I have no financial disclosures.
Family Health History Assignment

• How is knowing your family health history helpful?

• What did you learn from the assignment?

• What challenges did you face?

• Do you plan to share information with your family?

• Do you plan to share with your physician?
Discussion Outline

• Cancer genetic counseling

• Review process to identify families with hereditary disease

• Discuss clinical significance of hereditary cancer

• Review two practical cases
  • Assessment, medical management, family issues

• Discuss information learned (and not learned) from genetic testing

• Review significance of young adults with cancer
Genetic Counselors

- Genomics
- Psychiatric
- Population
- Pediatric
- Newborn
- Laboratory
- Adult
- Metabolic
- Hematology
- Health screening
- Cancer Prenatal
- Education
- Public
- Administration
- Research
- Cardiology
- Neurogenetics
Cancer genetic counseling and risk assessment is the **process** of **identifying** and **educating** individuals and their **families** at increased risk of developing cancer.

Cancer genetic counseling acknowledges the **psychosocial sequelae** associated with inherited disease.

Riley, J Genetic Counseling, 2012
Who is referred for GC?

• Any person with a family history of cancer suggestive of hereditary disease
• Any person who has a family member with a known gene mutation
• Any person who was diagnosed with cancer at an early age or who has more than one primary cancer type
• Any person who is considering alterations in medical care based on his or her family history of cancer
• Any person who is interested in learning more about genetic testing for cancer

Hampel, J Med Genetics, 2004
Clinical Genetics Assessment

Contracting → Assessment → Education

Testing disclosure → Yes → Genetic testing

Testing interpretation

NON-INFORMATIVE

INFORMATIVE

Medical management based on gene mutation

Medical management based on personal & family history

Long term follow-up

Long term follow-up
TWO ROADS DIVERGED IN A WOOD, AND I,

I took the one less traveled by,

AND THAT HAS MADE ALL THE DIFFERENCE.

~ Robert Frost
Accumulation of somatic genetic abnormalities over time
Sporadic cancer

Normal cell

Cancer cell

Hereditary cancer

Normal cell

Cancer cell

Time
Cancer Genetics Classification

- **Sporadic**
  - No known inherited predisposition to develop cancer

- **Hereditary**
  - High cancer risk
  - Single gene mutation

- **Familial**
  - Modest to low cancer risk
  - One or multiple gene mutations
Breast Cancer

Lung Cancer

Lichtenstein, New England Journal of Medicine, 2000
“Breast Cancer” genes identified to date account for ~20% of hereditary/familial risk.

Genes identified to date:

- **High risk (Frequency: rare)**
  - BRCA1, BRCA2, TP53, PTEN, STK11, CDH1, CHK2, PALB2

- **Moderate risk (Frequency: rare)**
  - BRIP1, BARD1, RAD51C, RAD51D, RAD50, ATM, MRE11A, RAD50, NBN

- **Low risk (Frequency: common)**
  - FGFR2, TNrC9, MAP3K1, CASP8

Stratton, Nature Genetics, 2008
Gene discovery

Positive changes in family medical care
Getting back to the basics
Documenting the Family History

Family Members

<table>
<thead>
<tr>
<th>No.</th>
<th>Full Name</th>
<th>Date of birth</th>
<th>Chronic health problems, serious illnesses, birth defects</th>
<th>Age at death &amp; cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Example</td>
<td>09/16/48</td>
<td>breast cancer @ 40 years; endometriosis</td>
<td>still living</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Family history reporting

Family history
Family history is non-contributory.

