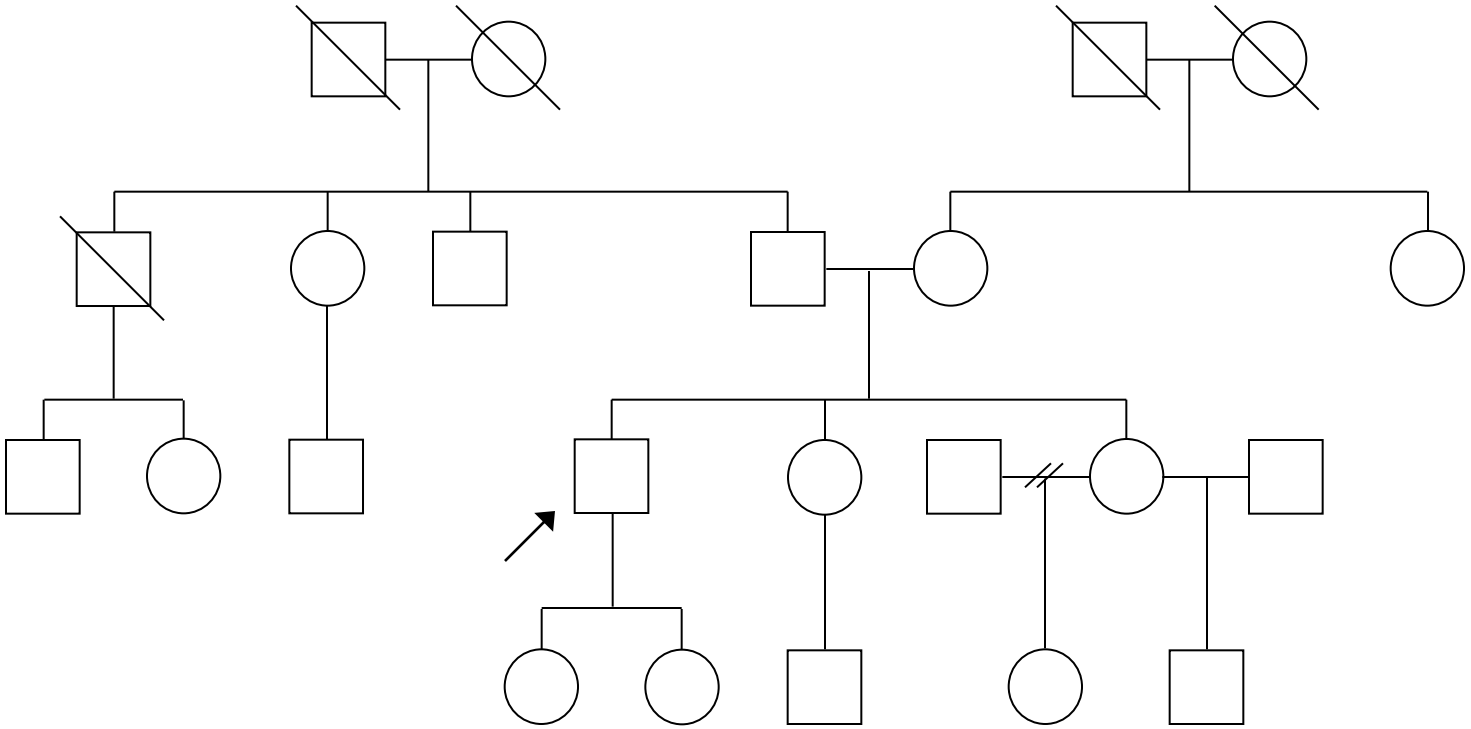
3) Elicit the following information for individuals represented in pedigree as required for clinical indications:

- Infertility, or no children by choice
- Consanguinity
- Pregnancies
- Pregnancy complications (note gestational age)
  - Miscarriages
  - Stillbirths
  - Ectopic pregnancies
  - Pregnancy terminations
  - Preterm birth
  - Preeclampsia
  - Bleeding/clotting complications

Adapted from: Bennett, R.L. (1999). *The Practical Guide to the Genetic Family History*. New York: Wiley-Liss.

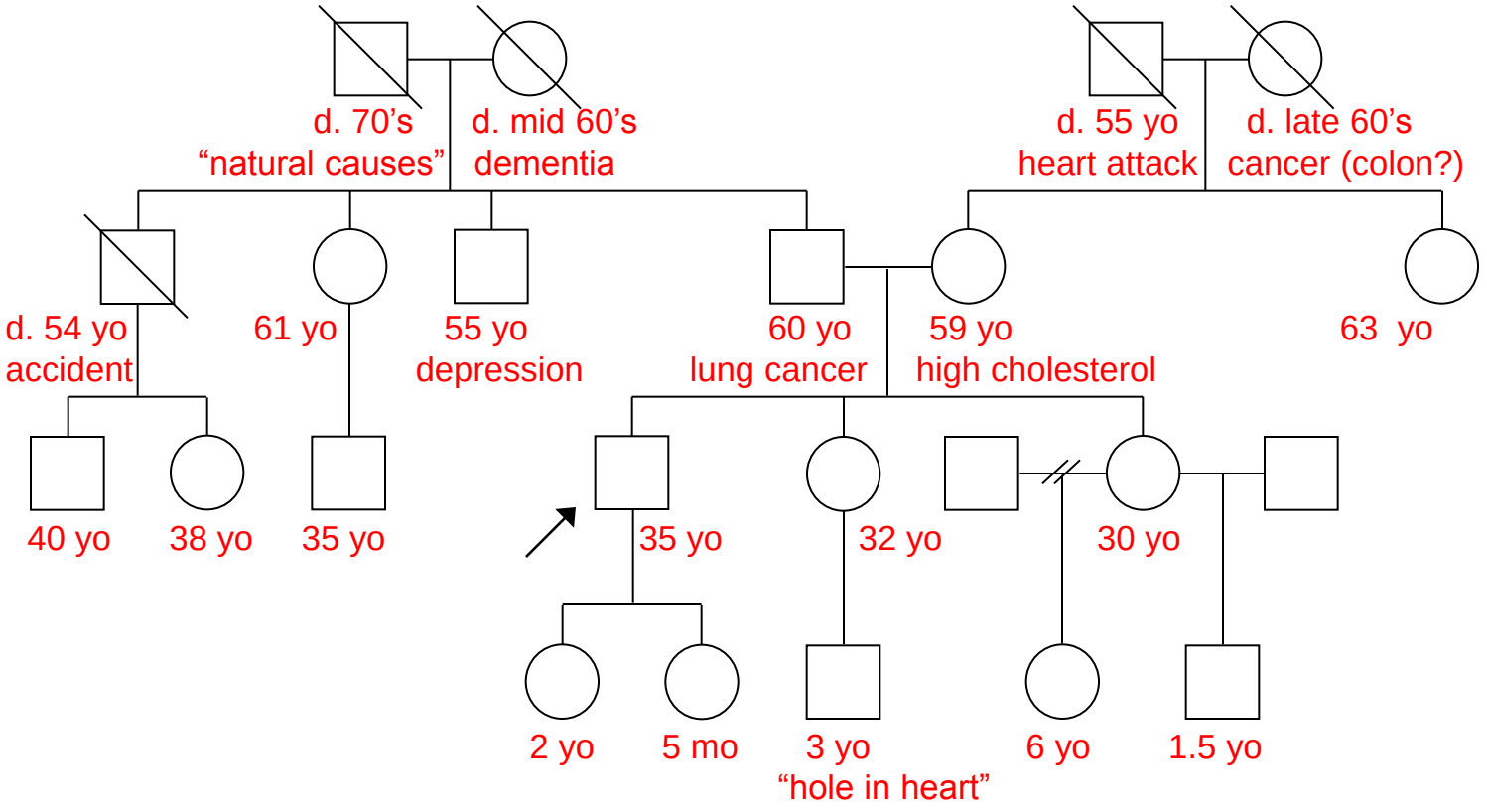
Collection

- Identification of patient
- Patient's first-, second-, and third-degree relatives
- Information on maternal and paternal relatives



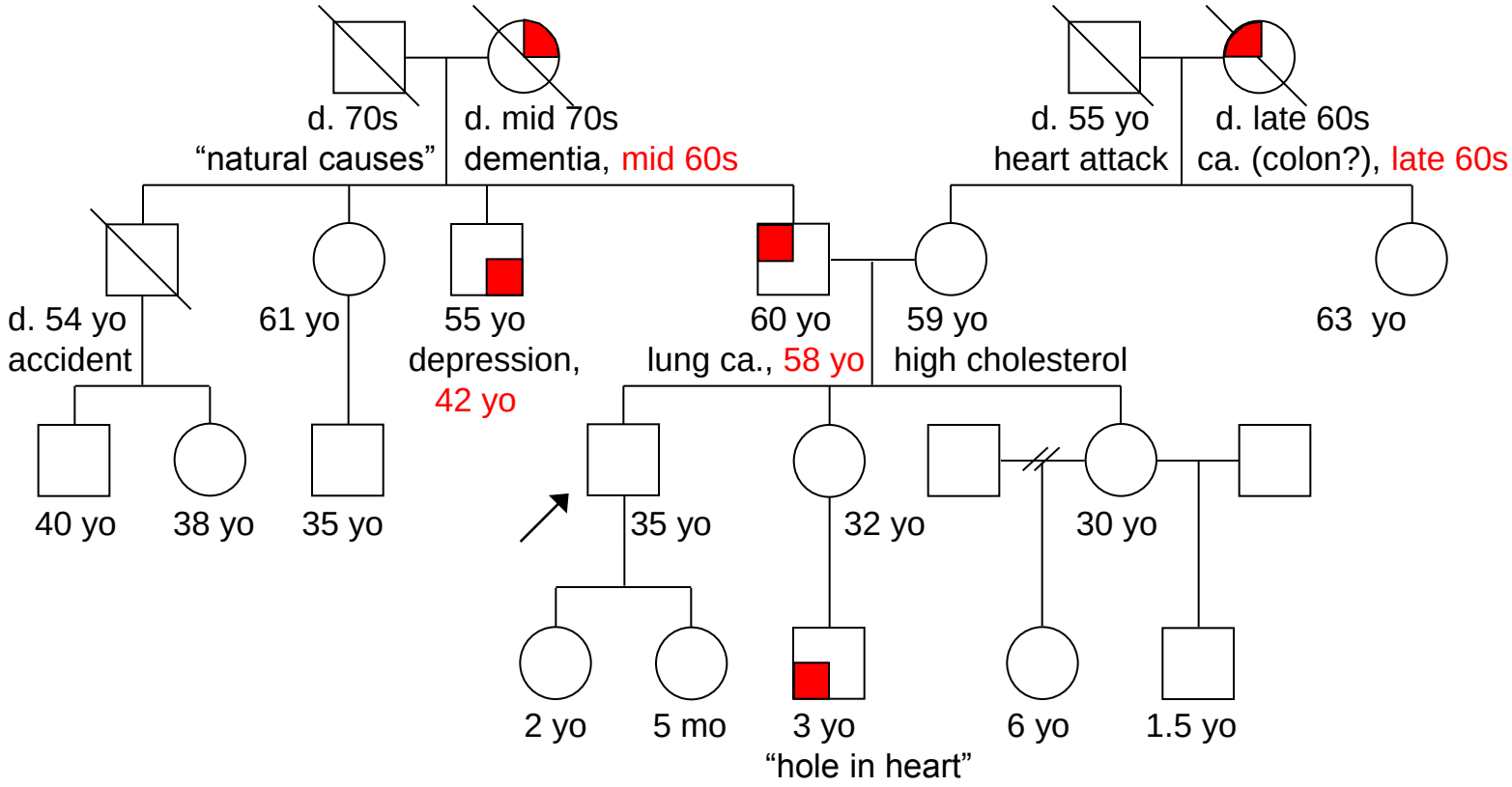
Collection

- Degree of relationship
  - Distinguish “full” from “half” relationships
- Age, birth date, or year of birth
- Relevant health information
- Age at, or year of death
- Cause of death



