

Hereditary Breast Cancer Risk

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Objectives

- ▶ Identify genes/hereditary conditions associated with breast cancer risk
- ▶ Describe current testing options for hereditary cancer (targeted vs. panel)
- ▶ Describe the importance of genetic testing for treatment planning and prevention of future cancer risk.

Genetic Counseling

- ▶ GC's are Master's level trained medical providers specializing in hereditary disorders
- ▶ National certification; state level licensure in some areas
- ▶ Cancer genetics is a subspecialty
- ▶ Typical consultations take ~90 minutes
 - ▶ Obtain pertinent personal medical history information
 - ▶ Construct genetic pedigree (3-generation family tree)
 - ▶ Risk assessment
 - ▶ Counseling: differential diagnosis, testing options, limitations and benefits, screening/management options, and address legal, privacy, psychosocial issues

Family history - ASCO

- ▶ Obtain family history of cancer/ precancerous conditions (3 generations)
 - ▶ 1st - Parents, siblings, children
 - ▶ 2nd - Grandparents, aunts/uncles, grandchildren, nieces/nephews
 - ▶ 3rd - first cousins, great- grandparents, -aunts/ uncles
- ▶ Document diagnosis, age of onset, current age/age of death
- ▶ Clarify diagnoses (ex. Cervical vs. uterine vs. ovarian cancer)
- ▶ **Update at least yearly**

Identifying Patients (NCCN)

- ▶ Personal diagnosis
 - ▶ Breast cancer <45
 - ▶ TNBC <60
 - ▶ Male breast cancer
 - ▶ Bilateral (first diagnosis under age 50)
 - ▶ Malignant phyllodes tumor
 - ▶ At any age PLUS family history:
 - ▶ breast, ovarian, pancreatic, prostate
 - ▶ Ancestry (Ashkenazi Jewish)
 - ▶ Individuals with multiple and/or rare cancers (ex. Sarcoma)

Identifying Patients

Best person to test in a family is an *affected* individual with the most significant history

Hereditary breast and ovarian cancer syndrome - BRCA1/2

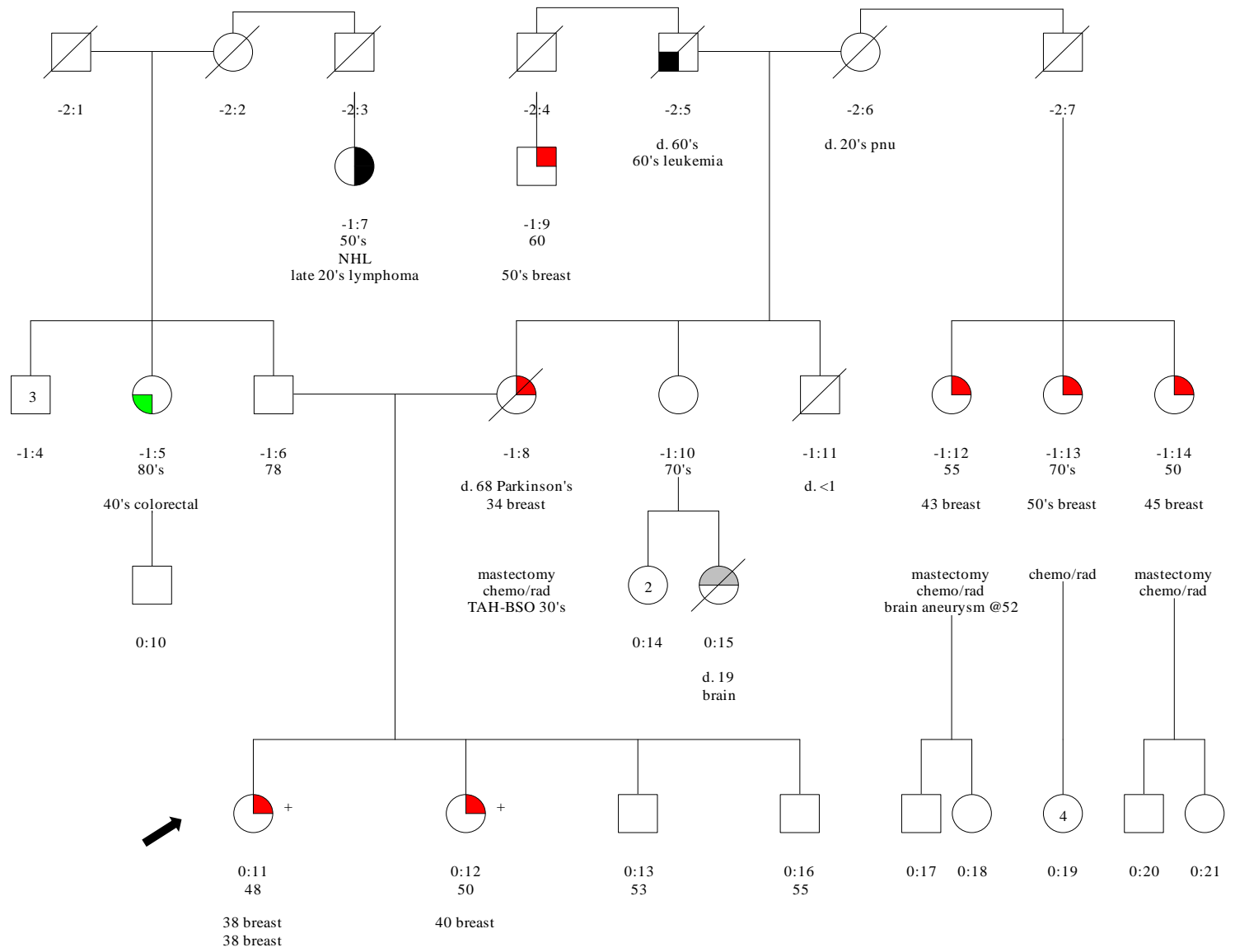
▶ BRCA1

- ▶ up to 50-87% risk for female breast cancer
 - ▶ up to 60% risk for second primary
- ▶ ~44% risk for ovarian cancer
- ▶ Others
 - ▶ Male breast: 1-2%
 - ▶ “elevated” risk for prostate and others

▶ BRCA2

- ▶ 45-70% risk for female breast cancer
 - ▶ up to 60% risk for second primary
- ▶ 10-20% risk for ovarian cancer
- ▶ Others
 - ▶ Male breast: up to 8%
 - ▶ Prostate: 17% for *early onset*
 - ▶ Pancreatic: up to 8%
 - ▶ Others

Breast Cancer



BRCA1

Cancer risks

- ▶ Breast
- ▶ Ovarian
- ▶ Others
 - ▶ Male breast
 - ▶ Prostate
 - ▶ ? Colon, pancreatic, others

Management

- ▶ Breast
 - ▶ MRI at age 25-29
 - ▶ Add mammogram at 30
 - ▶ Consider RR mastectomy
- ▶ Ovaries
 - ▶ Consider TV-US/ CA-125
 - ▶ RR BSO age 35-40
- ▶ Males
 - ▶ Consider PSA/DRE at 45
 - ▶ CBE at 35