OR

Family history
The patient mother’s had breast cancer. An aunt had stomach cancer, an uncle had lung cancer, and a cousin had ovarian cancer. Her grandmother also had ovarian cancer.
Key:
- Male, Female
- Deceased
- Cancer

MATERNAL GRANDMOTHER
MATERNAL GRANDFATHER
MATERNAL UNCLE
MATERNAL FIRST COUSIN – ONCE REMOVED

PATERNAL GRANDMOTHER
PATERNAL GRANDFATHER
PATERNAL UNCLE Colon CA – 78 years
PATERNAL AUNT

MOTHER
FATHER

28 PROBAND Colon Ca

DAUGHTER

SISTER
NEPHEW
MATERNAL GRANDMOTHER
Gastric Ca

MATERNAL GRANDFATHER

MATERNAL UNCLE
d. Colon CA – 45

MATERNAL COUSIN
Colon Ca - 38

MATERNAL FIRST COUSIN – ONCE REMOVED

MOTHER Uterine Ca

FATHER

PATERNAL GRANDMOTHER

PATERNAL UNCLE

PATERNAL GRANDFATHER

P

28 PROBAND
Colon Ca

DAUGHTER

SISTER

NEPHEW

Key

Male, Female

Deceased

Cancer
Evaluate each side of the family

What is her family based cancer risk?
Collecting pathology records...

Gastric Cancer –

Breast cancer --

Gastric Cancer –

Breast cancer --
Collecting pathology records...

Gastric Cancer – Gastrointestinal Stromal Tumor

Breast cancer -- Ductal cancer

Gastric Cancer – Diffuse; signet ring carcinoma

Breast cancer -- Lobular cancer
Collecting death certificates

<table>
<thead>
<tr>
<th>BIRTH</th>
<th>DEATH</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAME ON CERTIFICATE (FIRST)</td>
<td>NAME ON CERTIFICATE (FIRST)</td>
</tr>
<tr>
<td>(MIDDLE)</td>
<td>(MIDDLE)</td>
</tr>
<tr>
<td>(LAST)</td>
<td>(LAST)</td>
</tr>
<tr>
<td>ALSO KNOWN AS: (INDICATE IF NAME COULD BE REGISTERED UNDER ANOTHER NAME)</td>
<td>PLACE OF DEATH (CITY)</td>
</tr>
<tr>
<td></td>
<td>(COUNTY)</td>
</tr>
<tr>
<td>DATE OF BIRTH (MONTH)</td>
<td>DATE OF DEATH (MONTH)</td>
</tr>
<tr>
<td>(DAY)</td>
<td>(DAY)</td>
</tr>
<tr>
<td>(YEAR)</td>
<td>(YEAR)</td>
</tr>
<tr>
<td>PLACE OF BIRTH (CITY)</td>
<td>DATE OF BIRTH</td>
</tr>
<tr>
<td>(COUNTY)</td>
<td>AGE</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SEX</td>
</tr>
<tr>
<td></td>
<td>RACE</td>
</tr>
<tr>
<td>HOSPITAL</td>
<td>SPOUSE'S NAME (FIRST)</td>
</tr>
<tr>
<td></td>
<td>(MIDDLE)</td>
</tr>
<tr>
<td></td>
<td>(LAST)</td>
</tr>
<tr>
<td>FATHER'S NAME (FIRST)</td>
<td>FATHER'S NAME (FIRST)</td>
</tr>
<tr>
<td></td>
<td>(MIDDLE)</td>
</tr>
<tr>
<td></td>
<td>(LAST)</td>
</tr>
<tr>
<td>MOTHER'S NAME (FIRST)</td>
<td>MOTHER'S NAME (FIRST)</td>
</tr>
<tr>
<td></td>
<td>(MIDDLE)</td>
</tr>
<tr>
<td></td>
<td>(MAIDEN)</td>
</tr>
</tbody>
</table>

*Certified copies are computer generated and are valid for all legal purposes.

Legal Amendment Fee - $10.00. A filing fee is required to process adoptions, court orders and filing delayed certificate.

If the record is not found, no record statement will be issued and fees will be retained for search of the files.

Fees are retained and valid for one year from date received by this office.

