Four Questions

- What are the major health problems worldwide?
- Who pays to solve problems in health care?
- **How can technology solve health care problems?**
- How are health care technologies managed?
Three Case Studies

- Prevention of infectious disease
  - HIV/AIDS

- Early detection of cancer
  - Cervical Cancer
  - Ovarian Cancer
  - Prostate Cancer

- Treatment of heart disease
  - Atherosclerosis and heart attack
  - Heart failure
Outline

- The burden of cancer
- How does cancer develop?
- Why is early detection so important?
- Strategies for early detection
- Example cancers/technologies
  - Cervical cancer
  - Ovarian cancer
  - Prostate cancer
The Burden of Cancer: U.S.

- **Cancer:**
  - 2nd leading cause of death in US
  - 1 of every 4 deaths is from cancer

- **5-year survival rate for all cancers:**
  - 62%

- **Annual costs for cancer:**
  - $172 billion
    - $61 billion - direct medical costs
    - $16 billion - lost productivity to illness
    - $95 billion - lost productivity to premature death
U.S. Cancer Incidence & Mortality 2009

- New cases of cancer:
  - United States: 1,479,350
  - Texas: 98,200

- Deaths due to cancer:
  - United States: 562,340

www.cancer.org, Cancer Facts & Figures
2009 Estimated US Cancer Cases*

- **Prostate**: 25%
- **Lung & bronchus**: 15%
- **Colon & rectum**: 10%
- **Urinary bladder**: 7%
- **Melanoma of skin**: 5%
- **Non-Hodgkin lymphoma**: 5%
- **Kidney & renal pelvis**: 5%
- **Leukemia**: 3%
- **Oral cavity**: 3%
- **Pancreas**: 3%
- **All Other Sites**: 19%

**Men**: 766,130

**Women**: 713,220

- **Breast**: 27%
- **Lung & bronchus**: 14%
- **Colon & rectum**: 10%
- **Uterine corpus**: 6%
- **Non-Hodgkin lymphoma**: 4%
- **Melanoma of skin**: 4%
- **Thyroid**: 4%
- **Kidney & renal pelvis**: 3%
- **Ovary**: 3%
- **Pancreas**: 3%
- **All Other Sites**: 20%

### 2009 Estimated US Cancer Deaths*

<table>
<thead>
<tr>
<th>Location</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>30%</td>
<td>26%</td>
</tr>
<tr>
<td>Prostate</td>
<td>9%</td>
<td>5%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>All other sites</td>
<td>25%</td>
<td>25%</td>
</tr>
</tbody>
</table>

*ONS=Other nervous system.

Source: American Cancer Society, 2009.
Worldwide Burden of Cancer

- **Today:**
  - 11 million new cases every year
  - 6.2 million deaths every year (12% of deaths)

- **Can prevent 1/3 of these cases:**
  - Reduce tobacco use
  - Implement existing screening techniques
  - Healthy lifestyle and diet

- **In 2020:**
  - 15 million new cases predicted in 2020
  - 10 million deaths predicted in 2020
  - Increase due to aging population
  - Increase in smoking
Global Cancer Trends

Worldwide Burden of Cancer

- 23% of cancers in developing countries caused by infectious agents
  - Hepatitis (liver)
  - HPV (cervix)
  - H. pylori (stomach)
- Vaccination could be key to preventing these cancers
What is Cancer?

- Characterized by uncontrolled growth & spread of abnormal cells
- Can be caused by:
  - External factors:
    - Tobacco, chemicals, radiation, infectious organisms
  - Internal factors:
    - Mutations, hormones, immune conditions
Squamous Epithelial Tissue

- Squamous superficial cells
- Germinative cells
- Basement membrane
- Connective tissue
Precancer $\rightarrow$ Cancer Sequence
Histologic Images

Normal

Cervical Pre-Cancer
Fig 7.33 – The Metastatic cascade
The War on Cancer

- **1971 State of Union address:**
  - President Nixon requested $100 million for cancer research
- **December 23, 1971**
  - Nixon signed National Cancer Act into law
  - "I hope in years ahead we will look back on this action today as the most significant action taken during my Administration."
Change in the US Death Rates* by Cause, 1950 & 2001

* Age-adjusted to 2000 US standard population.