BRCA1 continued

Management

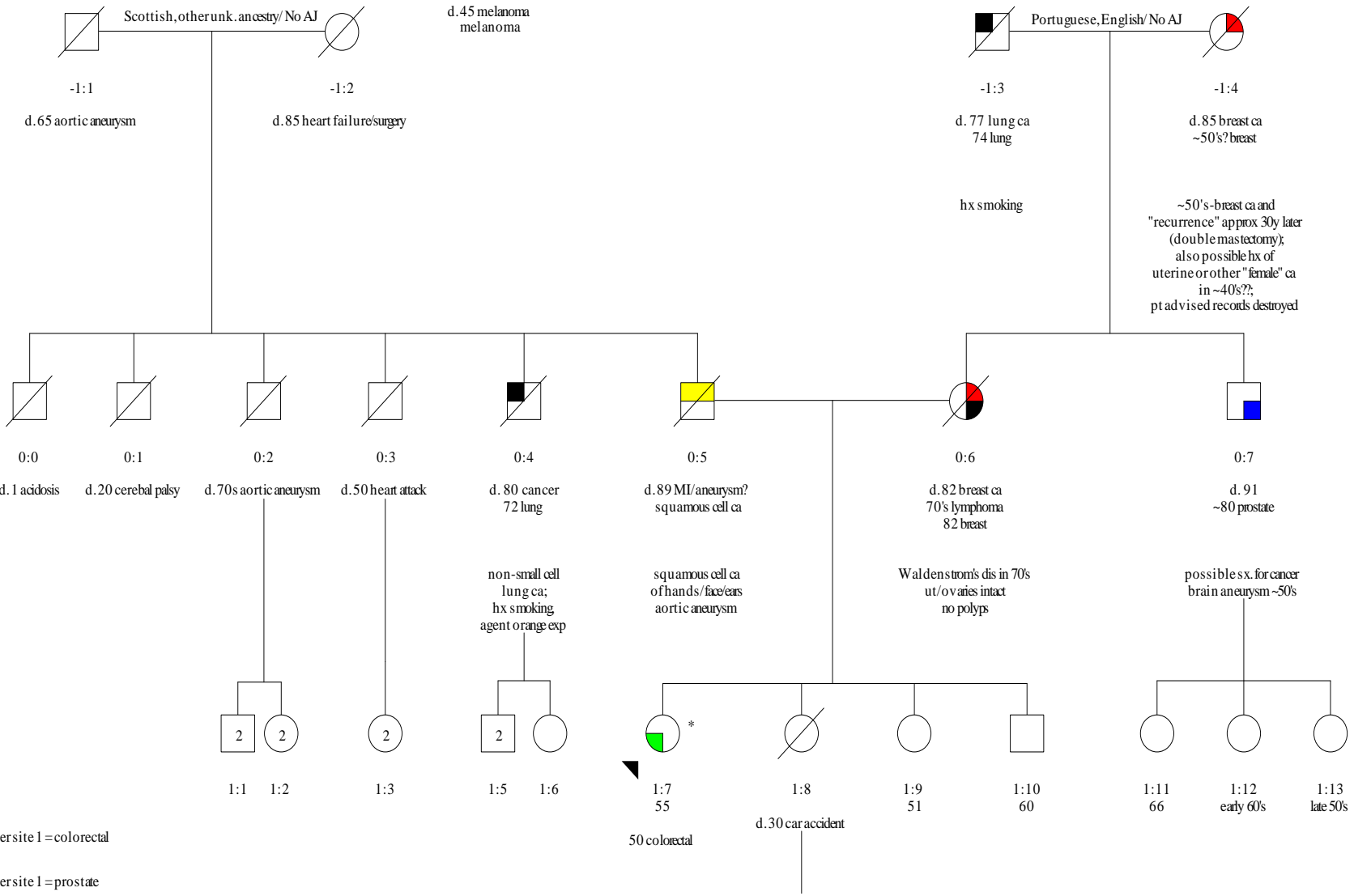
- ▶ Additional treatment option (clinical trial/ off label)
 - ▶ PARP inhibitors
- ▶ Identify at risk relatives, etc.
 - ▶ Early detection
 - ▶ Prevention

Colon Cancer?

50 yo woman diagnosed
with colon cancer...