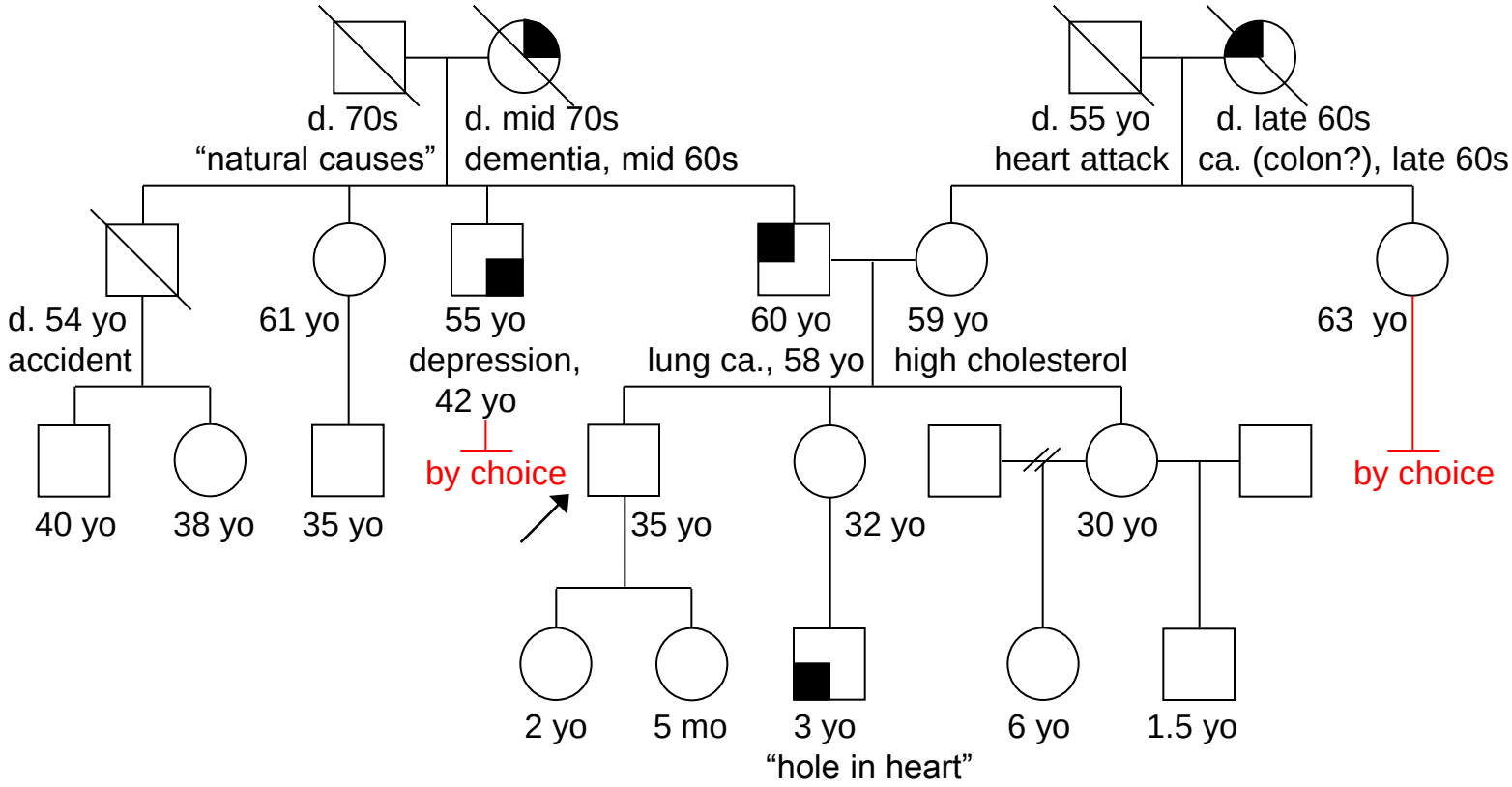
Collection

- Diagnosis, age at diagnosis
- Affected and unaffected individuals



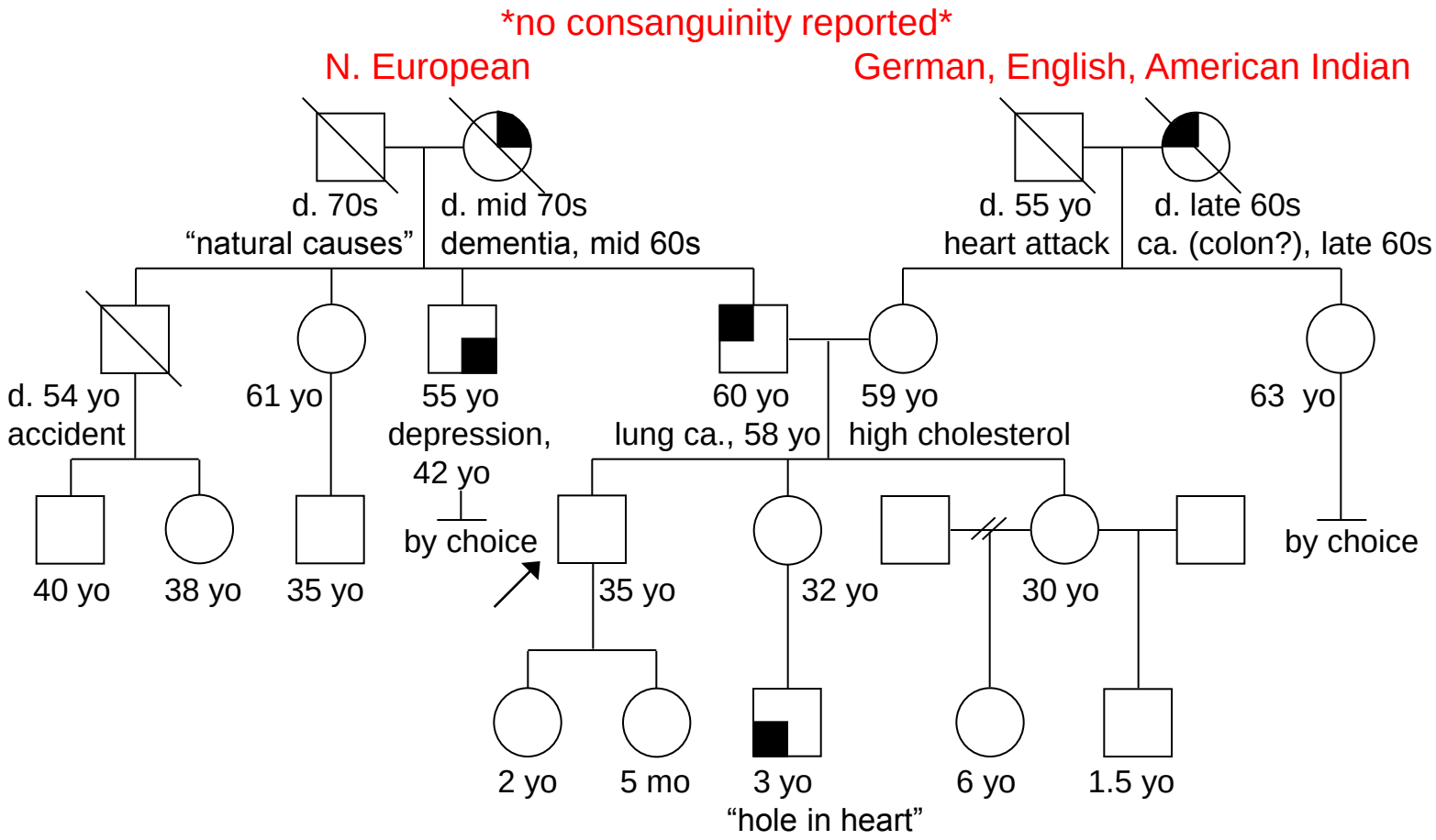
Collection

- Pregnancies
- Pregnancy complications (note gestational age)
- Infertility, or no children by choice



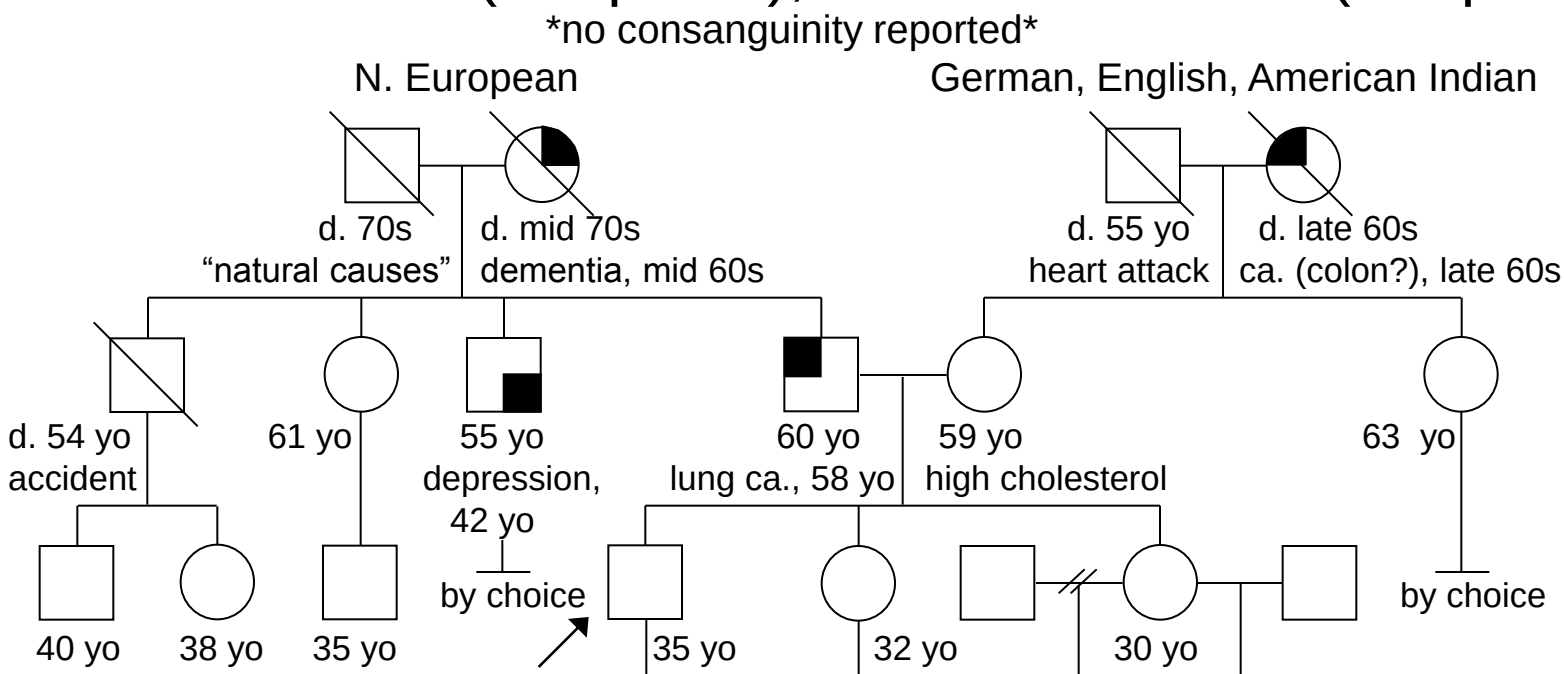
Collection

- Ancestral background for each biological grandparent
- Consanguinity



Collection

- Legend or key, if symbols are used to designate disease
- Date of collection (or update), name of collector (or updater)



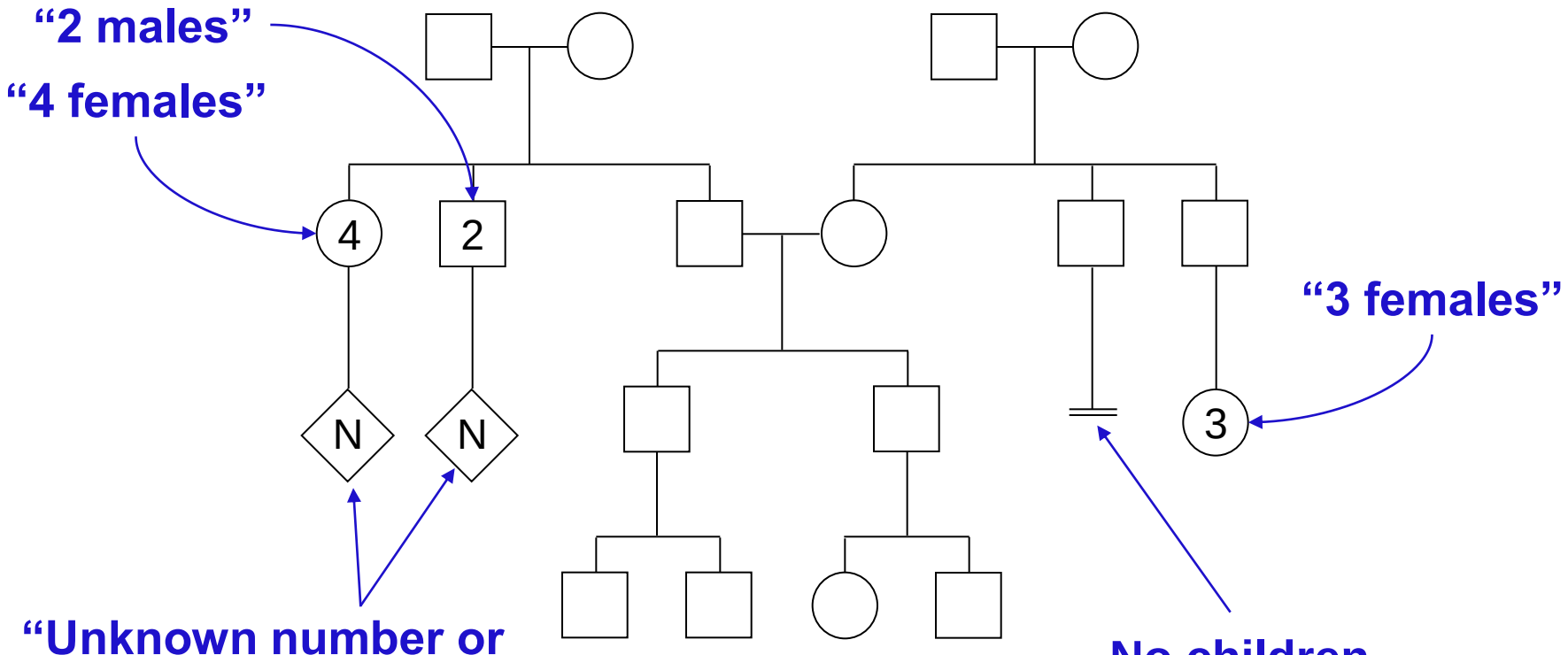
Key:

- dementia
- cancer
- depression
- born with "hole in heart"

Collected by: Jane Doe

Collected on: August 20, 2006

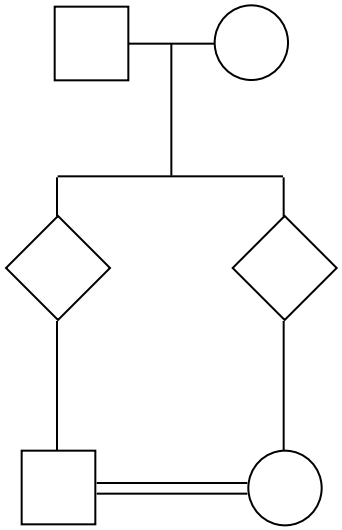
Additional Standard Pedigree Symbols



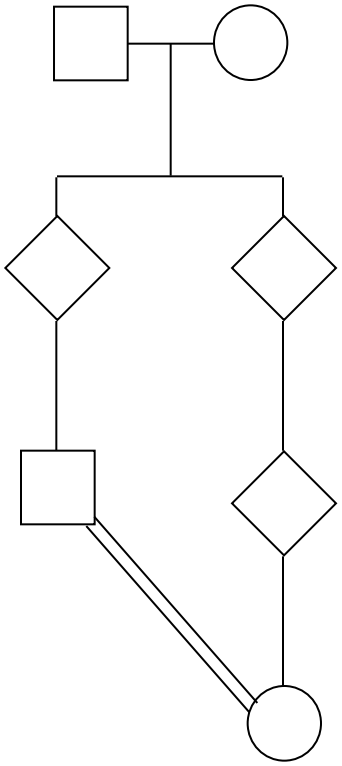
Bennett, et al. (1995). Recommendations for standardized human pedigree nomenclature. *Am J Hum Genet, 56*(3), 745-52.

Consanguinity: Relationships

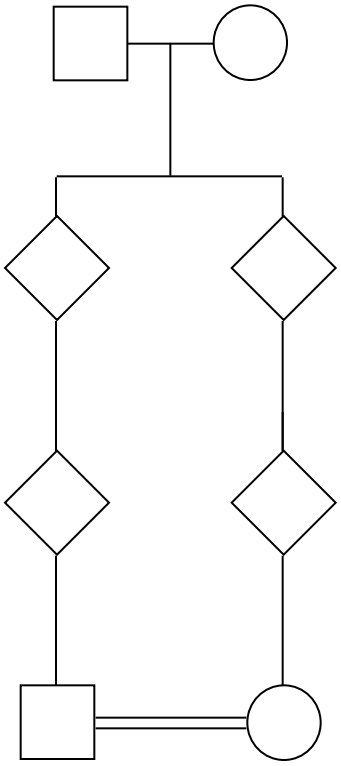
First cousins



First cousins once removed

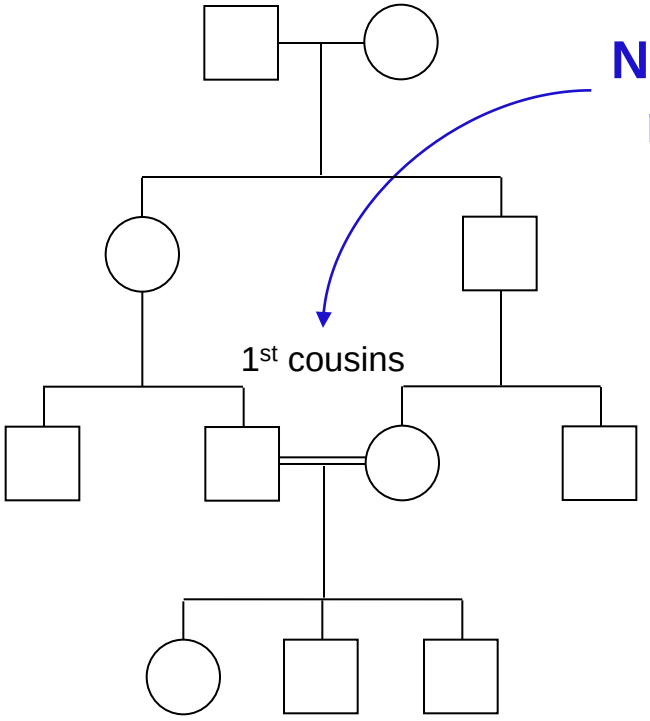


Second cousins



Bennett, R.L. (1999). *The Practical Guide to the Genetic Family History*. New York: Wiley-Liss.

Consanguinity: An Example



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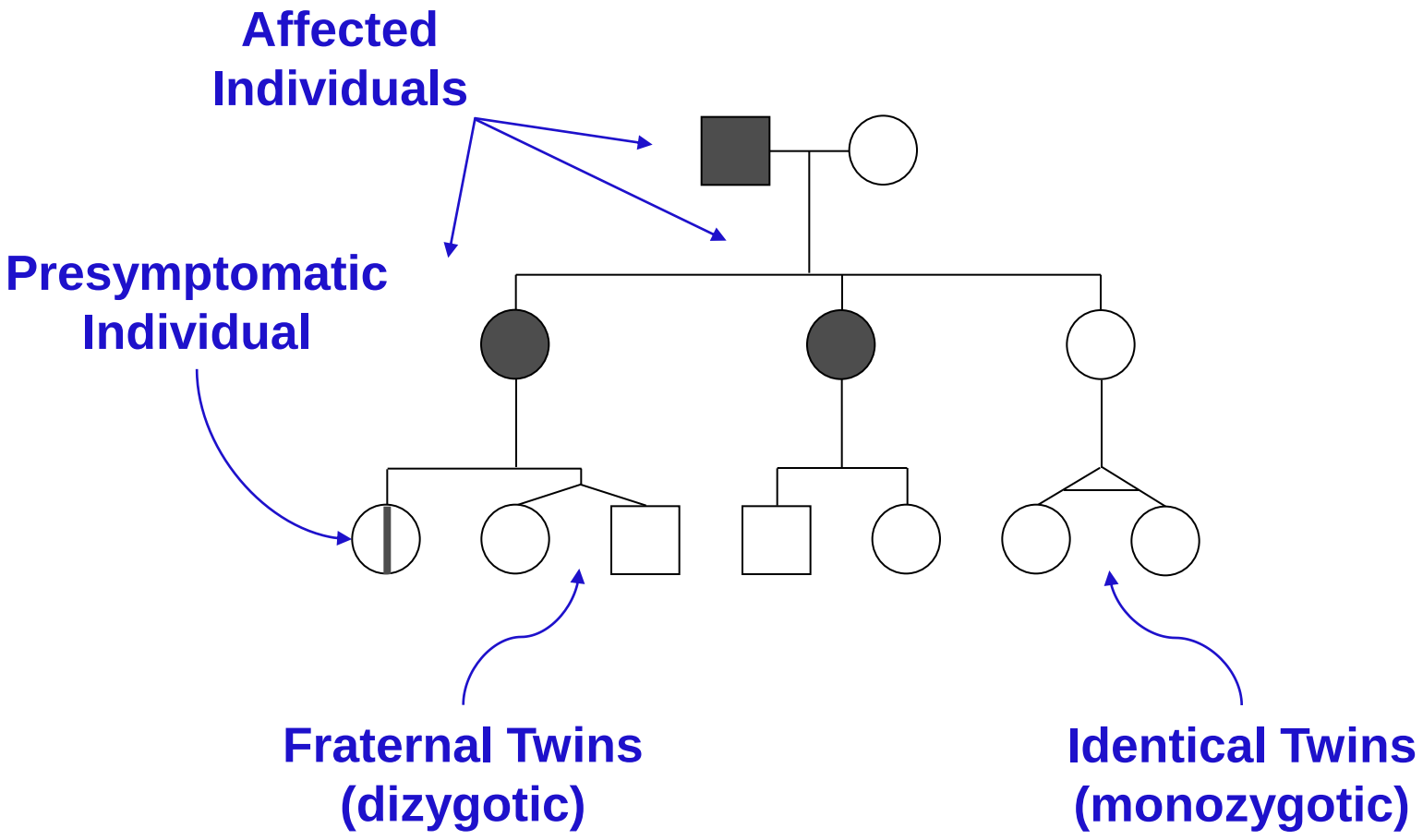

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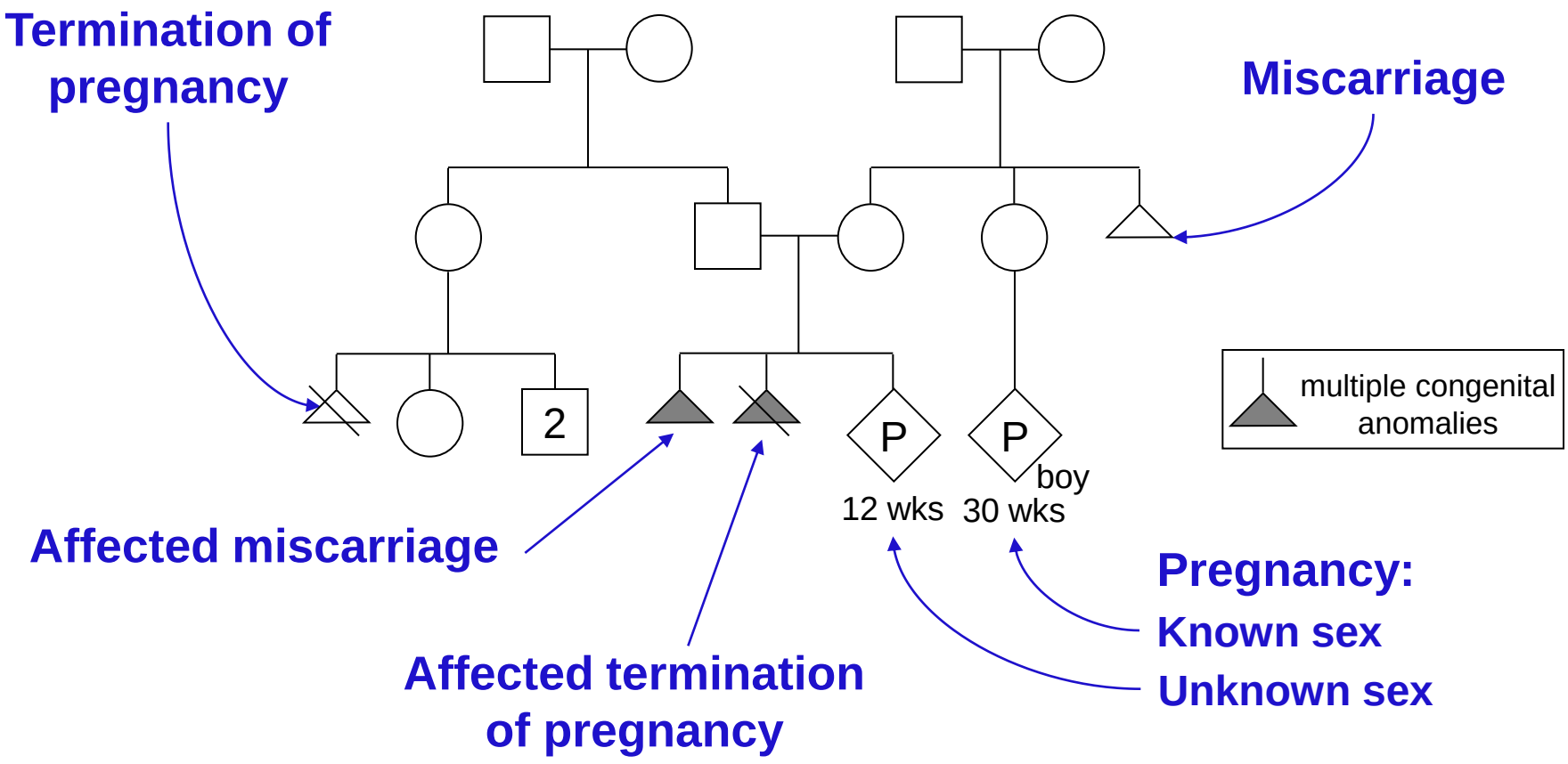