Sources: 1950 Mortality Data - CDC/NCHS, NVSS, Mortality Revised.
http://www.cdc.gov/nchs/data/nvsr/nvsr52/nvsr52_03.pdf
Change in the US Death Rates* by Cause, 1950 & 2001

<table>
<thead>
<tr>
<th>Cause</th>
<th>1950 Rate</th>
<th>2001 Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Diseases</td>
<td>586.8</td>
<td>245.8</td>
</tr>
<tr>
<td>Cerebrovascular Diseases</td>
<td>180.7</td>
<td></td>
</tr>
<tr>
<td>Pneumonia/Influenza</td>
<td>48.1</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>193.9</td>
<td></td>
</tr>
</tbody>
</table>

* Age-adjusted to 2000 US standard population.
Sources: 1950 Mortality Data - CDC/NCHS, NVSS, Mortality Revised.
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Change in the US Death Rates* by Cause, 1950 & 2001

* Age-adjusted to 2000 US standard population.
Change in the US Death Rates* by Cause, 1950 & 2001

Rate Per 100,000

Heart Diseases
- 1950: 586.8
- 2001: 245.8

Cerebrovascular Diseases
- 1950: 180.7
- 2001: 57.5

Pneumonia/Influenza
- 1950: 48.1
- 2001: 21.8

Cancer
- 1950: 193.9

* Age-adjusted to 2000 US standard population.
Sources: 1950 Mortality Data - CDC/NCHS, NVSS, Mortality Revised.
http://www.cdc.gov/nchs/data/nvsr/nvsr52/nvsr52_03.pdf
Change in the US Death Rates* by Cause, 1950 & 2001

Rate Per 100,000

<table>
<thead>
<tr>
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<th>1950</th>
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</tr>
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<tr>
<td>Heart Diseases</td>
<td>586.8</td>
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<tr>
<td>Diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia/Influenza</td>
<td>48.1</td>
<td>21.8</td>
</tr>
<tr>
<td>Cancer</td>
<td>193.9</td>
<td>194.4</td>
</tr>
</tbody>
</table>

* Age-adjusted to 2000 US standard population.

*Age-adjusted to the 2000 US standard population.

*Age-adjusted to the 2000 US standard population.

Rate Per 100,000

Prostate
Lung
Colon and rectum
Urinary bladder
Non-Hodgkin lymphoma

*Age-adjusted to the 2000 US standard population.
### Relative Survival* (%) during Three Time Periods by Cancer Site

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>50</td>
<td>52</td>
<td>63</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>75</td>
<td>78</td>
<td>87</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>50</td>
<td>57</td>
<td>62</td>
</tr>
<tr>
<td>Leukemia</td>
<td>34</td>
<td>41</td>
<td>46</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>12</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Melanoma</td>
<td>80</td>
<td>85</td>
<td>90</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>47</td>
<td>54</td>
<td>56</td>
</tr>
<tr>
<td>Ovary</td>
<td>37</td>
<td>41</td>
<td>53</td>
</tr>
<tr>
<td>Pancreas</td>
<td>3</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Prostate</td>
<td>67</td>
<td>75</td>
<td>98</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>73</td>
<td>78</td>
<td>82</td>
</tr>
</tbody>
</table>

*5-year relative survival rates based on follow up of patients through 2000.

Importance of Early Detection

Five Year Relative Survival Rates

- Local
- Regional
- Distant

Breast
Ovary
Cervix
Screening

- Use of simple tests in a healthy population
- Goal:
  - Identify individuals who have disease, but do not yet have symptoms
- Should be undertaken only when:
  - Effectiveness has been demonstrated
  - Resources are sufficient to cover target group
  - Facilities exist for confirming diagnoses
  - Facilities exist for treatment and follow-up
  - When disease prevalence is high enough to justify effort and costs of screening
Cancer Screening

- We routinely screen for 4 cancers:
  - Female breast cancer
    - Mammography
  - Cervical cancer
    - Pap smear
  - Prostate cancer
    - Serum PSA
    - Digital rectal examination
  - Colon and rectal cancer
    - Fecal occult blood
    - Flexible sigmoidoscopy, Colonoscopy
Yearly mammograms are recommended starting at age 40.