Your signature | Day Time Phone |
|---------------|---------------|

Address: [StREET | CITY | STATE | ZIP]

Purpose for which certified copy is to be used:

Your relationship to person identified on certificate (self, mother, spouse, etc.) if legal guardian, must provide guardianship papers.

If legal representative - indicate legal relationship.

WARNING: False application for a certified copy of a vital record is a felony punishable by a fine up to $5,000, five years in prison.
Physical examination

At present, physical examination is minimally useful.
Some notable exceptions:
Physical examination

At present, physical examination is minimally useful.
Some notable exceptions:

MEN2B  Peutz Jeghers syndrome  Cowden syndrome
Features of hereditary cancer

PERSONAL FEATURES
• Young age at diagnosis
• Multiple primary cancers in a single individual
• Unusual tumor histology
• Bilaterality in paired organs or multifocal disease
• Uncommon presentation of cancer
• Rare cancer types

FAMILY HISTORY FEATURES
• Multiple affected individuals - closely related to one another
• Cancers occurring in multiple generations
• Clusters of the same type of cancer
• Combination of cancers suggestive of a known syndrome
• Ethnic background known to be associated with increased risk for specific cancer syndrome(s)

Hampel, J Medical Genetics, 2004; NCCN 2011
Clinical significance

Hereditary cancer syndromes associated with highest cancer risk

• Offer intensified cancer surveillance
• Provide risk-reducing medical or surgical interventions
• Use genetic testing to assist with medical management and follow-up
• Identify at-risk family members
• Provide targeted therapy or chemoprevention
  – e.g. PARP inhibitors
Male, Female
Deceased
Cancer

Key

Male, Female
Deceased
Cancer
Case Discussions
Family 1

- Family Member 1: d. Pancreatic cancer - 51
  - Family Member 2: d. Heart disease
  - Family Member 3: Sally, 74 Healthy
  - Family Member 4: FATHER: d. Prostate Ca - 49
  - Family Member 5: MOTHER: Healthy - 75

- Michelle, 43 Breast CA- 40
- 36
- 38

- Jeanne, 42 Breast Ca- 38
  - 22

- 45 Ovarian ca - 41
  - 25

- 50 Healthy

- d. Heart disease - Elderly
“Breast Cancer” genes identified to date account for ~20% of hereditary/familial risk.

High risk
Frequency: rare
- BRCA1
- BRCA2
- TP53
- PTEN
- STK11
- CDH1
- CHK2
- PALB2
- ATM
- BRIP1
- BARD1
- MRE11A
- RAD51C
- RAD51D
- RAD50
- ATM
- MRE11A
- NBN
- FGFR2
- TNrC9
- MAP3K1
- CASP8

Moderate risk
Frequency: rare
- Hereditary
- Familial

Low risk
Frequency: common
- Hereditary
- Familial

Stratton, Nature Genetics, 2008
<table>
<thead>
<tr>
<th><strong>BRCA1</strong></th>
<th><strong>BRCA2</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td><strong>Women</strong></td>
</tr>
<tr>
<td>~ 40 - 80% breast cancer risk</td>
<td>~ 40 - 80% breast cancer risk</td>
</tr>
<tr>
<td>- ER- PR- Her2Neu -</td>
<td>- ER+ tumors</td>
</tr>
<tr>
<td>~ second primary breast ca</td>
<td>~ second primary breast ca</td>
</tr>
<tr>
<td>~ 40% ovarian cancer risk</td>
<td>~ 11 - 20% ovarian cancer risk</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td><strong>Men</strong></td>
</tr>
<tr>
<td>~ up to 40% prostate cancer</td>
<td>~ up to 40% prostate cancer</td>
</tr>
<tr>
<td>~ male breast cancer</td>
<td>~ male breast cancer</td>
</tr>
<tr>
<td><strong>Women and Men</strong></td>
<td><strong>Women and Men</strong></td>
</tr>
<tr>
<td>~ up to 7% pancreatic cancer</td>
<td>~ up to 7% pancreatic cancer</td>
</tr>
<tr>
<td>~ melanoma (skin &amp; eye)</td>
<td>~ melanoma (skin &amp; eye)</td>
</tr>
<tr>
<td>~ gastric cancer</td>
<td>~ gastric cancer</td>
</tr>
<tr>
<td>~ hepatobiliary tumors</td>
<td>~ hepatobiliary tumors</td>
</tr>
</tbody>
</table>
Medical Recommendations