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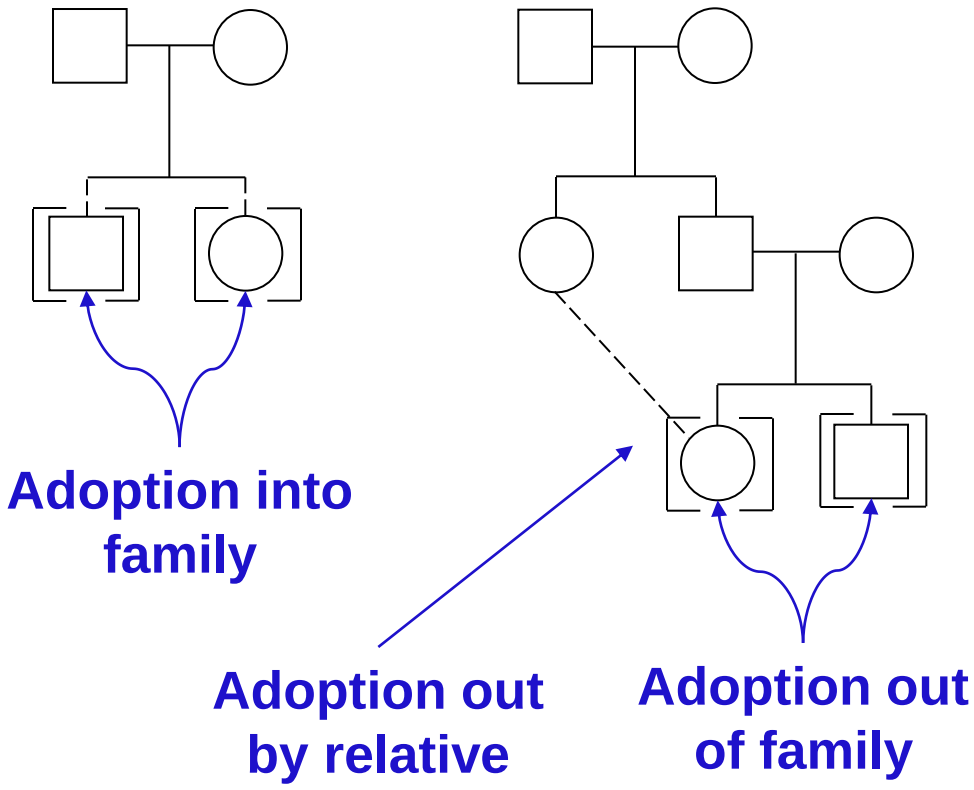

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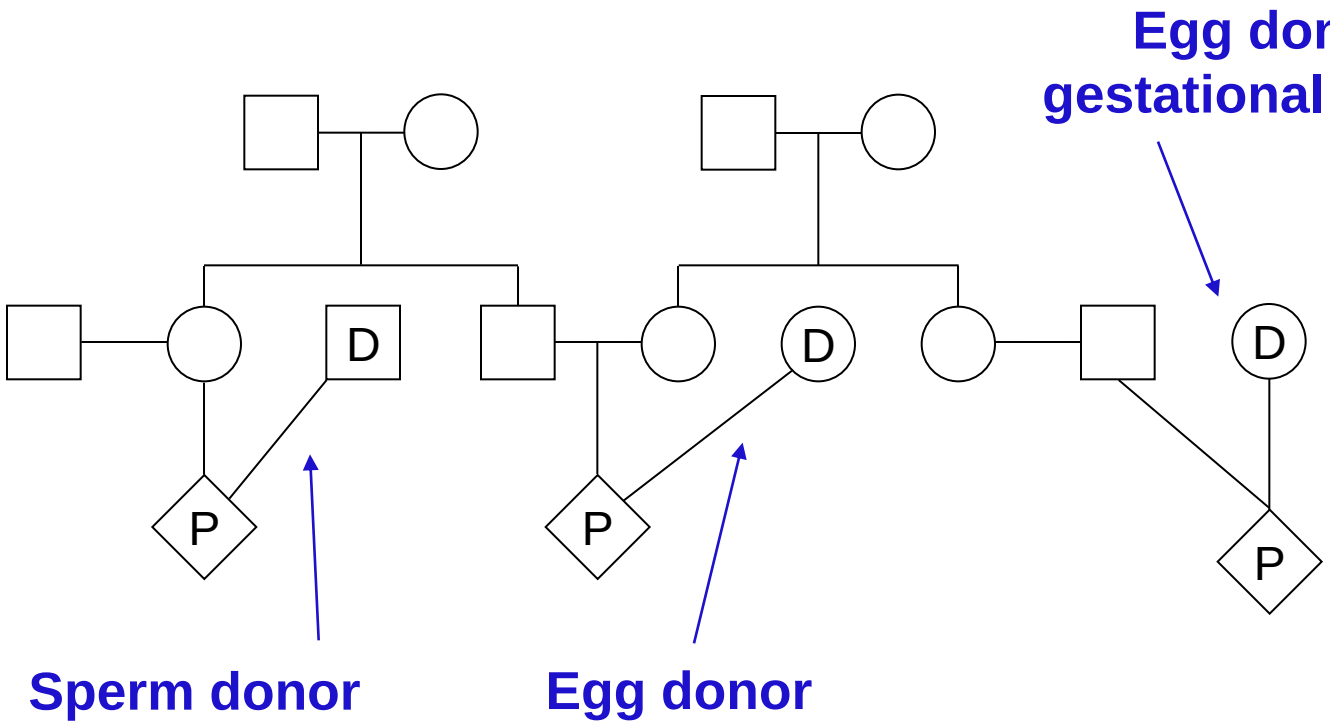


Bennett, et al. (1995). Recommendations for standardized human pedigree nomenclature. *Am J Hum Genet, 56*(3), 745-52.

Interpretation

2) Recognize Genetic Red Flags:

Do you think a condition present in a family may be genetic? Look for these clues:

- Family history of known or suspected genetic condition
- Multiple affected family members with same or related disorders
- Earlier age at onset of disease than expected
- Developmental delays or mental retardation

Interpretation

2) Recognize Genetic Red Flags (cont.):

Do you think a condition present in a family may be genetic? Look for these clues:

- Diagnosis in less-often-affected sex
- Multifocal or bilateral occurrence in paired organs
- One or more major malformations
- Disease in the absence of risk factors or after preventive measures

Interpretation

2) Recognize Genetic Red Flags (cont.):

Do you think a condition present in a family may be genetic? Look for these clues:

- Abnormalities in growth (growth retardation, asymmetric growth, excessive growth
- Recurrent pregnancy losses (2+)
- Consanguinity (blood relationship of parents)
- Ethnic predisposition to certain genetic disorders

Interpretation

Pedigrees

- Pedigree: uses standard symbols and terminology to represent a large amount of information in a diagram
- Preferred method of organizing and displaying family history
- Benefits:
  1) organize a great deal of information
  2) visualize inheritance patterns and familial clustering

Interpretation

1) Recognize basic inheritance patterns:

Multifactorial disorders

- Multiple genetic and environmental factors

Chromosomal disorders

- Extra/missing chromosomes
- Large-scale deletions or duplications
- Translocations

Single-gene disorders

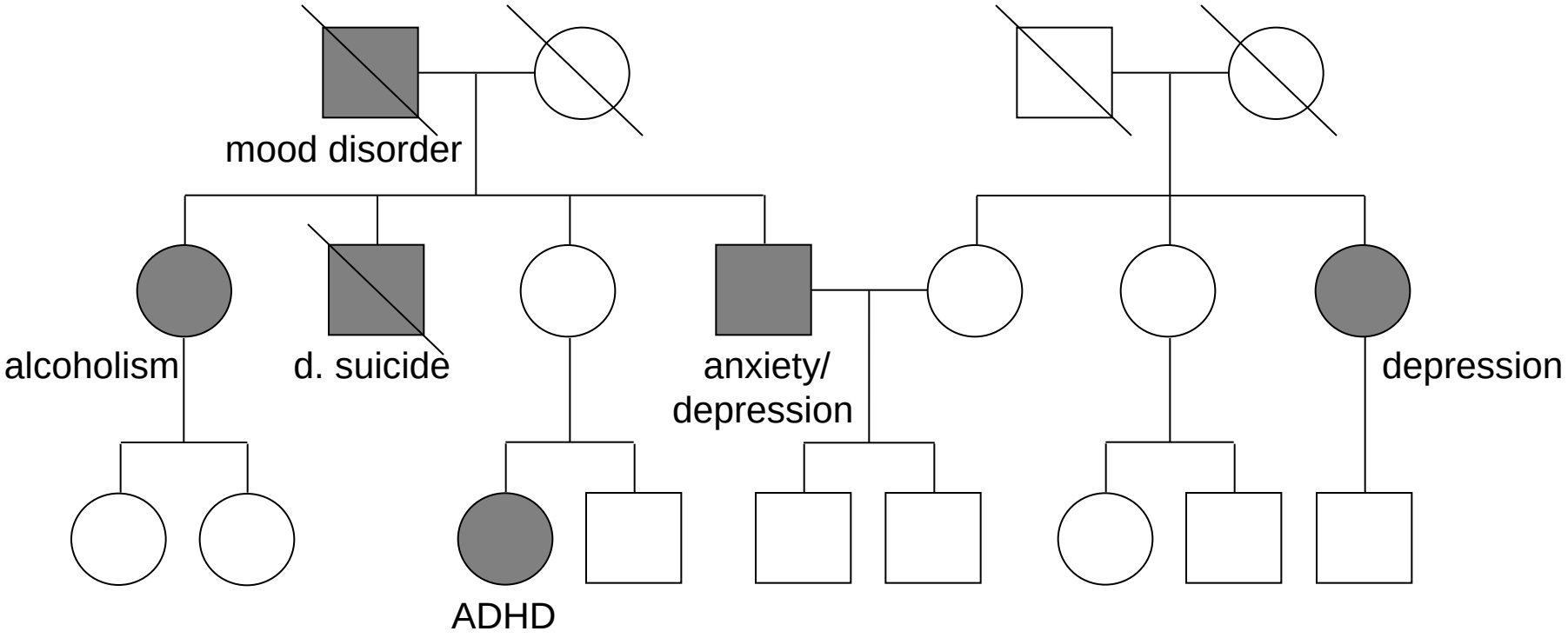
- Autosomal Dominant
- Autosomal Recessive
- X-Linked

Mitochondrial disorders

- Characterized by maternal transmission
- Usually neurological or neuromuscular symptoms