A clinical breast exam should be part of a periodic health examination, about every 3 years for women in their 20s and 30s. Asymptomatic women aged 40 and older should continue to undergo a clinical breast exam, preferably annually*.

Beginning in their early 20s, women should be told about the benefits and limitations of breast-self examination. Women should know how their breasts normally feel and report any breast changes promptly to their health care providers.

* Beginning at age 40 years, annual CBE should be performed prior to mammography.

* A mammogram within the past year. Note: Data from participating states and the District of Columbia were aggregated to represent the United States.
How do we judge efficacy of a screening test?

Sensitivity/Specificity
Positive/Negative Predictive Value
Sensitivity & Specificity

**Sensitivity**
- Probability that given DISEASE, patient tests POSITIVE
- Ability to correctly detect disease
- 100% - False Negative Rate

**Specificity**
- Probability that given NO DISEASE, patient tests NEGATIVE
- Ability to avoid calling normal things disease
- 100% - False Positive Rate
## Possible Test Results

<table>
<thead>
<tr>
<th></th>
<th>Test Positive</th>
<th>Test Negative</th>
<th># with Disease</th>
<th># without Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease Present</td>
<td>TP</td>
<td>FN</td>
<td>TP+FN</td>
<td>FP+TN</td>
</tr>
<tr>
<td>Disease Absent</td>
<td>FP</td>
<td>TN</td>
<td>#without Disease</td>
<td>#with Disease</td>
</tr>
<tr>
<td></td>
<td># Test Pos = TP+FP</td>
<td># Test Neg = FN+TN</td>
<td>Total Tested = TP+FN+FP+TN</td>
<td></td>
</tr>
</tbody>
</table>

Se = TP/(# with disease) = TP/(TP+FN)
Sp = TN/(# without disease) = TN/(TN+FP)
Example

- **Sputum microscopy:**
  - Procedure to detect lung cancer

- **Efficacy:**
  - 1,000 40-year-olds given the test
  - 28 people later proven to have lung cancer
  - 32 test positive, and of those 25 were truly positive

- **Calculate:**
  - Sensitivity & Specificity
## Possible Test Results

<table>
<thead>
<tr>
<th></th>
<th>Test Positive</th>
<th>Test Negative</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease Present</td>
<td>25</td>
<td>3</td>
<td># with Disease = 28</td>
</tr>
<tr>
<td>Disease Absent</td>
<td>7</td>
<td>965</td>
<td># without Disease = 972</td>
</tr>
<tr>
<td></td>
<td># Test Pos = 32</td>
<td># Test Neg = 968</td>
<td>Total Tested = 1,000</td>
</tr>
</tbody>
</table>

Se = 25/28 = 89%  Sp = 965/972 = 99.3%
As a patient:

What Information Do You Want?
Predictive Value

- **Positive Predictive Value**
  - Probability that given a POSITIVE test result, you have DISEASE
  - Ranges from 0-100%

- **Negative Predictive Value**
  - Probability that given a NEGATIVE test result, you do NOT HAVE DISEASE
  - Ranges from 0-100%

- Depends on the prevalence of the disease
### Possible Test Results

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<tr>
<td>Disease Absent</td>
<td>FP</td>
<td>TN</td>
<td># without Disease = FP+TN</td>
</tr>
<tr>
<td># Test Pos</td>
<td>TP+FP</td>
<td># Test Neg</td>
<td>Total Tested = TP+FN+FP+TN</td>
</tr>
<tr>
<td></td>
<td># Test Neg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**PPV** = \( \frac{TP}{# \text{ Test Pos}} = \frac{TP}{TP+FP} \)

**NPV** = \( \frac{TN}{# \text{ Test Neg}} = \frac{TN}{FN+TN} \)
Example

- **Sputum Microscopy:**
  - Procedure to detect lung cancer

- **Efficacy:**
  - 1,000 40-year-olds given the test
  - 28 people later shown to have lung cancer
  - 32 test positive, and of those 25 were truly positive

- **Calculate:**
  - Positive & Negative Predictive Value
## Possible Test Results