BRCA1 and BRCA2

Surveillance options
Mammography + Breast MRI – begin at 25 years
Ovarian cancer surveillance – Ultrasound + CA125 levels

Annual skin and eye evaluation
Prostate cancer surveillance – begin at 40 years

Risk reducing options
Bilateral mastectomy
Prophylactic Tamoxifen
Bilateral salpingo oophorectomy
Mutation Frequency

2.7% (2-3/100)  Ashkenazi Jewish ancestry
<1% (1 in 400)  Other Northern European ancestry

Likelihood of mutation increases with positive fm hx
Family 1

- **Jeanne**, 42
  - Breast Ca - 38
  - **BRCA1 +**
  - 22

- **Michelle**, 43
  - Breast Ca - 40
  - 36
  - 38

- **Sally**, 74
  - Healthy

- **FATHER**
  - d. Prostate Ca - 49

- **MOTHER**
  - Healthy - 75
  - 45
  - Ovarian ca - 41
  - 25

- d. Pancreatic ca - 51
- d. Heart disease
- d. Heart disease - Elderly
Family 1

- **BRCA1 +**
  - Michelle, 43
    - Breast CA - 40
  - Jeanne, 42
    - Breast CA - 38
    - Ovarian CA - 41
  - 50 Healthy

- **BRCA1 -**
  - FATHER
    - d. Prostate Ca - 49
  - MOTHER
    - Healthy - 75
  - 45
  - 25

- **Sally, 74**
  - Healthy

- d. Heart disease
  - d. Pancreatic CA - 51
  - d. Heart disease
  - d. Heart disease - Elderly
Clinical / Family Issues

What do we learn and not learn from genetic testing?

What do we offer family members with a mutation and at what age do we begin?

What factors play in the decision to pursue risk-reducing medical and surgical options?

What if a mutation had not been identified, how would the family be followed?

How do individuals make medical decisions?

How do families communicate information to one another?

How do family members work through differences in their approach?
Family 2

Gastric Ca- 64

Lobular Breast Ca – 38
Gastric Cancer - 46

Catherine
Diffuse Gastric Cancer - 29

Gastric Ca- 67

FATHER
d. Diffuse Gastric Ca- 42

MOTHER
Healthy - 69

Mary
36

9
7
4

Chris
33

1
Some inherited “GI” cancer syndromes

Lynch syndrome: MLH1, MSH2, MSH6, PMS2, EPCAM

Familial adenomatous polyposis: APC

MYH associated polyposis: MYH

Juvenile polyposis syndrome: BMPR1A, SMAD4

Cowden syndrome: Pten

Peutz-Jeghers syndrome: STK11

Hereditary diffuse gastric cancer: E-cadherin (CDH1)

Hereditary pancreatic cancer: BRCA2, PALB2

Li-Fraumeni syndrome: TP53

Hereditary GI stromal tumors: SDHB, SDHD, SDHC

Lindor, JNCI Monograph, 2008
Hereditary Diffuse Gastric Cancer syndrome (HDGC)

Tumor Spectrum
– Diffuse gastric cancer
  • Average age of onset = 38 years
  • Youngest reported age at diagnosis = 14 years
  • Risk for women (83%), for men (67%)
– Lobular breast cancer
  • ~ 40% lifetime risk
– Colon cancer
  • ~ ??? Increased risk