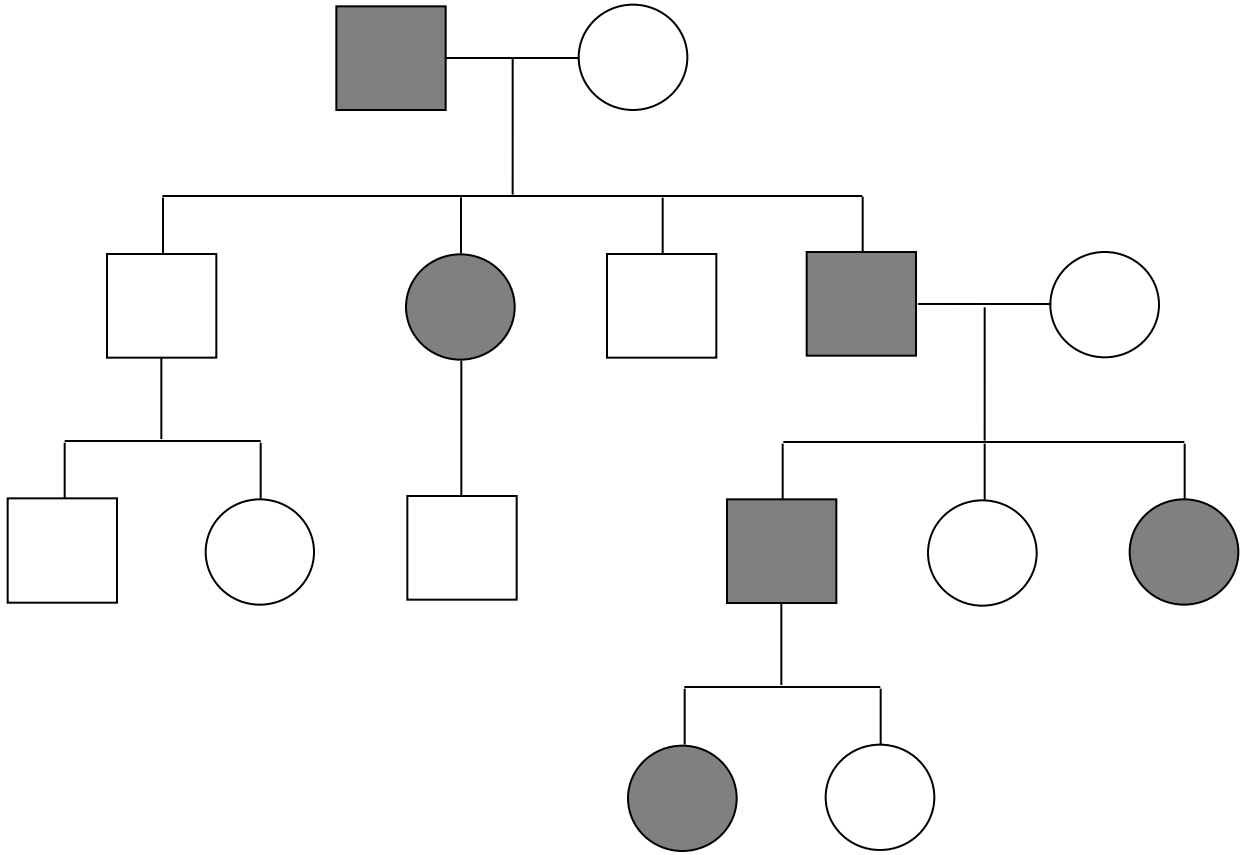
Multifactorial Inheritance

Familial Clustering



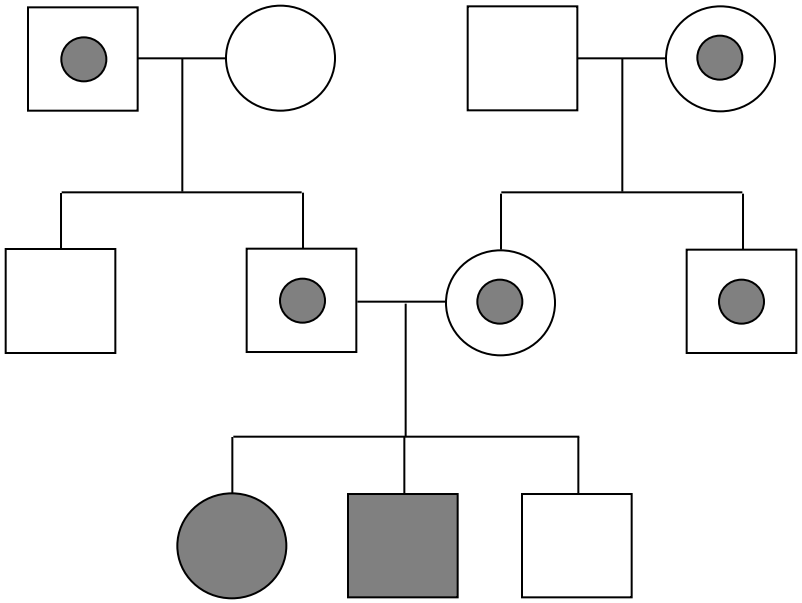
Single-gene Inheritance

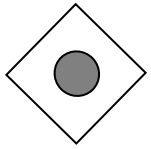
Autosomal Dominant



Single-gene Inheritance

Autosomal Recessive

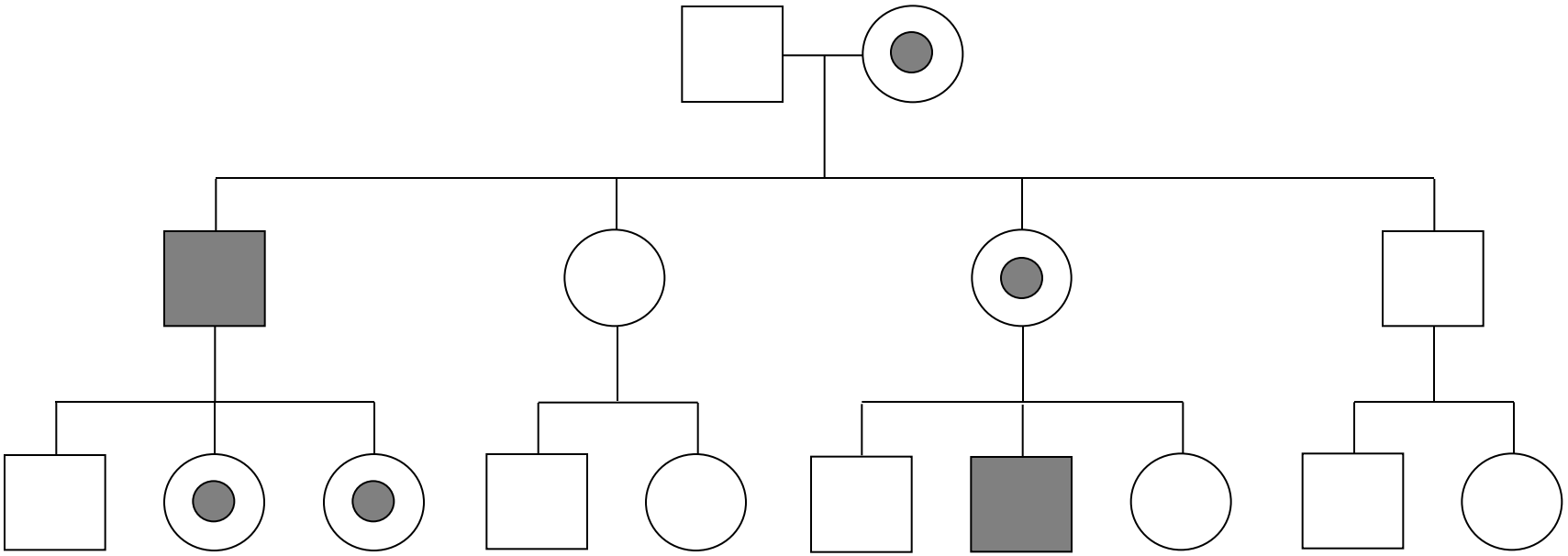




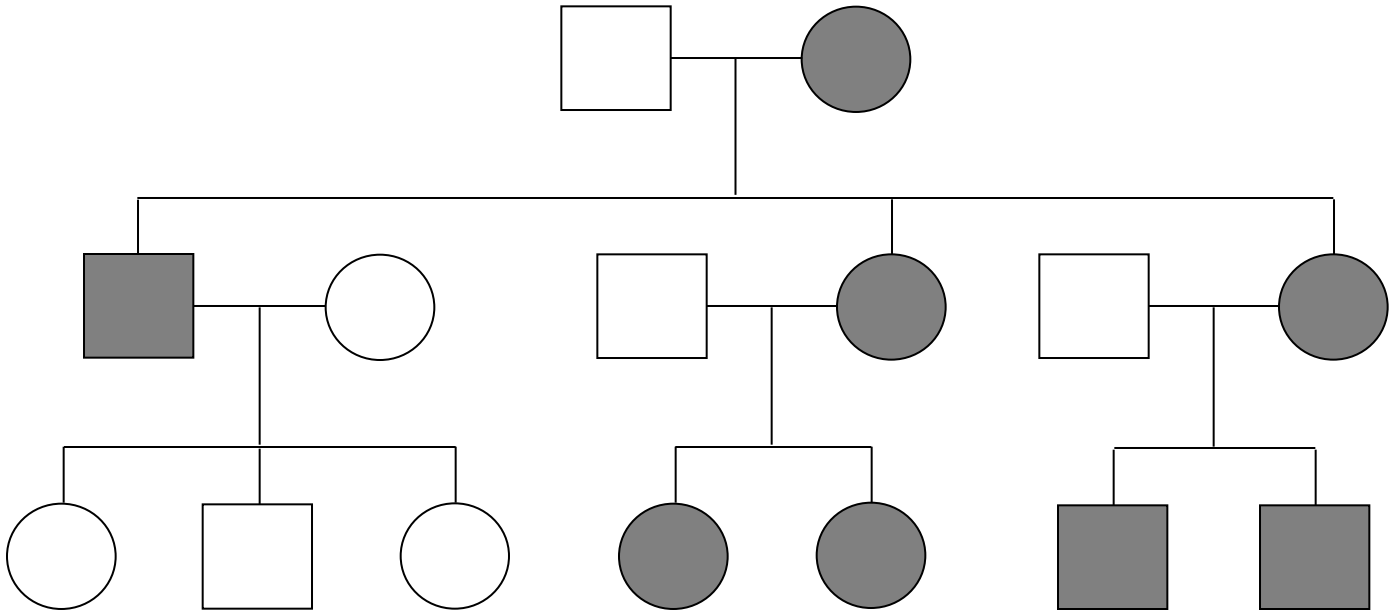
Carrier

Single-gene Inheritance

X-Linked

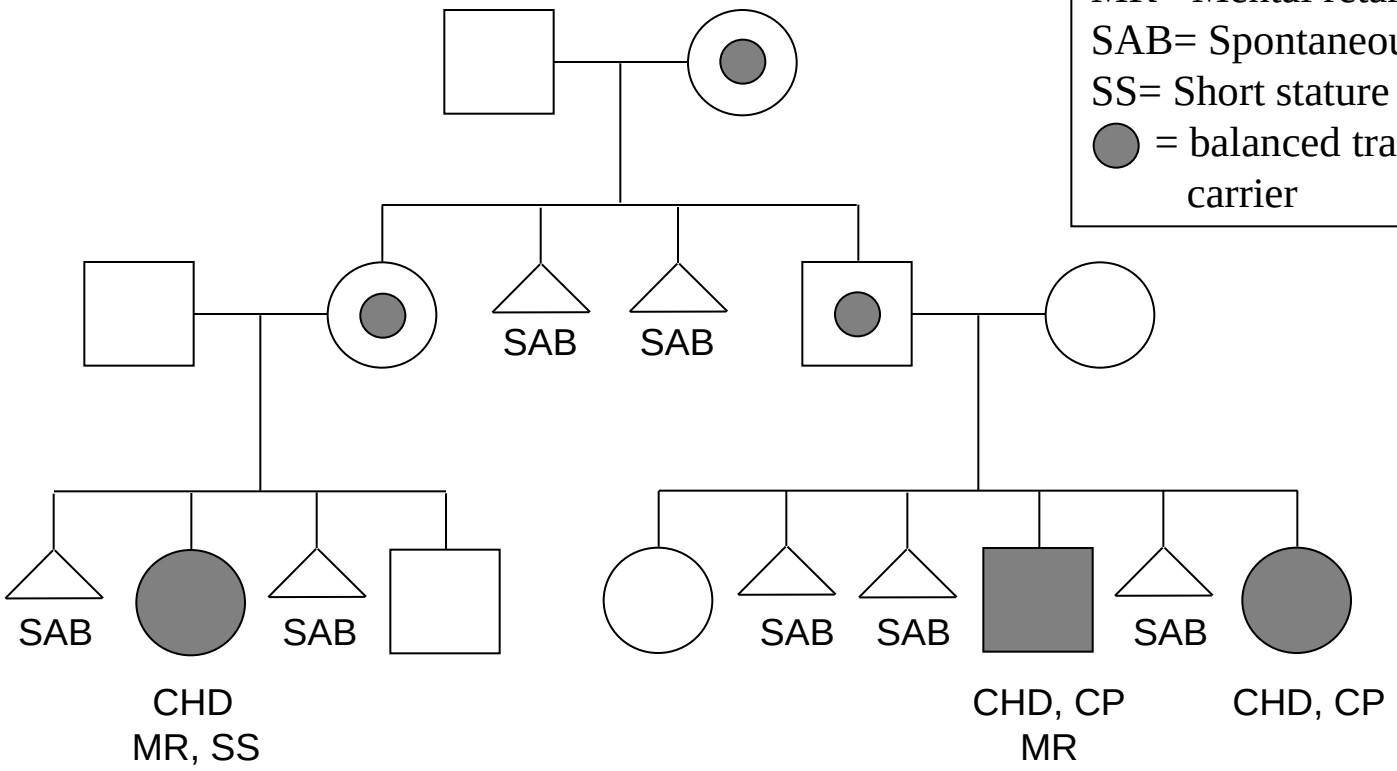


Mitochondrial Inheritance



Chromosomal Translocation

CHD= Congenital heart defect
CP= Cleft palate
MR= Mental retardation
SAB= Spontaneous abortion
SS= Short stature
● = balanced translocation carrier



Interpretation

Pedigrees or Checklists?

Crucial element: THE INFORMATION!

The method used must:

1) be reasonably accurate
2) be updated easily
3) allow for pattern detection and interpretation
4) provide clear communication and interpretation between healthcare providers

Genetics and Common Disorders: Implications for Primary Care and Public Health Providers. National Coalition of Health Providers Education in Genetics. April 2005.

Interpretation

Opportunities for Patient Education

Eliciting and summarizing family history information can:

- ✓ help the patient understand the condition in question
- ✓ clarify patient misconceptions
- ✓ help the patient recognize the inheritance pattern of the disorder
- ✓ demonstrate variation in disease expression (such as different ages at onset)
- ✓ provide a visual reminder of who in the family is at risk for the condition
- ✓ emphasize the need to obtain medical documentation on affected family members

Bennett, R.L. (1999). *The Practical Guide to the Genetic Family History*. New York: Wiley-Liss.