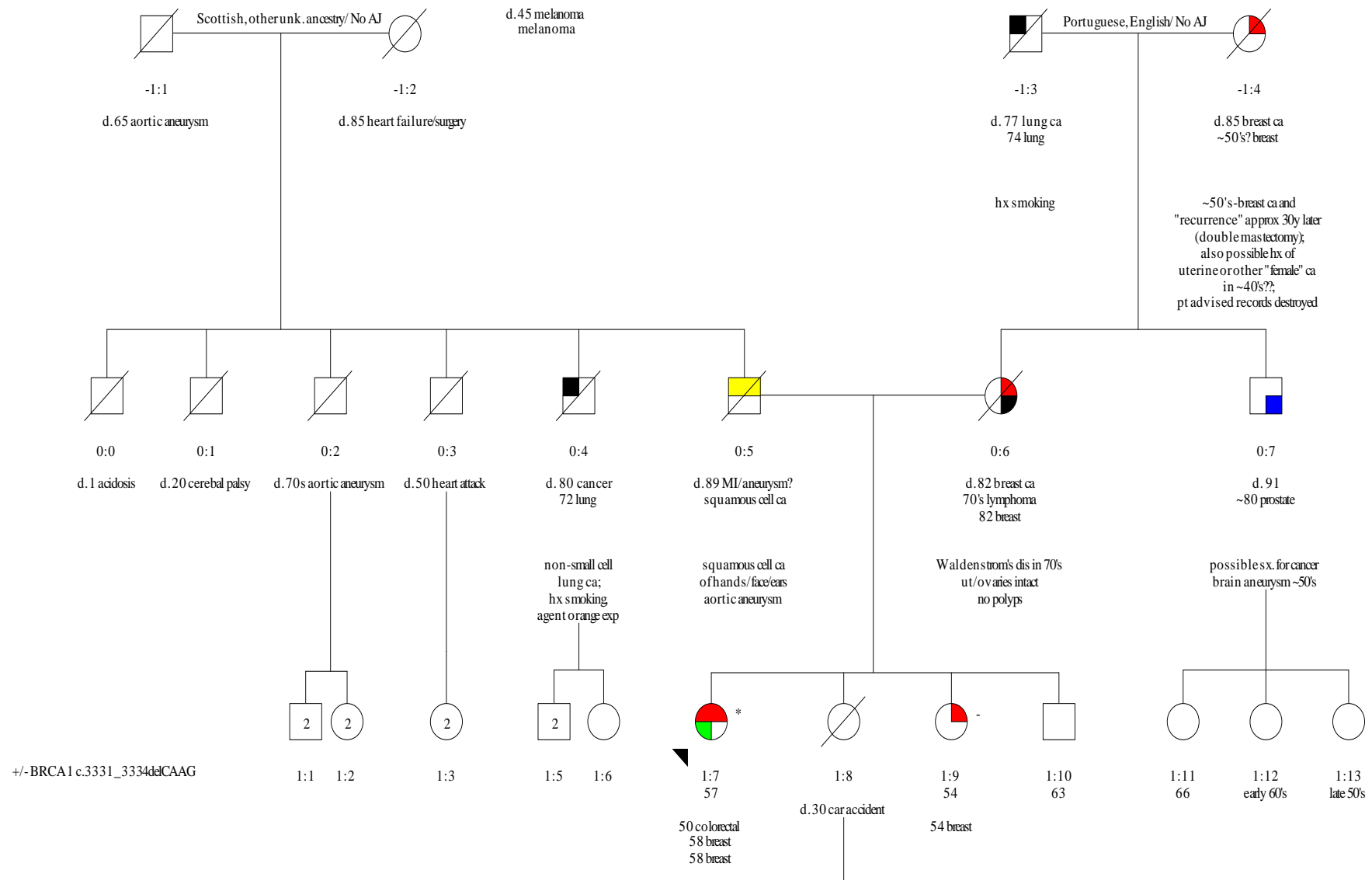
1-4

d.45 melanoma
melanoma



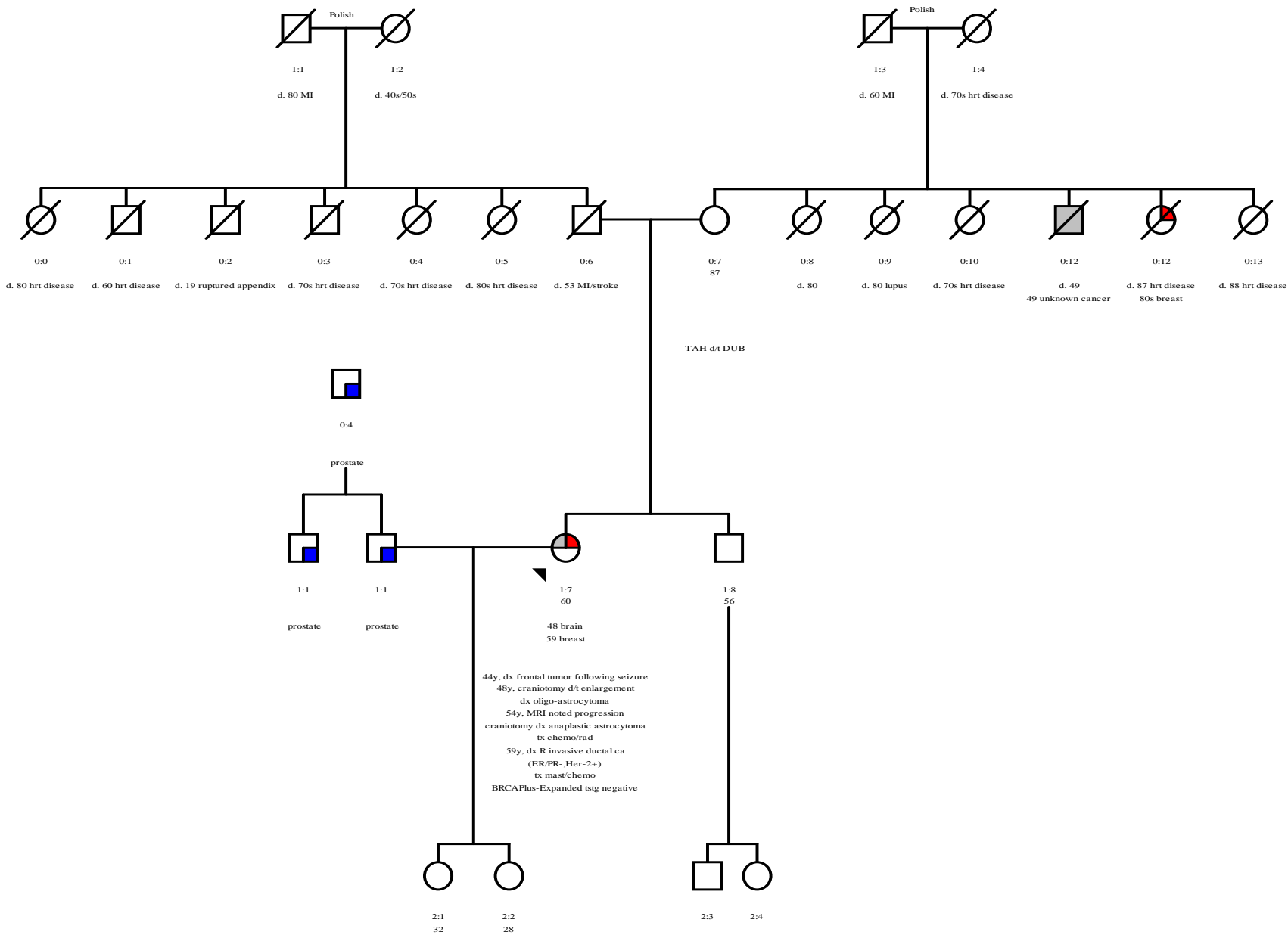
incersite 1 = colorectal

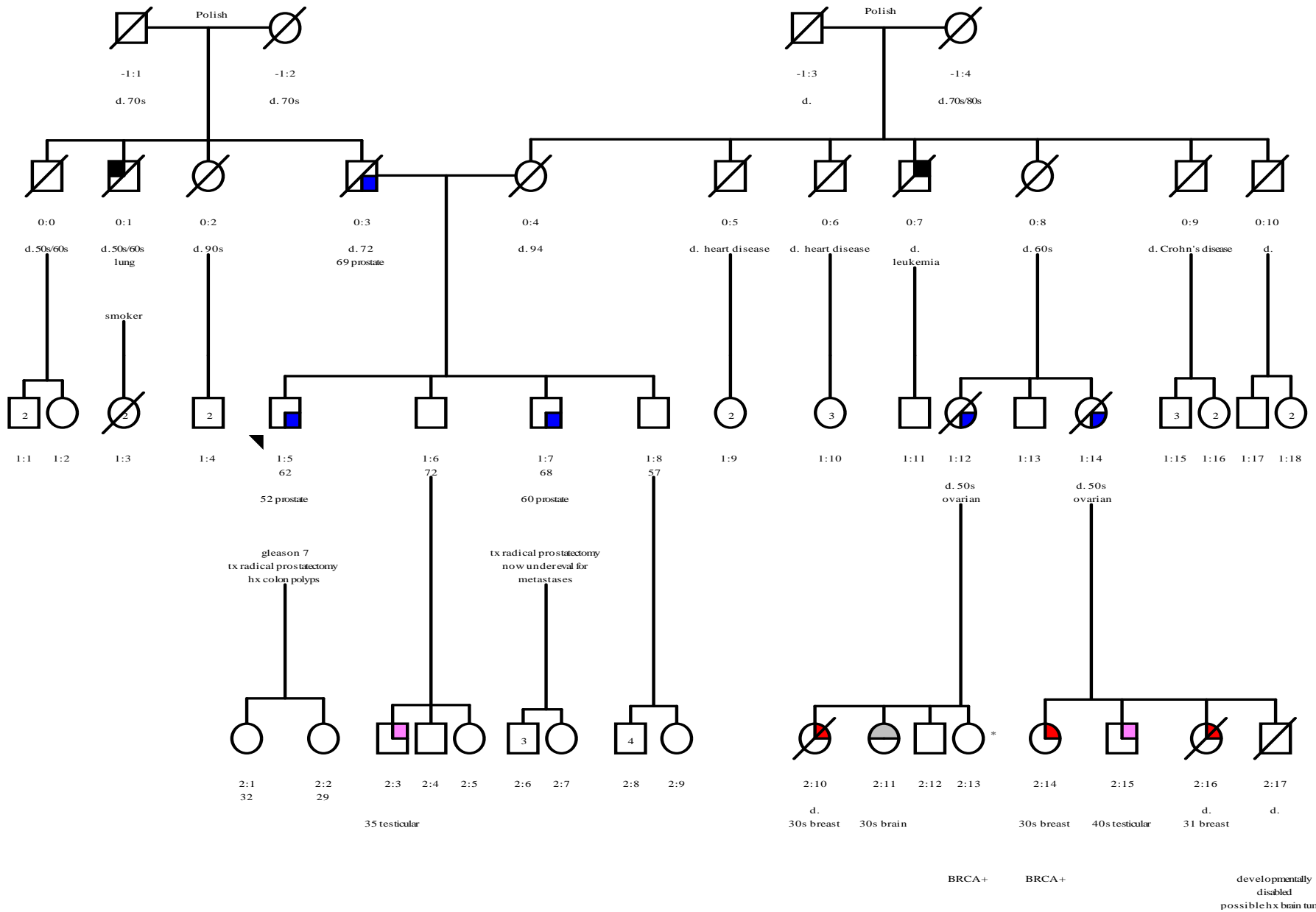
incersite 1 = prostate



Prostate Cancer?

- ▶ 62 yo male accompanied wife to CGS consult d/t her personal/family history
- ▶ Shared his personal and family history of prostate cancer
- ▶ Scheduled an individual consult and pursued testing





BRCA2

Cancer Risks

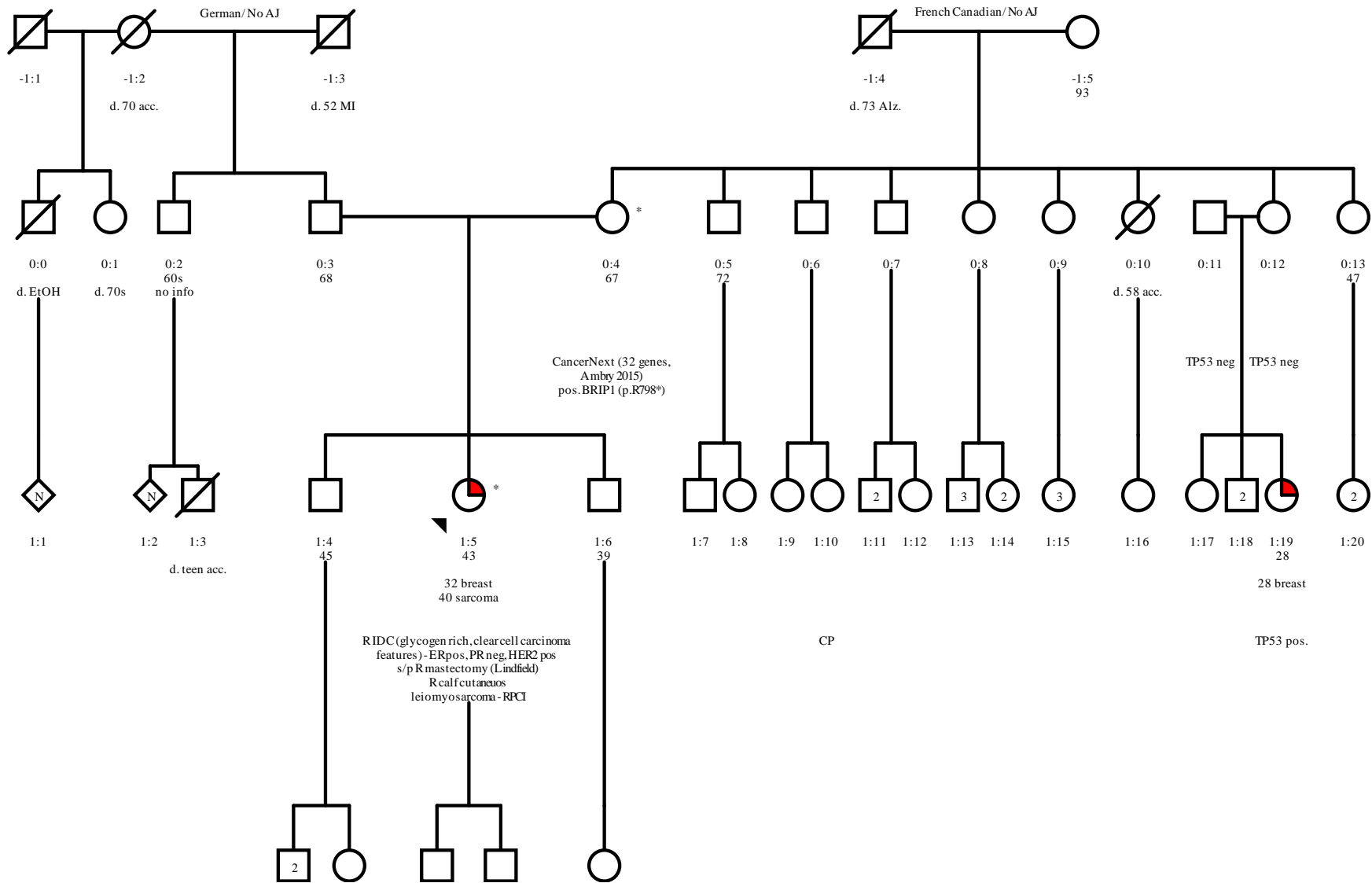
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 - ▶ Others