Genetics
– E(epithelial) cadherin (CDH1); 16q22.1
  • Mutations account for 1/3rd of hereditary diffuse gastric cancers

Pharoah et al, Gastroenterology 2001; Oliveria, Human mutation, 2002
## Medical Recommendations

<table>
<thead>
<tr>
<th>Surveillance options</th>
<th>Risk reducing options</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Endoscopy</td>
<td>- Gastrectomy</td>
</tr>
<tr>
<td>- Chromoendoscopy</td>
<td>- Mastectomy</td>
</tr>
<tr>
<td>- Mammography</td>
<td></td>
</tr>
<tr>
<td>- Breast MRI</td>
<td></td>
</tr>
<tr>
<td>- Colonoscopy</td>
<td></td>
</tr>
</tbody>
</table>

Lewis, Surgery, 2001; Carneiro, J Path, 2004
Family 2

- Catherine: Diffuse Gastric Cancer - 29
  - CDH1 -
- Mary: 36
- Chris: 33
- FATHER: d. Diffuse Gastric Ca- 42
- MOTHER: Healthy - 69
- Lobular Breast Ca – 38
  - Gastric Cancer - 46
- Gastric Ca- 67
- d. "Stomach Ca" - 35
- Gastric Ca- 64
Family 2 – example of common testing mistake

Gastric Ca- 64
Lobular Breast Ca – 38
Diffuse Gastric Cancer - 29
Gastric Ca- 67
Diffuse Gastric Cancer Ca- 42
Mary 36
CDH1 -

Catherine
Gastric Cancer - 46

FATHER
d. "Stomach Ca" - 35

MOTHER
Healthy - 69
Chris 33

9 7 4
3 1
Clinical / Family Issues

How should this family be followed given a gene mutation was not identified?

Should family members consider prophylactic gastrectomy?

How do we support them in their medical decision making?

Do individuals understand risk estimates?

What is the level of risk that individuals change behavior?

Does this risk level vary with each person?

How do family members work through differences in their approach?
Genetics Communication study

Exploring the experience of relatives with whom genetic test results are communicated

M Daly, S Montgomery R Bingler, A Barsevik, K Ruth; Fox Chase, Philadelphia PA

422 women receiving BRCA1 and BRCA2 gene testing results (probands) 2000 - 2003

Communication intervention
N = 137 (32 withdrew, 50 lost of follow-up)

Wellness control group
N = 112 (45 withdrew, 46 lost to follow-up)

Disclosure of test results

3-month follow-up with probands

4-month follow-up with relatives

Montgomery, Familial Cancer, 2013
Genetics Communication Study

1,046 1st / 2nd degree relatives identified

838 (80.1%) relatives received results

99% of probands shared with at least one relative

Probands’ communication
• Female relatives more likely to receive results than male relatives*
• Adult children more likely to receive results than parents/siblings*
• Positive/negative results more likely to be communicated than VUS

Relatives’ receipt and processing of information (manuscript in preparation)
• 26% of relatives cited **INCORRECT** test result
  • Most accurate with positive result – mutation identified*
  • Least accurate with VUS – variant of unknown significance identified
• 32% relatives reported difficulty understanding information
• 52% relatives reported intention to pursue genetic testing

* Statistically significant  \( p \leq 0.005 \)

Montgomery, Familial Cancer, 2013
• Perceived control – proband’s ability to communicate results
• Subjective norms – proband’s perception of relative’s opinion of testing

Montgomery, Familial Cancer, 2013
Cancer Genetic Testing

Tumor Analysis  Germline Analysis

Gene discovery

Positive changes in family medical care
Genetic analysis of tumors

Grade II, 1.0cm, ER-, PR-, Her2/Neu-

Grade II, 1.0cm, ER-, PR-, Her2/Neu-

Grade II, 1.0cm, ER-, PR-, Her2/Neu-
Genetic analysis of tumors

Grade II, 1.0cm, ER-, PR-, Her2/Neu-

Clinical testing
Used to identify targeted therapies

Grade II, 1.0cm, ER-, PR-, Her2/Neu-

Research studies
Distinguish the genetic characteristics of tumors

Grade II, 1.0cm, ER-, PR-, Her2/Neu-
Germline Genetic Testing – Key Points

• **ALWAYS START** genetic testing with an affected family member, when possible.