Interpretation

Complicating Factors in Interpretation

1) Missing information vs. unaffected relatives
2) Reliability of information
3) Non-traditional families
4) Unknown paternity
5) Adoption
6) Cultural definitions of family
7) Cultural biases
8) Consanguinity
9) Confidentiality

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Intervention

National Society of Genetic Counselors

1) Identify where more specific information is needed and obtain records

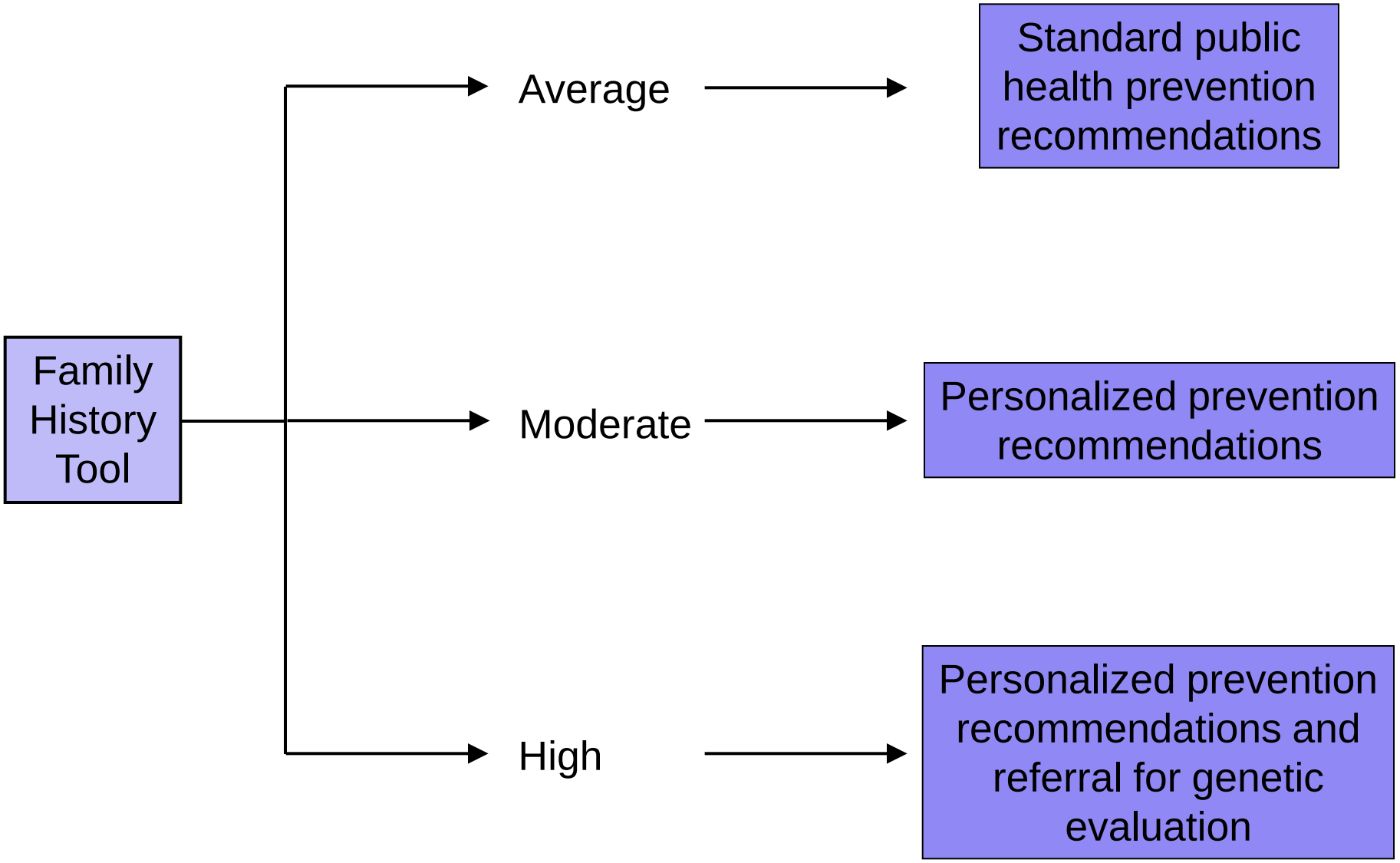
2) Assess general risks

3) Know when to refer to genetics professionals

4) Encourage the patient to talk to other family members

5) Update pedigree at subsequent visits

Risk Classification



Available Family History Tools

Surgeon General's Family History Initiative:

"My Family Health Portrait"

www.hhs.gov/familyhistory, familyhistory.hhs.gov

Available Family History Tools

"Family History: Resources and Tools" (CDC)

www.cdc.gov/genomics/public/famhistMain.htm

Available Family History Tools

AMA's Genetics & Molecular Medicine: Family History

www.ama-assn.org/ama/pub/category/2380.html

Family History

e-mail story | print story

HELPING DOCTORS HELP PATIENTS

The importance of a family history
Describes importance of family medical history in disease prevention and provides links to resources on how to collect family history information and generate a simple pedigree.

Prenatal screening questionnaire

Pediatric clinical genetics questionnaire

Adult family history form

Last updated: Jun 20, 2006
Content provided by: AMA Science

Available Family History Tools

"Your Family History- Your Future"

(NSGC, Genetic Alliance, ASHG)

YOUR FAMILY HISTORY – YOUR FUTURE

Your family history holds key information about your past and clues to your future health. Many of your physical traits (such as eye color, hair color, and height) are inherited. So, too, are risks for certain genetic conditions and health problems such as heart disease, diabetes, and some cancers. You may have noticed that some of your relatives are healthier and live longer than other relatives. You may also have noticed that some relatives have the same health problems. By collecting your family's health history, you can learn what health problems you may be at increased risk for in the future and how to reduce your risks. For instance, people at increased risk for heart disease may be able to reduce their risk through not smoking, regular exercise and diet. Finding out your family history can benefit both you and your relatives… and it can be fun too!

How to Find a Genetics Professional

1. National Society of Genetic Counselors

Find a counselor according to location, institution, or area of specialization

How to Find a Genetics Professional

2. GeneClinics

GeneTests

Welcome to the **GeneTests** Web site, a publicly funded medical genetics information resource developed for physicians, other healthcare providers, and researchers, available at no cost to all interested persons. Use of this Web site assumes acceptance of the terms of use.

www.geneclinics.org

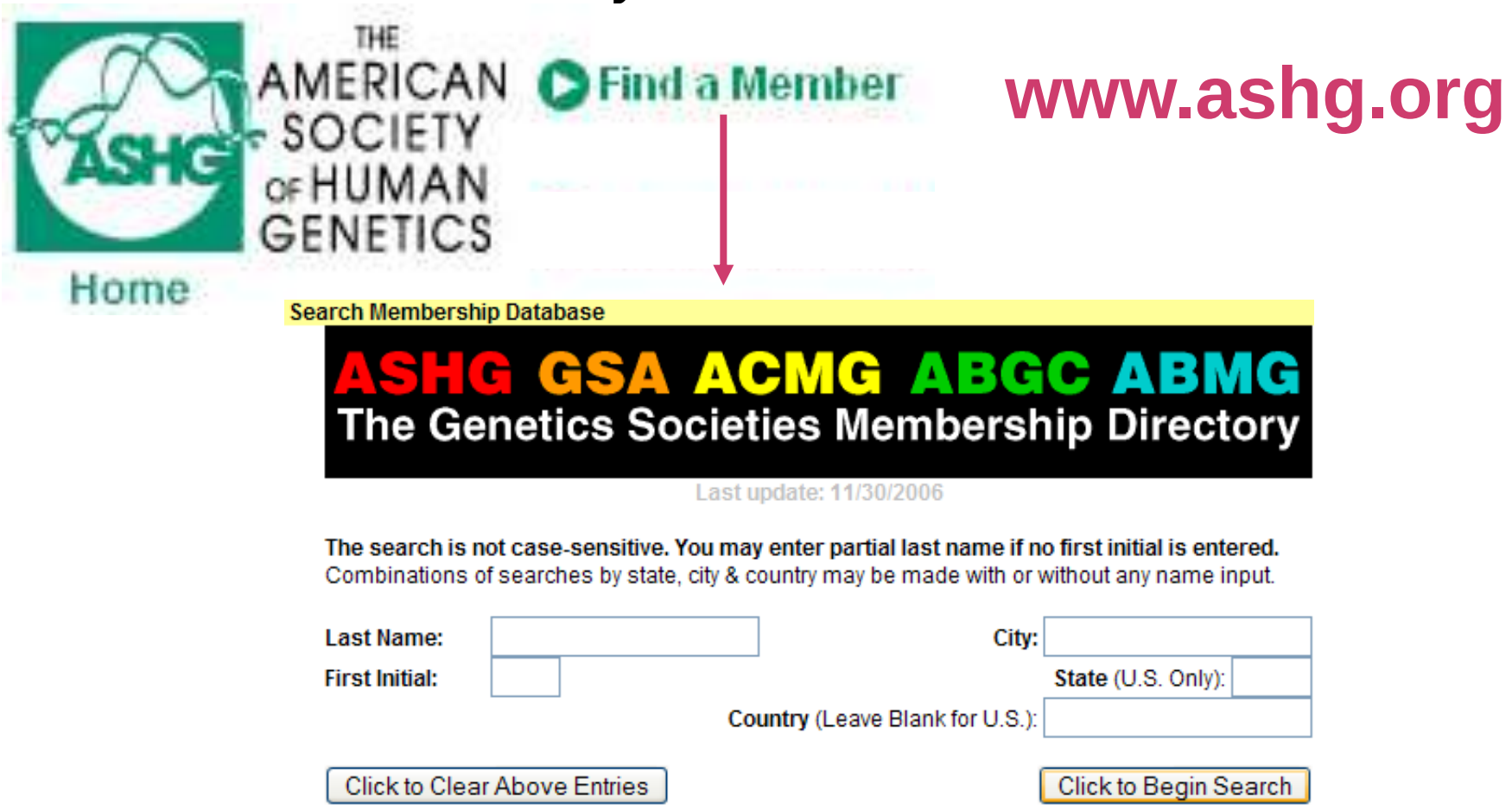
A voluntary listing of US and international genetics clinics providing genetic evaluation and genetic counseling

At This Site

- ***GeneReviews***
  Online publication of expert-authored disease reviews
- **Laboratory Directory**
  International directory of genetic testing laboratories
- **Clinic Directory**
  International directory of genetics and prenatal diagnosis clinics
- **Educational Materials**
  - Illustrated glossary
  - About genetic services
  - PowerPoint® slide presentations

How to Find a Genetics Professional

3. American Society of Human Genetics



www.ashg.org

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Case Examples

Saundra's Family

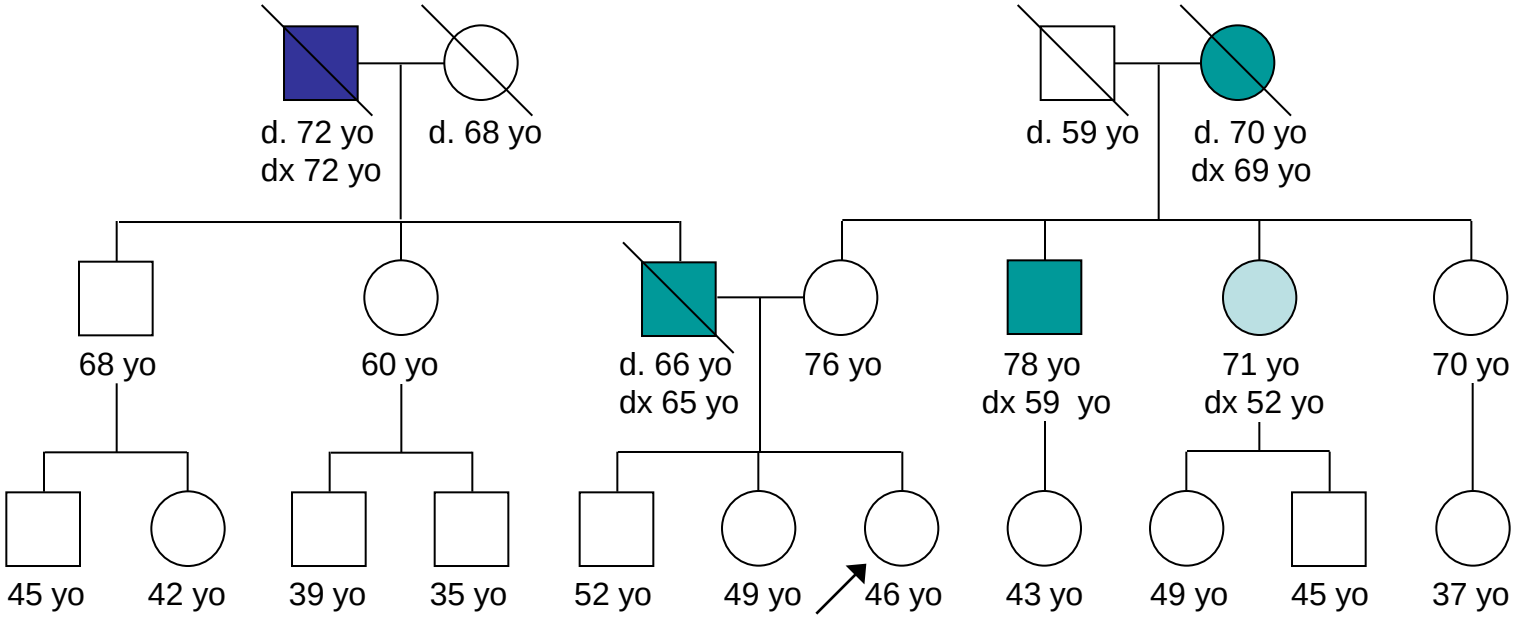
A new patient, Saundra, states that many individuals in her family have had cancer, especially colon cancer. She is certain that she is destined to develop cancer in the near future.

Saundra's Family

How can taking Saundra's family history help to assess her risk to develop colon cancer?