<table>
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<td>25</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td># with Disease = 28</td>
<td></td>
</tr>
<tr>
<td>Disease Absent</td>
<td>7</td>
<td>965</td>
</tr>
<tr>
<td></td>
<td># without Disease = 972</td>
<td></td>
</tr>
<tr>
<td>Total Tested</td>
<td># Test Pos = 32</td>
<td># Test Neg = 968</td>
</tr>
<tr>
<td></td>
<td>Total Tested = 1,000</td>
<td></td>
</tr>
</tbody>
</table>

Se = 25/28 = 89%
Sp = 965/972 = 99.3%
PPV = 25/32 = 78%
NPV = 965/968 = 99.7%
Dependence on Prevalence

- Prevalence – is a disease common or rare?
  - $p = (\# \text{ with disease})/\text{total } \#$
  - $p = (TP+FN)/(TP+FP+TN+FN)$

- Does our test accuracy depend on $p$?
  - $Se/Sp$ do not depend on prevalence
  - $PPV/NPV$ are highly dependent on prevalence

- $PPV = pSe/[pSe + (1-p)(1-Sp)]$
- $NPV = (1-p)Sp/[(1-p)Sp + p(1-Se)]$
Is it Hard to Screen for Rare Disease?

- **Sputum Microscopy:**
  - Procedure to detect lung cancer

- **Efficacy:**
  - 1,000 40-year-olds given the test
  - 28 people later shown to have lung cancer
  - 32 test positive, and of those 25 were truly positive

- **Calculate:**
  - Prevalence of lung cancer
Is it Hard to Screen for Rare Disease?

- **Sputum Microscopy:**
  - Usually offered to older smokers

- **Efficacy:**
  - 1,000 20-year-olds given the test
  - Prevalence of lung cancer is expected to be 2.8/1000

- **Calculate:**
  - Sensitivity & Specificity
  - Positive & Negative Predictive Value
  - Suppose a 20 yo has a positive test. What is the likelihood that they have lung cancer?
### Possible Test Results

<table>
<thead>
<tr>
<th></th>
<th>Test Positive</th>
<th>Test Negative</th>
<th># with Disease = 2.8</th>
<th># without Disease = 997.2</th>
<th>Total Tested = 1,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease Present</td>
<td>2.5</td>
<td>.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease Absent</td>
<td>6.98</td>
<td>990.2</td>
<td># Test Pos = 9.48</td>
<td># Test Neg = 990.5</td>
<td></td>
</tr>
</tbody>
</table>

Se = 2.5/2.8 = 89.3%  
Sp 990.2/997.2 = 99.3%  
PPV = 2.5/9.48 = 26.3%  
NPV = 990.2/990.5 = 99.97%
Cervical Cancer

Early Detection
Cervical Cancer: 2004

- 10,520 new cases in US
- 3,900 deaths in US

Signs and symptoms:
- Abnormal vaginal bleeding

Risk Factors:
- Failure to obtain regular Pap smears
- HPV infection
  - Sex at an early age
  - Multiple sexual partners
- Cigarette smoking
Cervical Cancer: World

- **Incidence:**
  - 510,000 new cases per year worldwide
  - 80% of cases occur in the developing world
  - Highest incidence in:
    - Central and South America
    - Southern Africa
    - Asia

- **Mortality:**
  - 288,000 deaths per year worldwide
  - 2nd leading cause of female cancer mortality worldwide
Global Burden of Cervical Cancer

Age-standardized incidence / 100,000 population

- < 9.3
- < 16.1
- < 23.8
- < 35.8
- < 93.9
Cervical Cancer
What Initiates Transformation?

- Infection with Human Papilloma Virus (HPV)
  - Most common sexually transmitted disease
  - Asymptomatic HPV infections can be detected in 5-40% of women of reproductive age
- HPV infection is the central causative factor in squamous cell carcinoma of the cervix
  - HPV infections are transient; most young women clear them with no ill effects
  - If HPV infection persists past age 30, there is greater risk of developing cervical cancer
  - Many viral subtypes (70)
    - 13 most commonly linked to cervical cancer
      - HPV 16, 18
In a wart or benign infection, the HPV chromosomes are stably maintained in the basal epithelium as plasmids (left). Integration of viral DNA into a host chromosome alters the environment of the viral genes and disrupts control of their expression. Unregulated reproduction of viral proteins tends to drive the host cell into S phase helping to generate a cancer (right).
How Do We Detect Early Cervical Cancer?