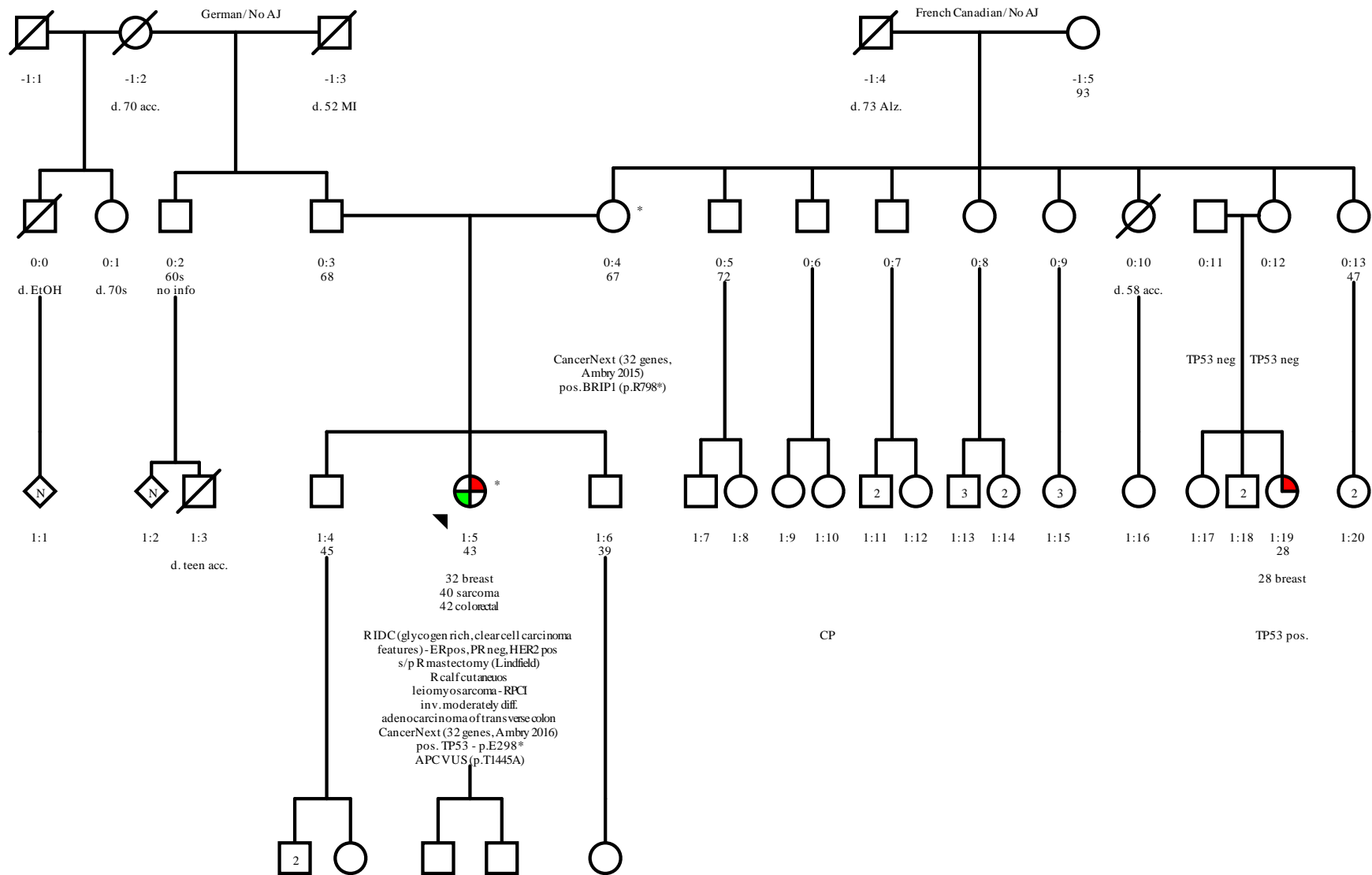
Management

- ▶ Additional treatment option (clinical trial/ off label)
 - ▶ PARP inhibitors
- ▶ Consideration of pancreatic cancer screening
- ▶ Identification of at-risk family members
 - ▶ Early detection
 - ▶ Prevention
 - ▶ Family planning (Fanconi Anemia)

Young, multiple cancers

- ▶ 43 yo female
- ▶ **Breast cancer** diagnosed at age 32 – treated in community
- ▶ **Leiomyosarcoma** diagnosed at age 40 – treated at Roswell Park!
- ▶ Eventual referral from community to CGS





Li-Fraumeni syndrome

- ▶ SBLA
 - ▶ Sarcoma
 - ▶ Breast/brain
 - ▶ Leukemia (acute)/ lymphoma
 - ▶ Adrenocortical carcinoma

Li-Fraumeni syndrome

Cancer risks

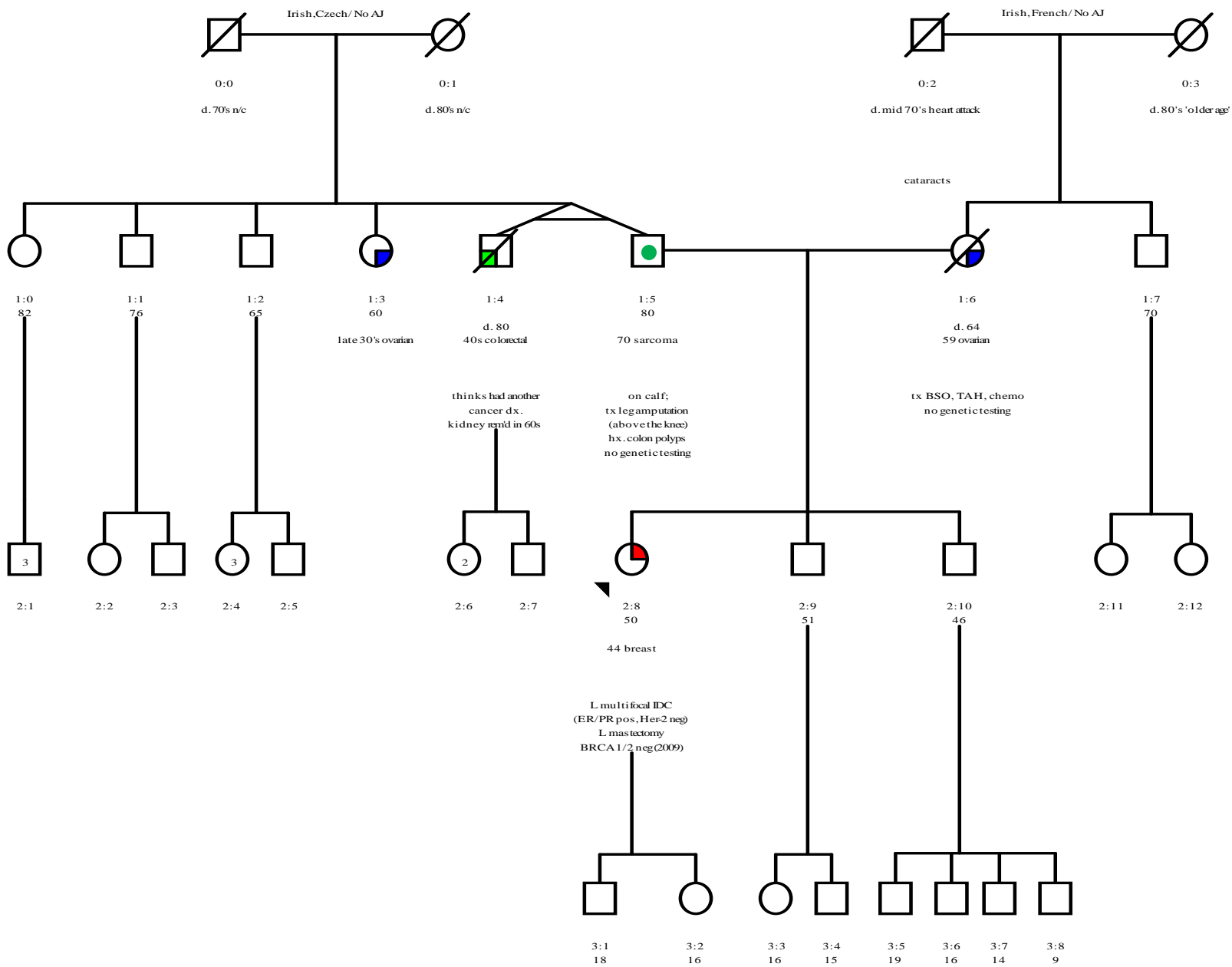
- ▶ >90% cancer risk by age 60
- ▶ Risk for multiple malignancies
- ▶ Almost every type of cancer has been reported
- ▶ Malignancy risk in early life