1) Identify specific relatives with colon or other cancers
2) Identify the ages at the diagnosis of cancer
3) Identify family members who have not had cancer
4) Identify the side (or sides) of the family on which cancer is present

Saundra's Family



Colon cancer

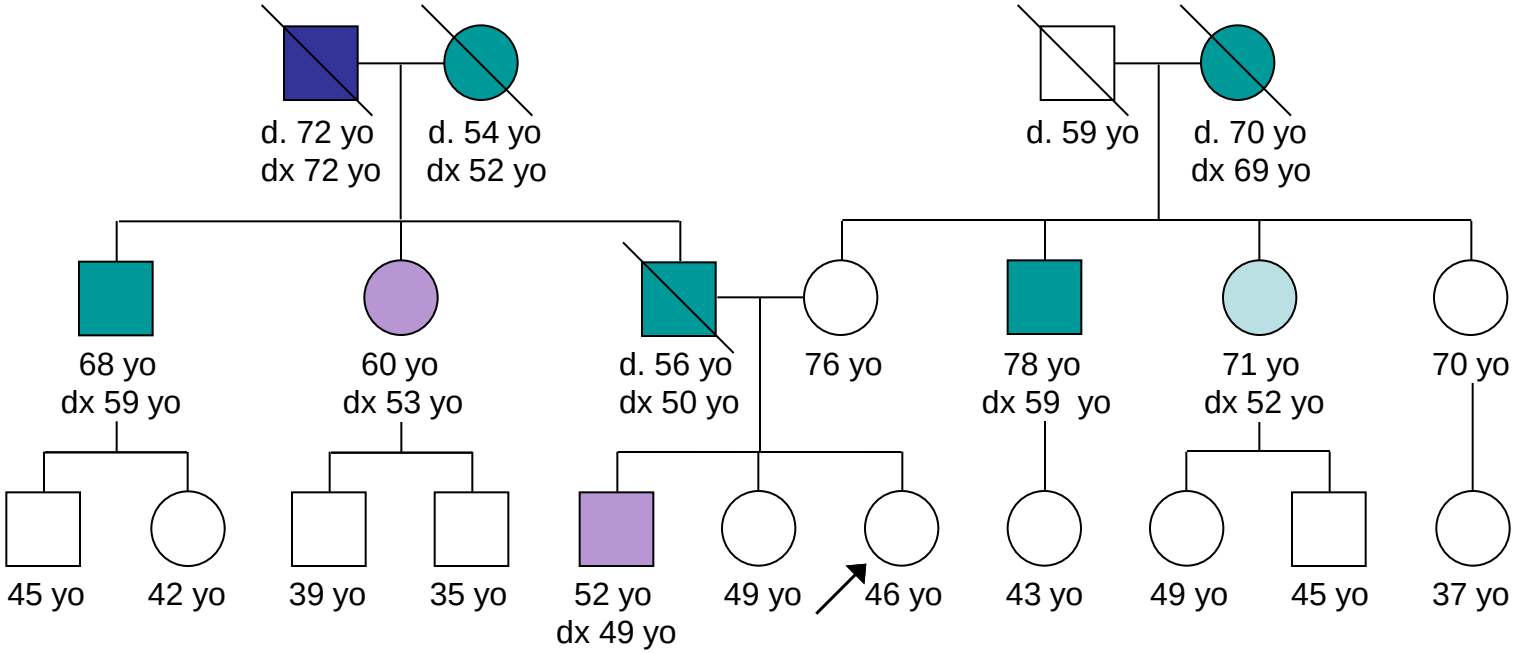
Lung cancer

Melanoma

Do you think that Saundra has a low, moderate, or high risk of developing colon cancer based on her family history?

How did you assess her risk?

Saundra's Family



Colon cancer

Lung cancer

Melanoma

Colon polyps

Do you think that Saundra has a low, moderate, or high risk of developing colon cancer based on her family history?

How did you assess her risk?

Saundra's Family

⇩ Factors **decreasing** risk of genetic basis to condition in first scenario

- Cancers common in general population
- Affected relatives are older at diagnosis
- Cancer on both sides of family

⇧ Factors **increasing** risk of genetic basis to condition in second scenario

- Affected relatives are relatively young at diagnosis
- Multiple affected relatives concentrated on same side of family

Saundra's Family

Utility of family history tools:

- **Collection**

  Focus on diagnoses and ages, as well as affected and unaffected individuals

- **Interpretation**

  Consider red flags: multiple affected family members, early age at onset

- **Implementation**

  Assessment of risk alters recommended surveillance

Toby's Family

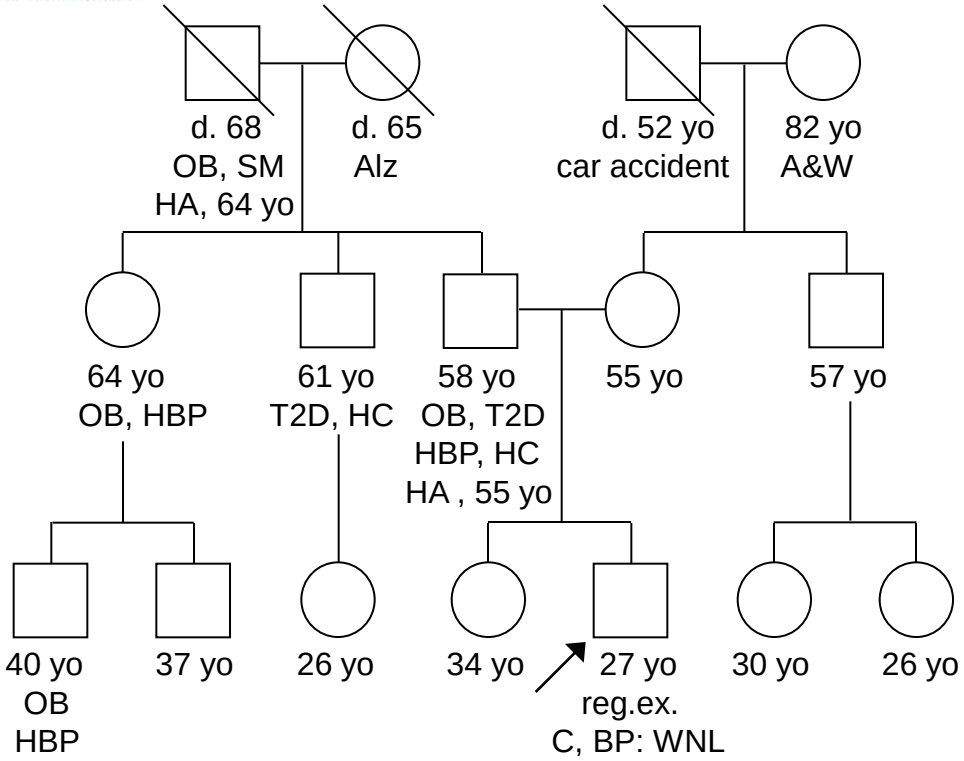
During a routine visit, Toby mentions that he is extremely conscious of his physical health because he does not want to get heart disease like the other members of his family.

Toby's Family

How can taking Toby's family history help to assess his risk to develop heart disease?

1) Identify specific relatives with heart disease and associated complications
2) Identify the ages at onset of disease
3) Identify the presence or absence of risk factors in relatives with heart disease

Toby's Family

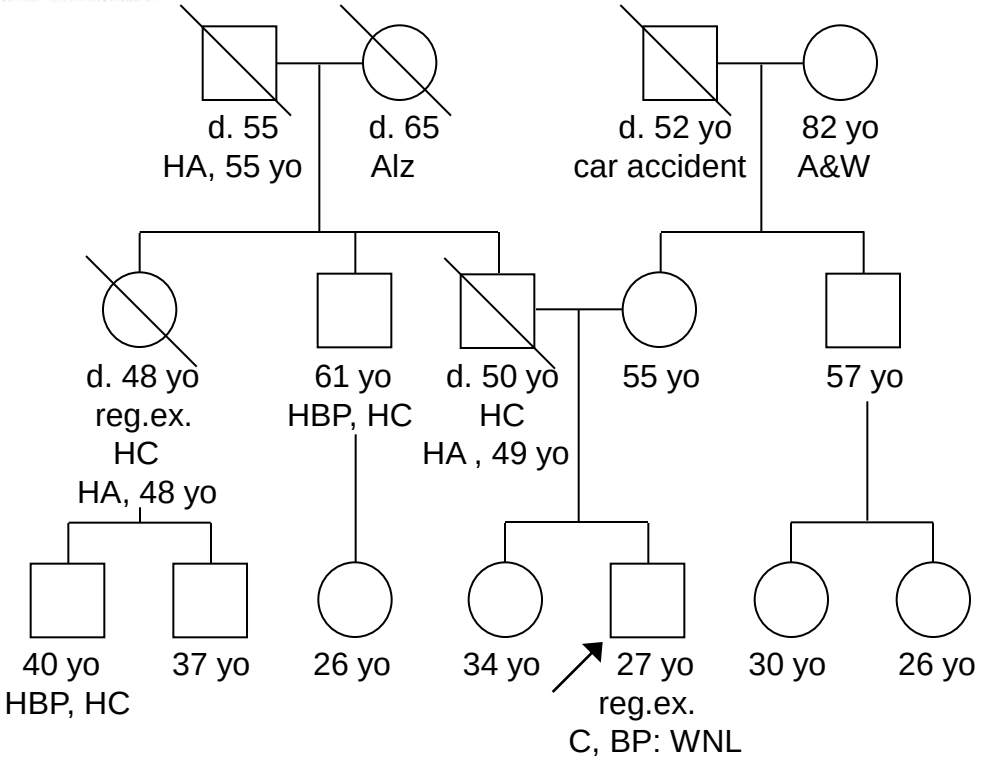


A&W: alive and well
Alz: Alzheimer's
HA: heart attack
HBP: high blood pressure
HC: high cholesterol
OB: obese
RegEx: regular exercise
SM: smoker
T2D: type 2 diabetes

Do you think that Toby has a low, moderate, or high risk of developing heart disease based on his family history?

How did you assess his risk?

Toby's Family



A&W: alive and well
Alz: Alzheimer's
HA: heart attack
HBP: high blood pressure
HC: high cholesterol
OB: obese
RegEx: regular exercise
SM: smoker

Do you think that Toby has a low, moderate, or high risk of developing heart disease based on his family history?

How did you assess his risk?

Toby's Family

⇩ Factors **decreasing** risk of genetic basis to condition in first scenario

- Affected family members have multiple risk factors, some of which are environmental
- Affected relatives are older at diagnosis

⇧ Factors **increasing** risk of genetic basis to condition in second scenario

- Affected relatives are relatively young at diagnosis
- Disease in the absence of risk factors

Toby's Family

Utility of family history tools:

- **Collection**

  Focus on diagnoses and ages at onset; also consider presence or absence of risk factors

- **Interpretation**

  Consider red flags: multiple affected family members, early age at onset, disease in the absence of risk factors and in the less-often-affected sex

- **Implementation**

  Assessment of risk alters recommended testing and health management

Baby Maria's Family

Maria (one month old) was born with a cleft lip and palate (CL/P). CL/P is commonly isolated, but can also be a part of a number of different inherited syndromes.

Baby Maria's Family

How can taking Maria's family history help assess whether her CL/P is isolated or syndromic?

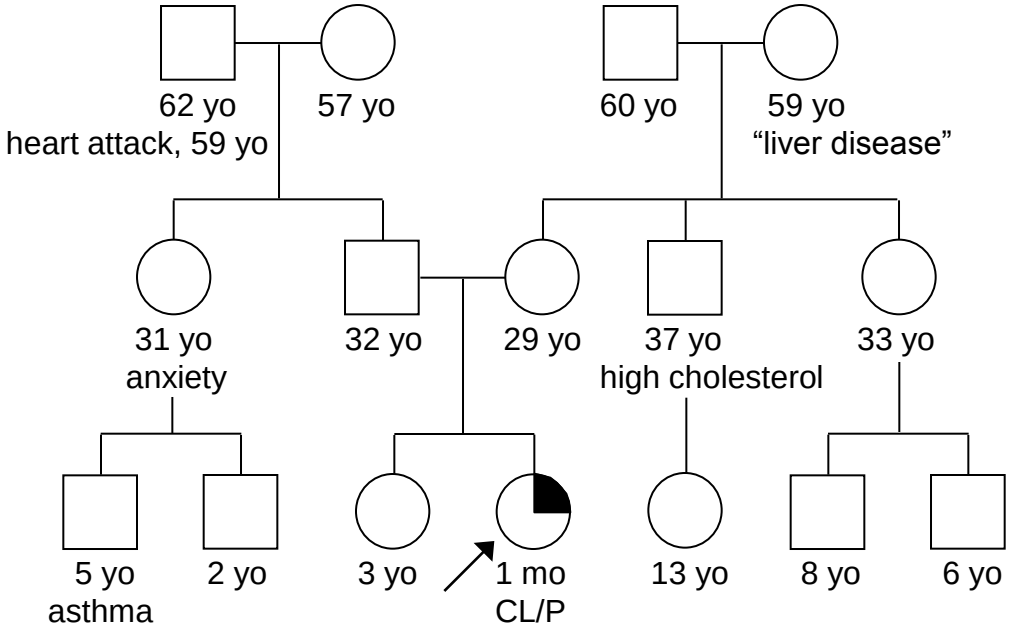
1) Identify whether features are present in other family members that are suggestive of a syndrome
2) If features are present, identify an inheritance pattern

Why is this helpful?

⇨ Better management of associated health problems

⇨ Determine recurrence risk for future children

Baby Maria's Family



Key:

Cleft lip and palate

Do you think that there is a low, moderate, or high chance that Maria's cleft lip and palate is due to an inherited condition?