Pap Smear
(The most successful cancer-screening test in medical history)

Colposcopy + Biopsy
Screening Pap Smear

- Each slide: 50,000-300,000 cells
- Cytotechnologists review < 100 slides per day
- 10% of "normal" slides re-screened
- Se = 62%
- Sp = 78%
- False negative smears account for 3% of U.S. Cervical Cancer cases/year
Screening Guidelines for the Early Detection of Cervical Cancer, American Cancer Society 2009

Screening should begin approximately three years after a woman begins having vaginal intercourse, but no later than 21 years of age.

Screening should be done every year with regular Pap tests or every two years using liquid-based tests.

At or after age 30, women who have had three normal test results in a row may get screened every 2-3 years with cervical cytology (either conventional or liquid-based Pap test) alone, or every 3 years with a human papillomavirus DNA test plus cervical cytology.

Women 70 and older who have had three or more consecutive Pap tests in the last ten years may choose to stop cervical cancer screening.

Screening after a total hysterectomy (with removal of the cervix) is not necessary unless the surgery was done as a treatment for cervical cancer.
Trends in Recent* Pap Test Prevalence (%), by Educational Attainment and Health Insurance Status, Women 18 and Older, US, 1992-2002

Detecting Cervical Pre-Cancer

Se = 95%
Sp = 44%
Cervical Cancer

- **Screening:**
  - Annual Pap smear

- **Diagnosis**
  - Colposcopy + Biopsy

- **Treatment:**
  - Surgery, radiation therapy, chemotherapy

- **5 year survival**
  - Localized disease: 92% (56% diagnosed at this stage)
Trends in Cervical Cancer Incidence

China, Shanghai

Puerto Rico

Denmark


Incidence: 100, 50, 25, 10, 5, 2.5, 1
Trends in Cervical Cancer Incidence

USA

New Zealand

Slovakia

Black

White

Maori

Non-Maori
Trends in Cervical Cancer Mortality

USA

Poland

Cuba


Black

White

1 2.5 5 10 25 50 100

100 50 25 10 5 2.5 1

1 2.5 5 10 25 50 100

1 2.5 5 10 25 50 100

1 2.5 5 10 25 50 100
New Technologies for Cervical Cancer

- Liquid Based Pap testing
- Automated Pap smear screening
- HPV Testing
- VIA
- HPV Vaccine
Liquid Based Pap Smear

- Rinse collection device in preservative fluid
- Process suspension of cells to deposit a monolayer of cells on a microscope slide
Liquid Based Pap Smear

- Gentle dispersion breaks up blood, mucous, non-diagnostic debris, and mixes sample
- Negative pressure pulse draws fluid through filter to collect a thin, even layer of cells
- Monitor flow through filter during collection to prevent cells from being too scant or too dense
- Cells then transferred to a glass slide
Automated Pap Smear Screening

TriPath Care Technologies

http://www.tripathimaging.com/usproducts/index.htm
HPV Testing

- The DNAwithPap Test is FDA-approved for routine adjunctive screening with a Pap test for women age 30 and older.
- Digene
  - [http://www.digene.com](http://www.digene.com)
<table>
<thead>
<tr>
<th></th>
<th>Step Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><strong>Release Nucleic Acids</strong></td>
</tr>
<tr>
<td></td>
<td>Clinical specimens are combined with a base solution which disrupts the virus or</td>
</tr>
<tr>
<td></td>
<td>bacteria and releases target DNA. No special specimen preparation is necessary.</td>
</tr>
<tr>
<td>2</td>
<td><strong>Hybridize RNA Probe with Target DNA</strong></td>
</tr>
<tr>
<td></td>
<td>Target DNA combines with specific RNA probes creating RNA:DNA hybrids.</td>
</tr>
<tr>
<td>3</td>
<td><strong>Capture Hybrids</strong></td>
</tr>
<tr>
<td></td>
<td>Multiple RNA:DNA hybrids are captured onto a solid phase coated with universal</td>
</tr>
<tr>
<td></td>
<td>capture antibodies specific for RNA:DNA hybrids.</td>
</tr>
<tr>
<td>4</td>
<td><strong>Label for Detection</strong></td>
</tr>
<tr>
<td></td>
<td>Captured RNA:DNA hybrids are detected with multiple antibodies conjugated to</td>
</tr>
<tr>
<td></td>
<td>alkaline phosphatase. Resulting signal can be amplified to at least 3000-fold.</td>
</tr>
<tr>
<td>5</td>
<td><strong>Detect, Read and Interpret Results</strong></td>
</tr>
<tr>
<td></td>
<td>The bound alkaline phosphatase is detected with a chemiluminescent dioxetane</td>
</tr>
<tr>
<td></td>
<td>substrate. Upon cleavage by alkaline phosphatase, the substrate produces light</td>
</tr>
<tr>
<td></td>
<td>that is measured on a luminometer in Relative Light Units (RLUs).</td>
</tr>
</tbody>
</table>
Sensitivity of HPV Testing