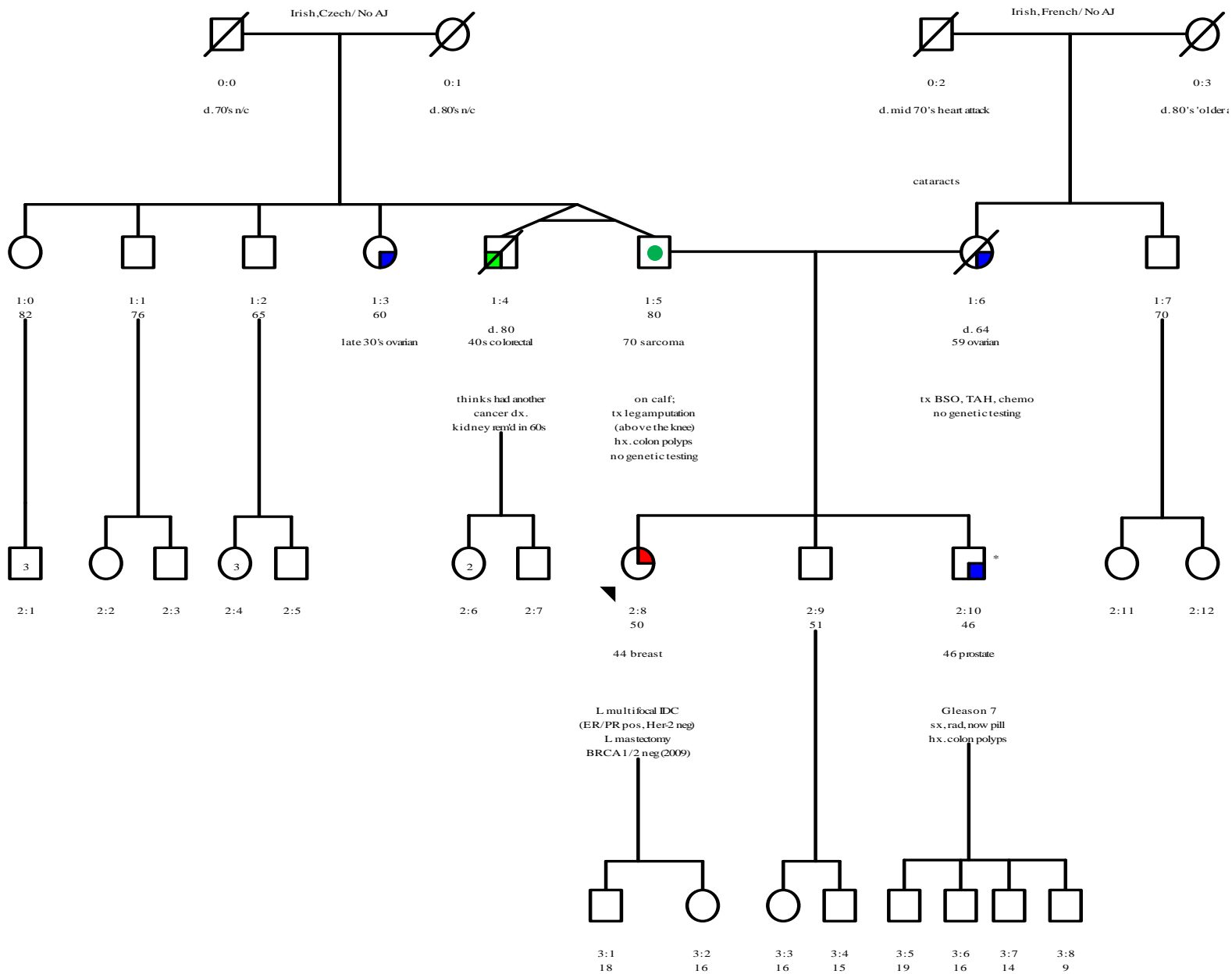
Management

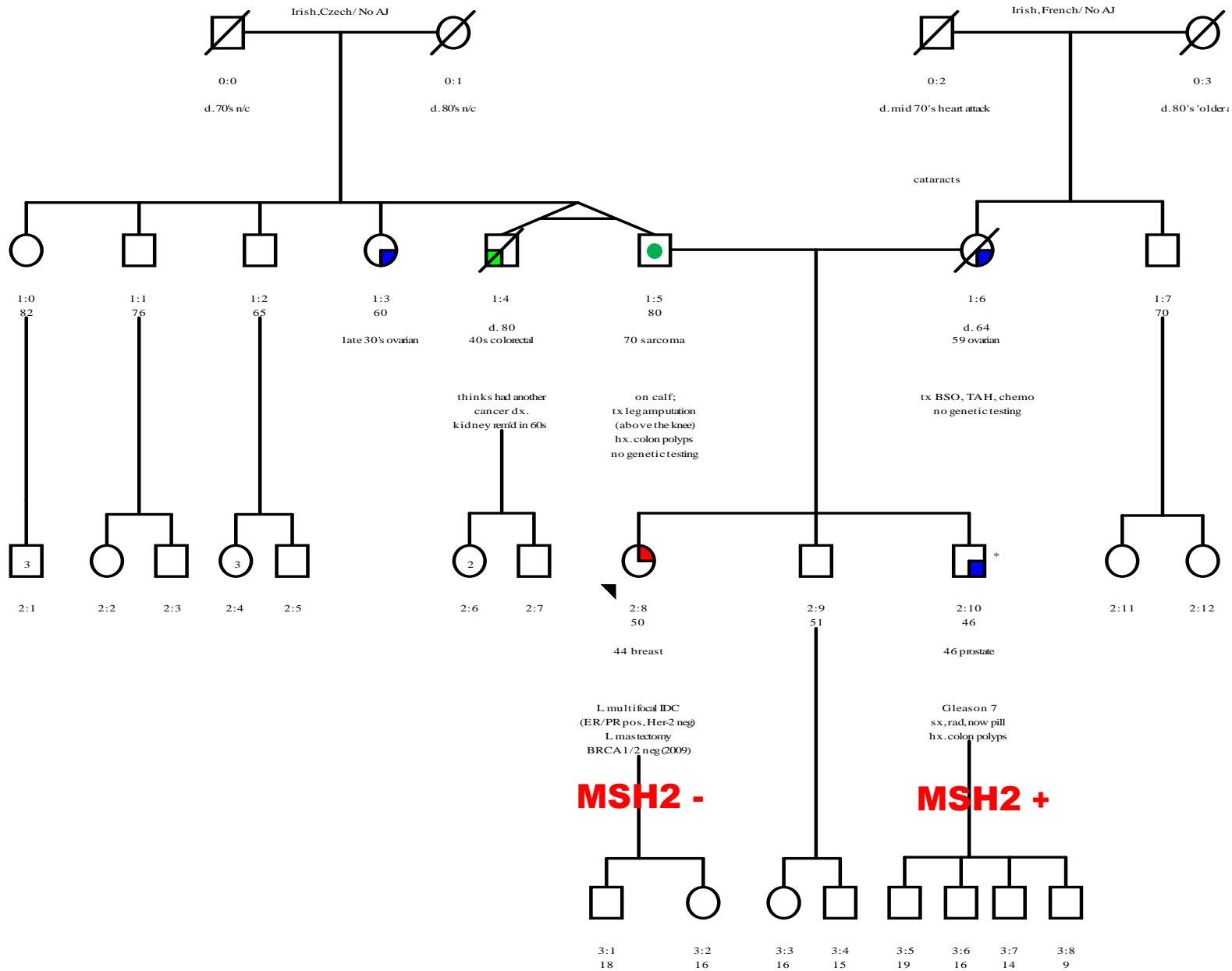
- ▶ FULL BODY and brain MRI yearly (at time of dx.)
- ▶ Breast MRI (age 20) and mammogram (age 30)
- ▶ Colonoscopy (age 25 q2-5y)
- ▶ Dermatologic exam (age 18)
- ▶ Avoid radiation
- ▶ Trials – blood work, others
- ▶ Two adolescent sons – proactive management

Who to test?