• For most families with hereditary cancer, the underlying gene mutation will not be found, at present.

• The test results are considered informative or non-informative.

• Be **VERY CAUTIOUS** with interpreting a NEGATIVE test result.

What prior information is known to aid in the interpretation?
Genetic Testing

Gene A

Copy 1

Copy 2

Mutation specific analysis

Gene A

Copy 1

Copy 2

Sequencing

Gene A

Copy 1

Copy 2

Deletion/duplication analysis
Genetic Testing Results

- Positive - mutation identified
  - New information

- Negative - No mutation identified
  - Interpretation depends on prior knowledge

- Variant of unknown clinical significance (VUS)
Genetic testing for cancer risk

Cancer genetics assessment and education

Personal and/or family history consistent with hereditary cancer

Known gene mutation in family
- Mutation specific analysis only
  - No mutation
    - Test result is INFORMATIVE, true negative
      - No increase in cancer risk due to side of the family with mutation
      - At-risk family members may pursue genetic testing
  - Deleterious mutation
    - Test result is INFORMATIVE true positive
      - Cancer risks based on penetrance & expressivity data
      - At-risk family members may pursue genetic testing

No known mutation in family
- Full gene(s) analysis
  - No mutation
    - Test result is NON-INFORMATIVE
    - Cancer risks based on personal & family history
    - At-risk family members should NOT pursue genetic testing
  - Variant of unknown clinical significance (VUS)
    - Test result is NON-INFORMATIVE
    - Cancer risks based on personal & family history
    - At-risk family members should NOT pursue genetic testing

Modified from Cancer Genetics Risk Assessment and Counseling (PDQ®); Figure 2; National Cancer Institute
Chromosome Analysis

Genetic Testing

- Single gene testing
  - CGH
  - 3-4 gene testing
- Gene panels
- Whole Exome Sequencing
- Whole genome Sequencing

Specialty testing for rare disorders

Broader application for complex disease & personal use
TECHNOLOGY

- Provider & public genetics education
- Outcome & communication research
- Penetrance / Expressivity studies
- Ethics Public policy regulation
- Cross discipline training

Information Access
MIND THE GAP
Individual factors to consider with genetic testing

WHERE
- at birth
- clinic

WHEN

HOW
- process
- geneticist

WHO
- physician
- specialist

WHAT
- targeted
- agreement
- decision maker

WHY
- Multi-disciplinary team
- delivery
- research setting
- healthy state

UTILITY
- agreement
- complete
- follow-up
- outcome
- select
- decision maker

PERSONAL
- at diagnosis
- at birth
- at clinic
Cherish the exception… young adults with cancer
Table 1. Leading Causes of Death Due to Disease, Age 20 to 39 Years, United States 2005, in Rank Order by Gender