Study of 5,671 women age >30 years

http://www.digene.com/images/sens.png
## Comparison of Various Techniques

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pap smear</td>
<td>60-80%</td>
<td>45-70%</td>
</tr>
<tr>
<td>Colposcopy</td>
<td>90-100%</td>
<td>20-50%</td>
</tr>
<tr>
<td>Digene HPV Test</td>
<td>80-90%</td>
<td>57-89%</td>
</tr>
<tr>
<td>VIA</td>
<td>67-79%</td>
<td>49-86%</td>
</tr>
</tbody>
</table>
HPV Vaccine

2006:
- Gardasil vaccine to prevent HPV infection was licensed for use in girls & women ages 9-26 in USA and 48 other countries
- Protects against 2 strains of HPV responsible for 70% of cervical cancers

Non-infectious vaccine
- Made by inserting gene for protein found in the HPV capsid into a different virus or yeast. Recombinantly produced HPV capsid protein self-assembles into virus like particles (VLPs).
HPV Vaccine

- **Gardasil**
  - Protects against new HPV infections
  - Not effective for women who have already been exposed to HPV
  - Given as a series of 3 shots over a 6 months
  - Cost: $360
  - This cost is a barrier even in developed countries, and is likely to limit its immediate impact in developing countries
<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Vaccine</th>
<th>Location</th>
<th>Participants</th>
<th>Projected End</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merck</td>
<td>VLPs of L1 protein from HPV 6/11/16/18, made in yeast, aluminum adjuvant</td>
<td>U.S., S. America, Europe</td>
<td>17,800 women, 16 to 26 years old</td>
<td>2007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>U.S., S. America, Europe, Asia</td>
<td>3800 women, 24 to 45 years old</td>
<td>2008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>U.S., S. America, Europe, Asia, Africa</td>
<td>3700 men, 16 to 24 years old</td>
<td>2008</td>
</tr>
<tr>
<td>GSK</td>
<td>VLPs of L1 protein from HPV 16/18, made in baculovirus, AS04 adjuvant</td>
<td>U.S., S. America, Europe, Asia Pacific</td>
<td>18,000 women, 15 to 25 years old</td>
<td>2010</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Costa Rica (run by NCI)</td>
<td>12,000 women, 18 to 25 years old</td>
<td>2010</td>
</tr>
</tbody>
</table>
HPV & Cervical Cancer

- Do condoms prevent HPV?
- Do we still need to screen women who have been vaccinated?
Summary of Cancer

- The burden of cancer
  - Contrasts between developed/developing world

- How does cancer develop?
  - Cell transformation → Angiogenesis → Motility
    → Microinvasion → Embolism → Extravasation

- Why is early detection so important?
  - Treat before cancer develops → Prevention

- Accuracy of screening/detection tests
  - Se, Sp, PPV, NPV
Summary of Cervical Cancer

- Cervical cancer
  - 2nd Leading cause of cancer death in women in world
  - Caused by infection with HPV
  - Precancer → cancer sequence
  - Precancer is very common

- Screening & Detection
  - Pap smear; colposcopy + biopsy
  - Reduces incidence and mortality of cervical cancer
  - Insufficient resources to screen in developing countries

- New technologies
  - Automated reading of Pap smears → reduce FN rate
  - HPV testing
  - VIA