- ▶ 50 yo female w/ history early-onset breast cancer and mother with ovarian cancer
- ▶ BRCA1/2 negative (2010) – prior to multigene panels







Lynch syndrome

Cancer risks

- ▶ Risk for breast cancer NOT well defined!
- ▶ Risks
 - ▶ Colon: up to 80%
 - ▶ Uterine: up to 60%
 - ▶ Ovarian: up to 24%
 - ▶ Others: stomach, pancreatic, ureter, renal pelvis, skin, brain

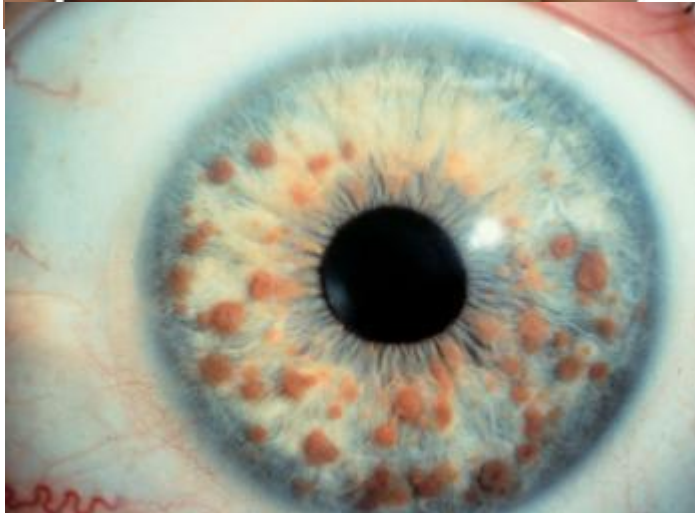
Management

- ▶ NO recommendations for breast
- ▶ Colonoscopy every 1-2 years starting at 25
- ▶ Consider prophylactic TAH-BSO
- ▶ Other? – per fhx.

Personal and family history of NOT cancer....

- ▶ 44 year old recently diagnosed with breast cancer
- ▶ Personal history:
 - ▶ Astrocytoma
 - ▶ Freckling
 - ▶ CALs
 - ▶ Skin bumps
- ▶ Fhx. mother diagnosed with a GIST, brother diagnosed with glioblastoma

Neurofibromatosis type 1



Neurofibromatosis type 1

Cancer Risks

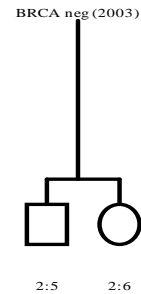
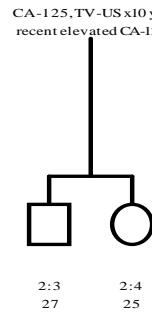
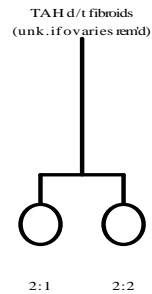
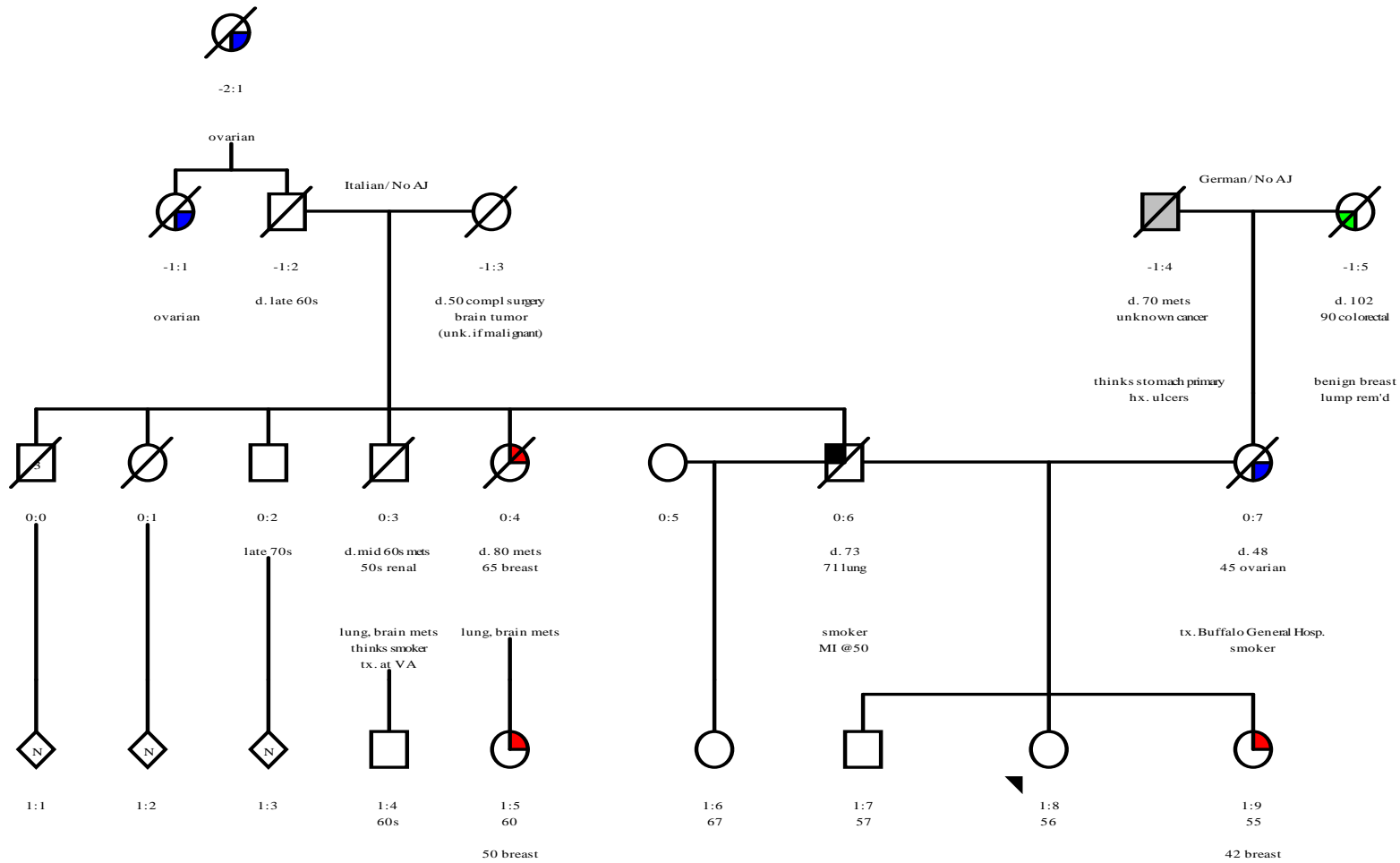
- ▶ Breast cancer
 - ▶ 4x increased risk at <50
- ▶ GISTs
- ▶ Brain tumors/cancer
- ▶ Optic nerve
- ▶ Malignant peripheral nerve sheath tumors

Management

- ▶ Mammogram and MRI from 30-50
- ▶ Annual PE with developmental screen
- ▶ Annual dermatologic exam
- ▶ Annual ophthalmologic
- ▶ Regular BP eval

Family History

- ▶ 56 yo female
- ▶ Mother diagnosed with ovarian cancer; GYN screening w/ CA-125 and TV-US yearly
- ▶ Recent elevated CA-125 (165)
- ▶ Referral to Roswell Park – negative CT