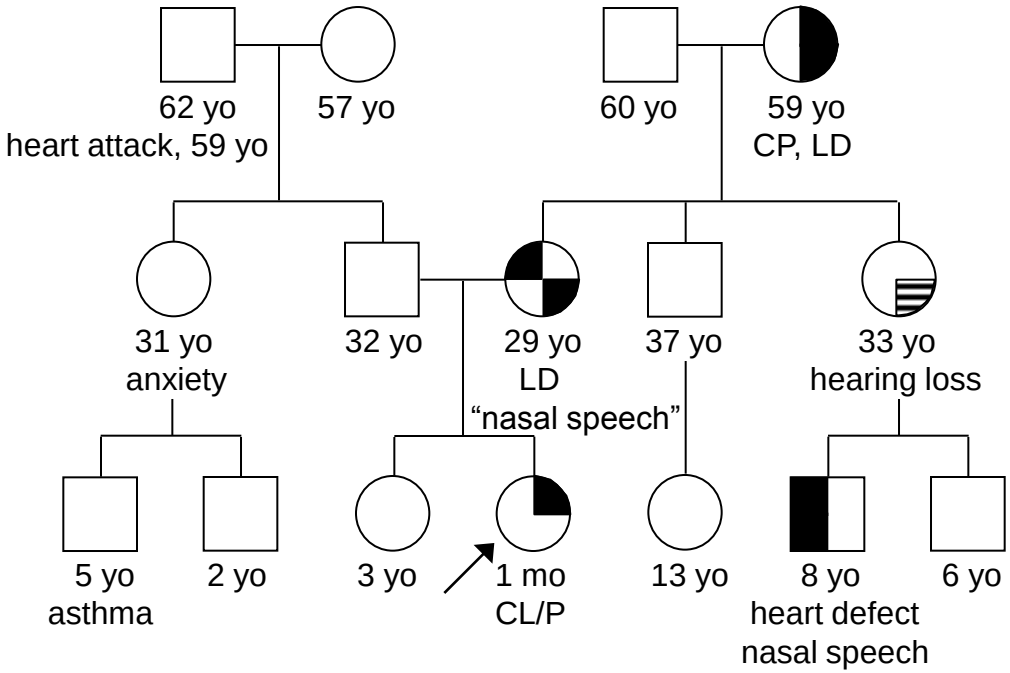
How did you assess this chance?

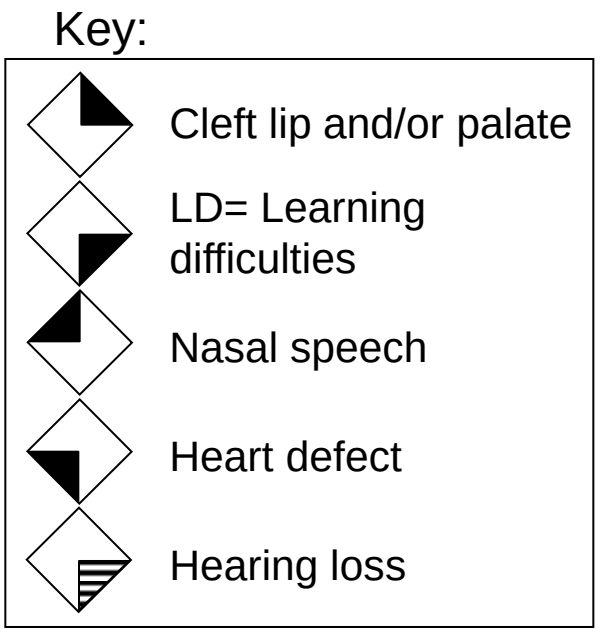
Baby Maria's Family

Isolated Cleft Lip and/or Palate:

- 1 in 1000 births (0.1%)
- Recurrence risks
  - Maria's sibling: 2%-8%
  - Maria's child: 4%-6%

Baby Maria's Family





Do you think that there is a low, moderate, or high chance that Maria's cleft lip and palate is due to an inherited condition?

How did you assess this chance?

Baby Maria's Family

22q Deletion syndrome:

- Deletion of submicroscopic deletion of ch. 22q
- Inheritance: autosomal dominant
- Recurrence risks:
  - Maria's sibling: 50%
  - Maria's child: 50%
- Primary features:

Congenital heart defects	Immune deficiency
Cleft lip and palate	Hypocalcemia
Learning difficulties	Characteristic facies

Baby Maria's Family

⇩ Factors **decreasing** risk of inherited syndrome in first scenario

- Presence of non-specific health conditions common in the general population
- Features on both maternal and paternal sides
- No clear inheritance pattern or family clustering

⇧ Factors **increasing** risk of inherited syndrome in second scenario

- Clustering of potentially related features
- Several genetic red flags are present
- Clear autosomal dominant inheritance

Baby Maria's Family

Utility of family history tools:

- **Collection**

  Specifically ask about features that are often seen in syndromes associated with CL/P

- **Interpretation**

  Consider red flags: multiple affected family members, early age at onset, developmental delays, one or more major malformation

- **Implementation**

  Presence of a syndrome can alter recurrence risks and health management for the patient and family members

Anne and Geoff

Anne and Geoff want to start a family. Following ACOG guidelines, Anne's physician makes cystic fibrosis (CF) carrier screening available to all her patients, and recommends screening to her patients who are Northern European (including Ashkenazi Jewish) or who have a family history of CF.

American College of Obstetricians and Gynecologists, American College of Medical Genetics. Preconception and prenatal carrier screening for cystic fibrosis: clinical and laboratory guidelines. Washington, DC: ACOG; Bethesda (MD): ACMG; 2001.

Anne and Geoff

How can Anne and Geoff's family histories help the physician decide whether to recommend CF carrier testing or simply make it available to Anne and Geoff?

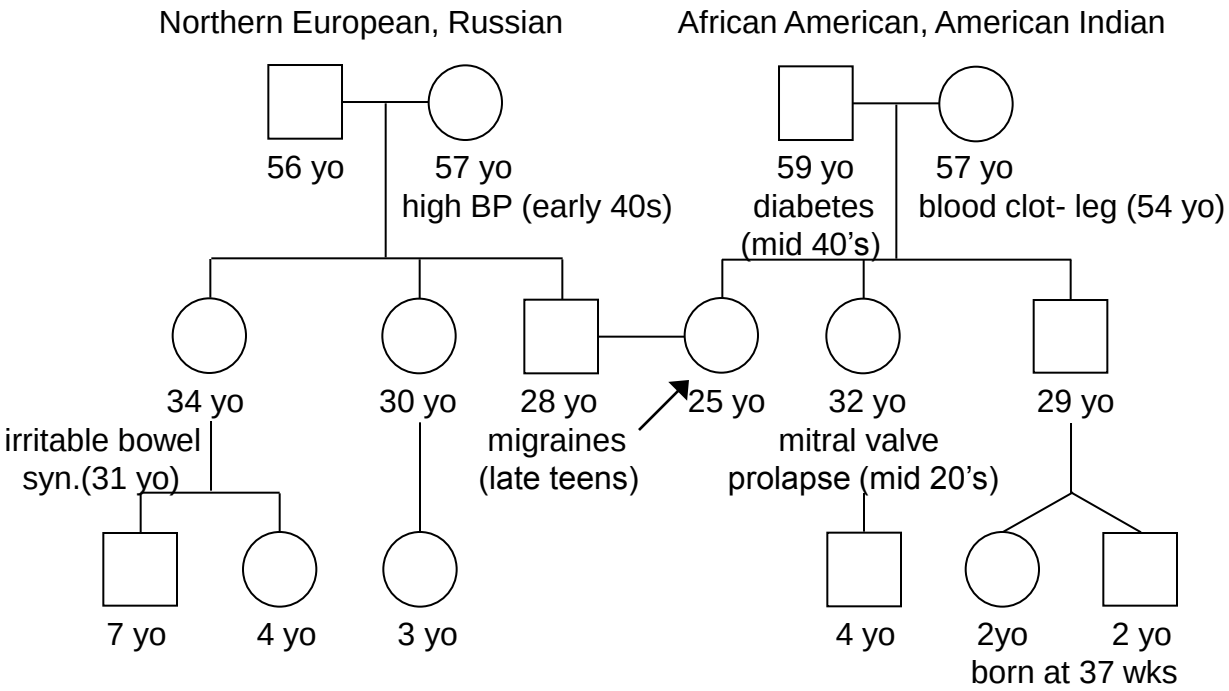
1) Identify whether CF is present in the family
2) Determine whether Anne or Geoff are of ancestries for which CF carrier screening is recommended
3) Identify other family members who may consider carrier testing

Anne and Geoff

Cystic Fibrosis:

- Multisystem disease
  - Pulmonary: accumulation of mucus
  - Digestive: malnutrition and constipation
  - Reproductive: bilateral absence of vas deferens (infertility)
- Inheritance: autosomal recessive
- Average life span: young adulthood

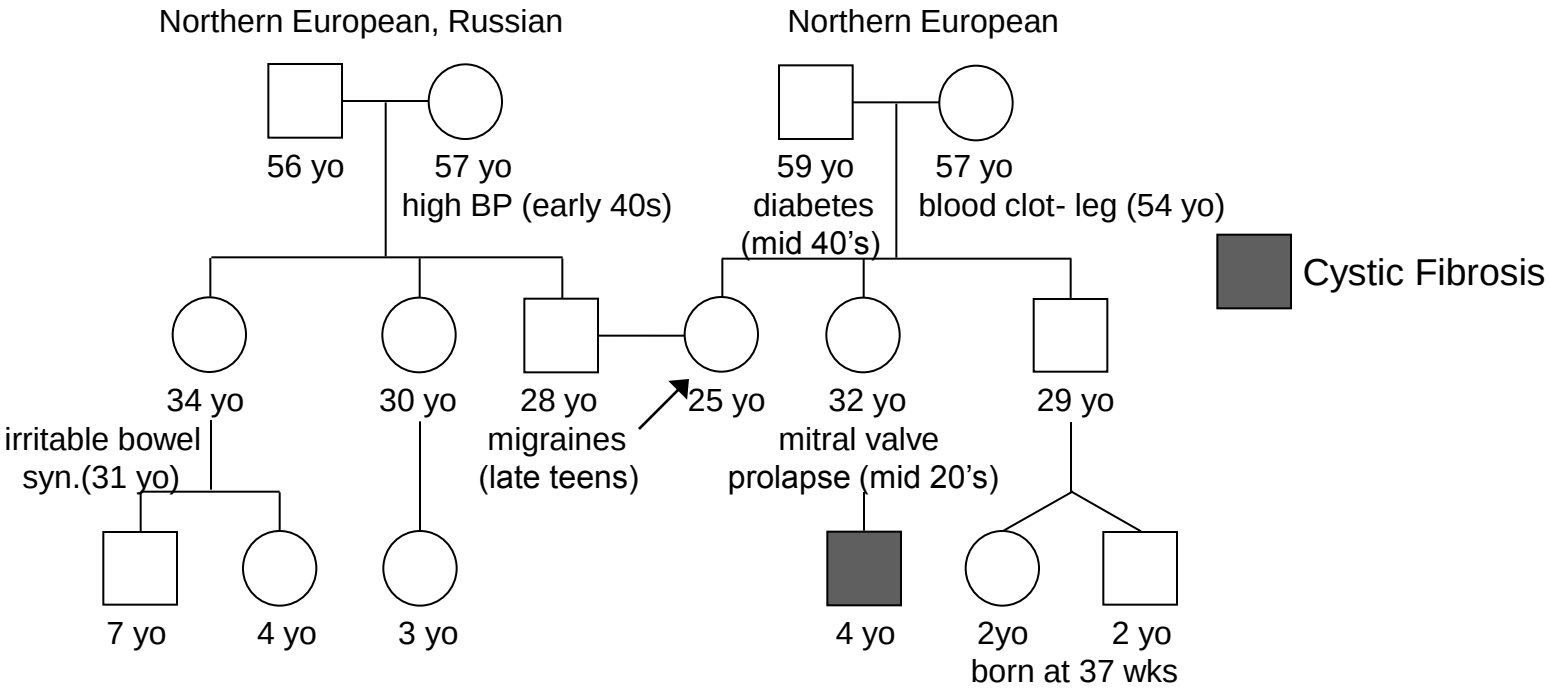
Anne and Geoff



Do you think that there is a low, moderate, or high chance that either Geoff or Anne are carriers of a CF mutation?

How did you assess this chance?

Anne and Geoff



Do you think that there is a low, moderate, or high chance that either Geoff or Anne are carriers of a CF mutation?

How did you assess this chance?

Anne and Geoff

⇩ Factors **decreasing** risk of being a CF carrier in first scenario

- Anne's ancestry has a lower carrier frequency
- No family history

⇧ Factors **increasing** risk of being a CF carrier in second scenario

- Both Anne and Geoff are of Northern European ancestry
- Positive family history: Anne's nephew (second-degree relative) has CF

Anne and Geoff

Utility of family history tools:

- **Collection**

  Elicit ancestry of biological grandparents, relevant health information

- **Interpretation**

  Consider red flags: known family history, ethnic predisposition; autosomal recessive inheritance

- **Implementation**

  Assessment of risk determines whether carrier testing is offered; may also consider prenatal testing, pregnancy surveillance, or preparation for CF management

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