<table>
<thead>
<tr>
<th>Males and Females</th>
<th>Deaths</th>
<th>Females</th>
<th>Deaths</th>
<th>Males</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Suicide</td>
<td>10,482</td>
<td>Neoplasms</td>
<td>4,888</td>
<td>Suicide</td>
<td>8,520</td>
</tr>
<tr>
<td>2 Neoplasms</td>
<td>9,310</td>
<td>Heart disease</td>
<td>2,519</td>
<td>Heart disease</td>
<td>5,536</td>
</tr>
<tr>
<td>3 Heart disease</td>
<td>8,055</td>
<td>Suicide</td>
<td>1,962</td>
<td>Neoplasms</td>
<td>4,442</td>
</tr>
<tr>
<td>4 HIV disease</td>
<td>3,142</td>
<td>HIV disease</td>
<td>1,069</td>
<td>HIV disease</td>
<td>2,073</td>
</tr>
<tr>
<td>5 Diabetes mellitus</td>
<td>1,514</td>
<td>Cerebrovascular disease</td>
<td>643</td>
<td>Diabetes mellitus</td>
<td>903</td>
</tr>
<tr>
<td>6 Cerebrovascular disease</td>
<td>1,359</td>
<td>Diabetes mellitus</td>
<td>611</td>
<td>Cerebrovascular disease</td>
<td>716</td>
</tr>
<tr>
<td>7 Chronic liver disease</td>
<td>1,049</td>
<td>Congenital anomalies</td>
<td>393</td>
<td>Chronic liver disease</td>
<td>685</td>
</tr>
<tr>
<td>8 Congenital anomalies</td>
<td>920</td>
<td>Chronic liver disease</td>
<td>364</td>
<td>Congenital anomalies</td>
<td>527</td>
</tr>
</tbody>
</table>

NOTE. Accidents and homicides excluded.

Bleyer, Barr. Cancer in Young Adults 20 -39 Years of Age: Overview. Seminars in Oncology; 2009
# Young Adults With Cancer


<table>
<thead>
<tr>
<th>Rank</th>
<th>Females and Males</th>
<th>Rate</th>
<th>Females</th>
<th>Rate</th>
<th>Males</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>All cancer</td>
<td>757.8</td>
<td>All cancer</td>
<td>936.0</td>
<td>Testis cancer</td>
<td>583.9</td>
</tr>
<tr>
<td>1</td>
<td>Breast cancer</td>
<td>126.5</td>
<td>Breast cancer</td>
<td>255.0</td>
<td>Testis cancer</td>
<td>114.9</td>
</tr>
<tr>
<td>2</td>
<td>Melanoma</td>
<td>84.8</td>
<td>Thyroid cancer</td>
<td>140.5</td>
<td>Melanoma</td>
<td>64.7</td>
</tr>
<tr>
<td>3</td>
<td>Thyroid cancer</td>
<td>83.6</td>
<td>Melanoma</td>
<td>105.6</td>
<td>Non-Hodgkin lymphoma</td>
<td>56.5</td>
</tr>
<tr>
<td>4</td>
<td>Testis cancer</td>
<td>58.6</td>
<td>Uterine cervix cancer</td>
<td>85.2</td>
<td>Colorectal cancer</td>
<td>39.8</td>
</tr>
<tr>
<td>5</td>
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<td>31.6</td>
<td>Oral cavity cancer†</td>
<td>18.7</td>
</tr>
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<td>Ovary cancer</td>
<td>31.5</td>
<td>Kidney cancer</td>
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</tr>
<tr>
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<td>87%</td>
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<td>Oral cavity cancer†</td>
<td>13.8</td>
<td>AML</td>
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</tr>
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<td>Kidney cancer</td>
<td>13.1</td>
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<td>11.4</td>
</tr>
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<td>15.5</td>
<td>AML</td>
<td>11.0</td>
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<td>9.8</td>
</tr>
<tr>
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<td>Bone sarcoma</td>
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<td>Bone sarcoma</td>
<td>7.7</td>
</tr>
<tr>
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<td>6.1</td>
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<td>90%</td>
<td></td>
<td>94%</td>
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</table>

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**Figure 4.** Incidence of invasive cancer by race/ethnicity, 1992–2005, age 20–39 years by 5-year intervals, US SEER13, Kaposi sarcoma excluded.
Figure 10. Improvement in 5-year relative survival rates

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Figure 5 | Breast cancer survival rates in US women, by age at diagnosis. a | Data for all patients, by individual year of age at diagnosis. The yellow background zone indicates the 15–39-year age range. b | By stage and extent of disease
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