BRCA1 and BRCA2 positive

Cancer Risks

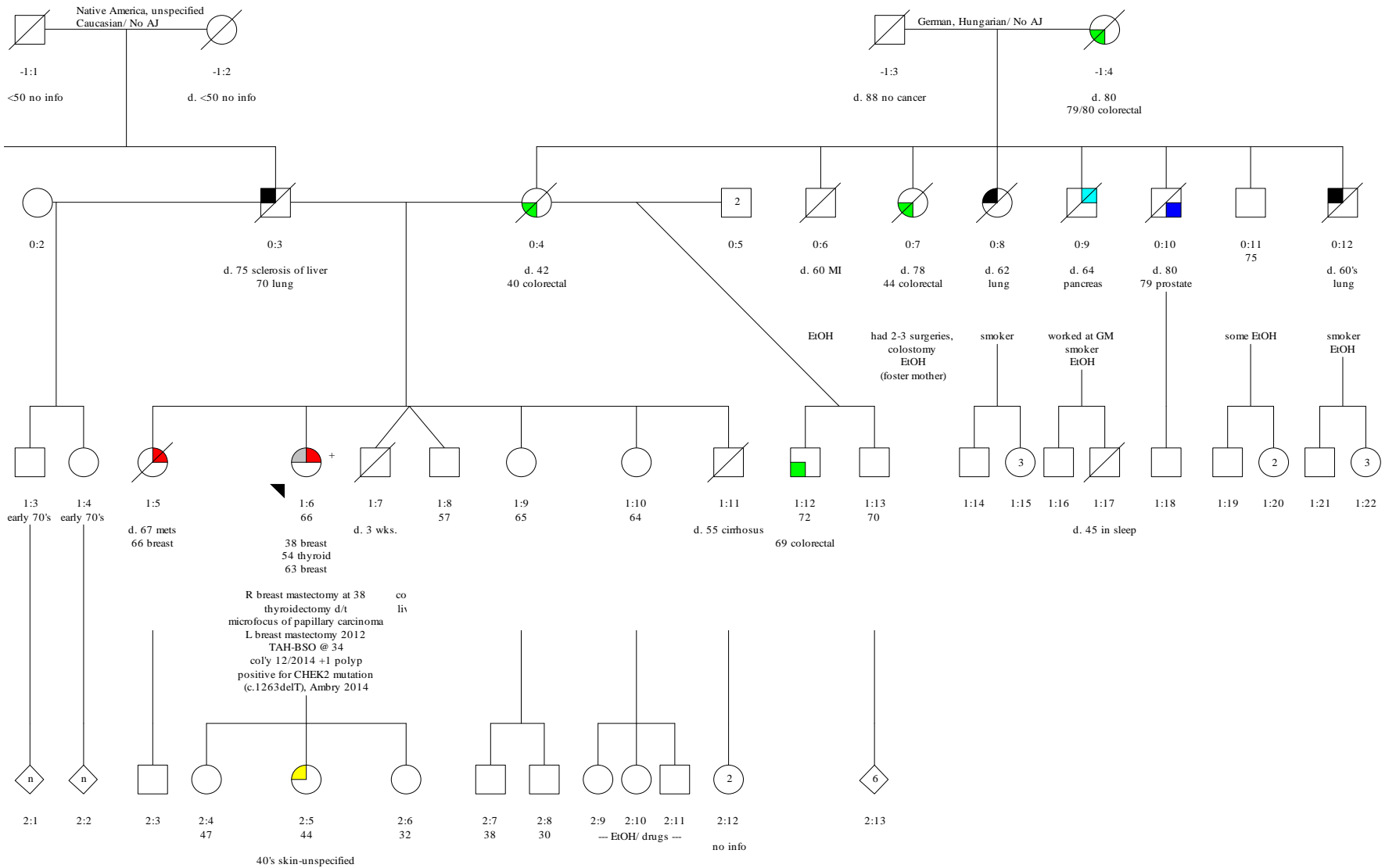
- ▶ Quote highest risk associated with each BRCA1 and BRCA2 – not additive
- ▶ More common in those with Ashkenazi Jewish ancestry
 - ▶ 1 in 40 carrier frequency

Management

- ▶ As both BRCA1 and BRCA2 pos
- ▶ At risk relatives (sibs/kids)
 - ▶ 50% risk for EACH BRCA1 and BRCA2

Multiple primaries

- ▶ Personal history
 - ▶ Breast at 38
 - ▶ Thyroid at 54
 - ▶ Breast at 63 (opposite breast)
- ▶ Family history
 - ▶ Multiple relatives with colon cancer



CHEK2

Cancer Risks

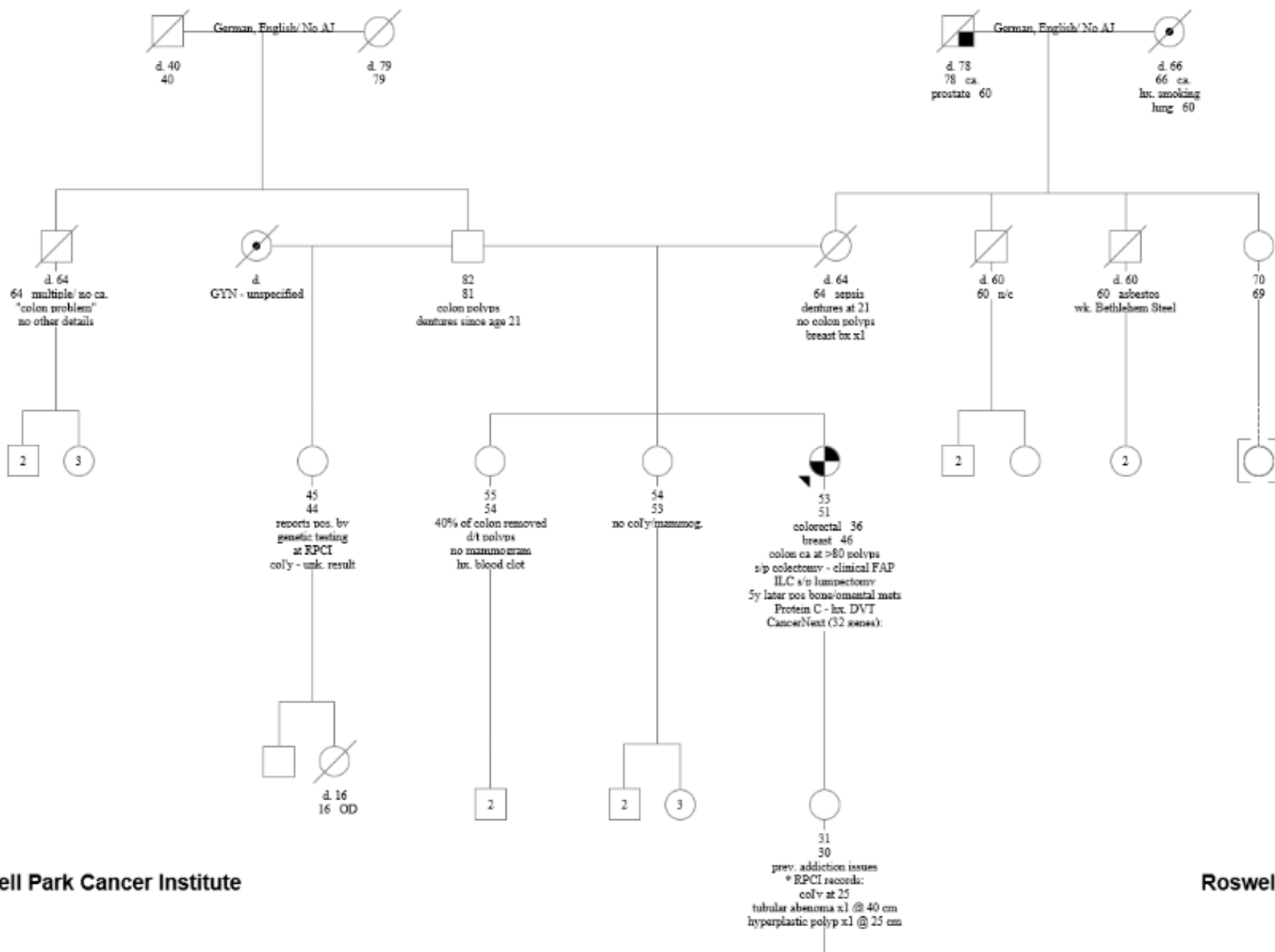
- ▶ Breast cancer
 - ▶ 2-3x
- ▶ Colon cancer
 - ▶ 2x
- ▶ Others
 - ▶ Uterine
 - ▶ Thyroid
 - ▶ Prostate
 - ▶ Melanoma
 - ▶ More!

Management

- ▶ Breast MRI in addition to mammograms
- ▶ Colonoscopy at age 40 and continue every 5 years
- ▶ Other
 - ▶ Based on fhx.

Family history

- ▶ 51 yo female with metastatic breast cancer
 - ▶ First diagnosed with colon cancer 36
 - ▶ >80 polyps – clinically managed as FAP
 - ▶ Breast cancer diagnosed at 46 – just under 5 years later was found to have diffuse metastatic disease



MUTYH Associated Polyposis

Cancer Risks

- ▶ Colon polyps (<100)/cancer
- ▶ Duodenal polyps/cancer (5%)
- ▶ OTHERS – not well defined

Management

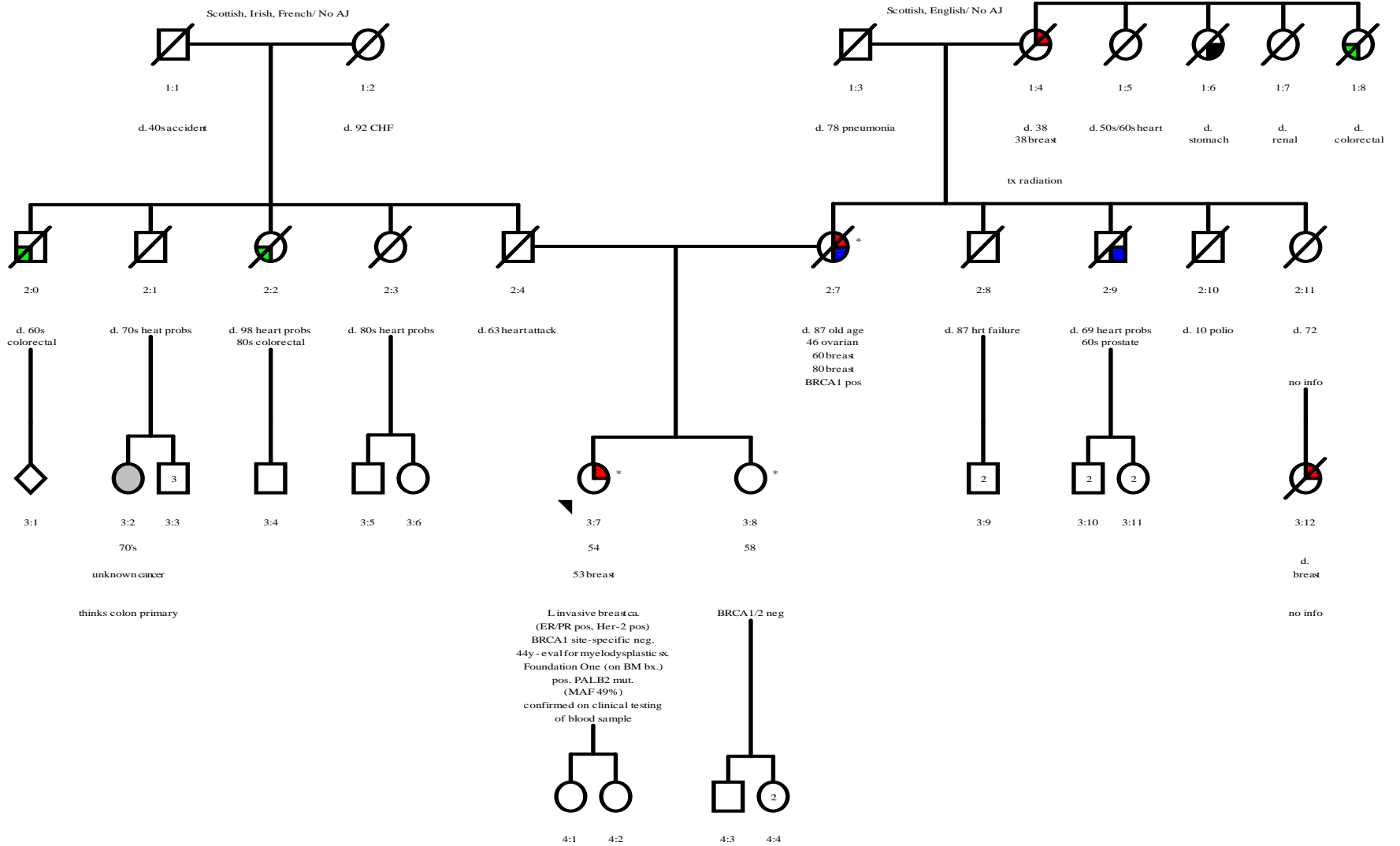
- ▶ Colonoscopy at 25-30; every 2-3y
- ▶ Upper endoscopy at 30-35
- ▶ Others – per fhx.
- ▶ Autosomal Recessive
 - ▶ 25% risk to siblings
 - ▶ Risk to children depends on partner's status (1% carrier frequency)

Tumor testing

- 54 yo female w/ recent diagnosis of breast cancer
- Previous negative testing for familial BRCA1 mutation
- Evaluation for myelodysplastic syndrome – had Foundation One testing on blood sample

Somatic testing

- ▶ Analysis of the genetic make up of cancer cells
- ▶ Reflect acquired (somatic) changes in the cancer cells
- ▶ MAY identify alterations that are hereditary



PALB2

Cancer Risks

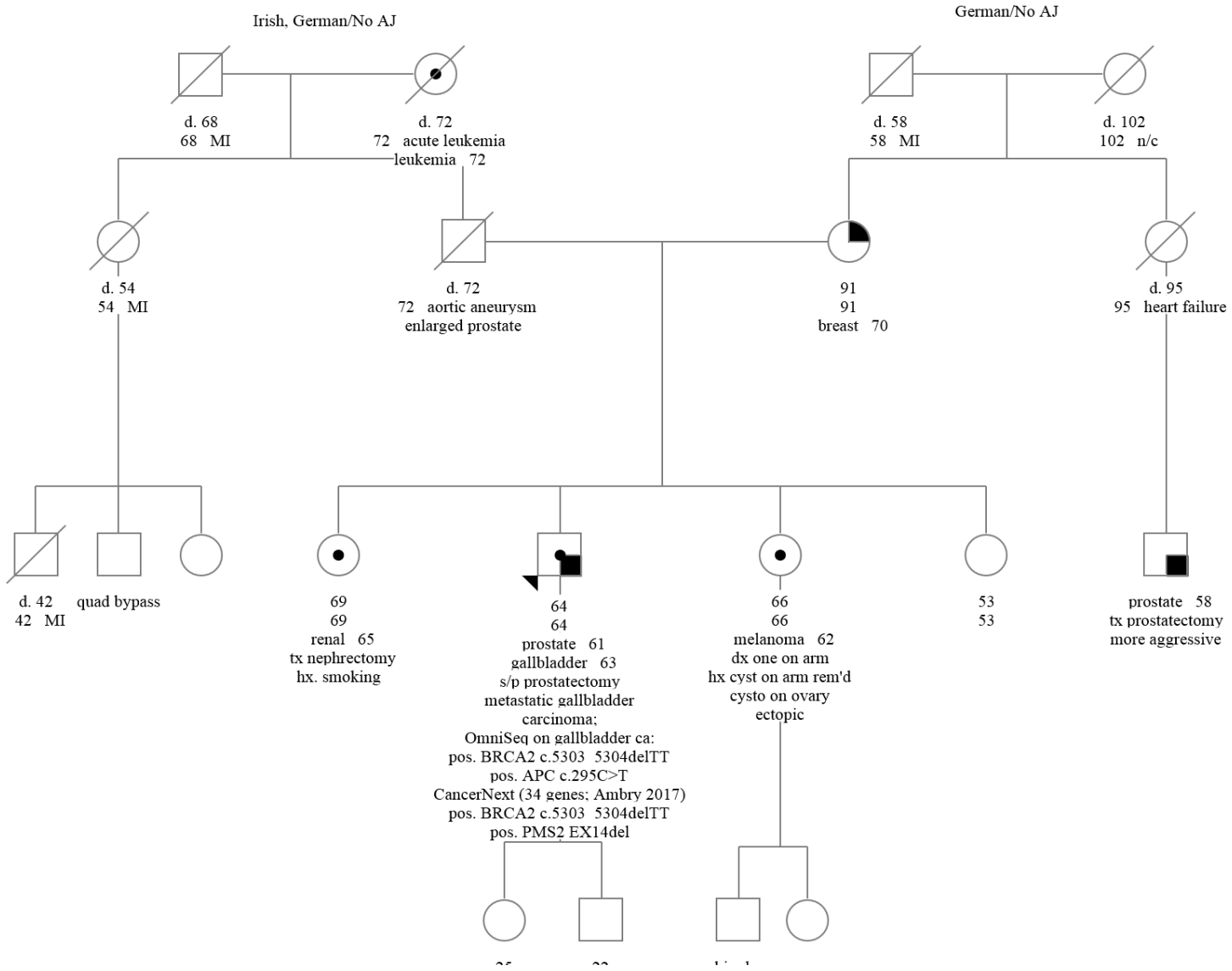
- ▶ Breast
 - ▶ 2-4x
- ▶ Pancreatic
 - ▶ “elevated”
- ▶ ?Prostate, Ovarian

Management

- ▶ Breast MRI and mammogram
- ▶ Pancreatic screenings in the presence of a fhx.
- ▶ Others – per fhx.

Somatic testing

- ▶ 64 yo male
 - ▶ Prostate cancer
 - ▶ Metastatic gallbladder cancer at 63
 - ▶ Tumor testing – BRCA2 pos.



BRCA2 and PMS2

Cancer Risks

- ▶ BRCA2
 - ▶ Breast/ovarian
 - ▶ Prostate
- ▶ Lynch
 - ▶ Colon, Uterine, Ovarian, Pancreatic, Renal, Prostate, ?breast

Management

- ▶ BRCA2
- ▶ Lynch
- ▶ Children at 50% risk for *each* condition!
- ▶ Treatment
 - ▶ Olaparib
 - ▶ Keytruda

Tumor testing - cautions

- ▶ refer based on personal/ family history and separately based on result
- ▶ germline mutations may be revealed or masked by testing tumor
- ▶ blood sample = germline testing

Genotype: Phenotype

- ▶ Multiple genes – all cause higher breast cancer risk
- ▶ May or may not be associated with other health/cancer risks
- ▶ Same genetic change in different individuals = different outcomes
- ▶ NOT 100% risk to develop cancer!

Value

- ▶ Surgical decision making
- ▶ Risk reducing surgeries/
enhanced screenings
- ▶ Targeted therapies!

QUESTIONS?

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