CS/PoliSci/Statistics C79

Societal Risks & The Law

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March 19, 2013
Calculating Risk

- Understanding of probability, models for risk and simple methods to combine information
- Empirical estimates of Risk (see next slides)
- How do we perceive risk, and what are biases associated with various perception and methods of assessing risk?
- Insuring against a bad event
- **Mitigating Risk**
- **Negative Consequences of Mitigating Risk**
- **Mitigating Risk on One Person Affects Risk of Other Persons**
Counting Events (Empirical Risk Assessment)

• Epidemics: number of infected (predict the epidemic forwards), numbers recovered, numbers died (case fatality rate), assess the impact of possible intervention strategies (vaccination etc)

• Adverse effects from pharmaceuticals (safety is different from drug efficacy, rare events, pooling studies)

• Civilian casualties in times of conflict (how many have died and how, poor data sources). How many children were abducted during the El Salvadorian conflict (and where are they)? What are the risks to health to refugees and how can be protect them?

• What are your chances of surviving an avalanche?
Moula massacre, Syria, May 26, 2012, 32 (?) children killed
STOP BURYING THE DEAD

Each year thousands of deaths from violence and conflict go unrecorded.

Article 36 joins other organisations under the Every Casualty banner, in calling on States to accept a legal responsibility to identify, record and acknowledge these deaths. It is time for governments to stop burying the impact of violence and to stand up for its victims.

Endorse the Every Casualty Charter, to stop the truth from being buried with the dead.
How do we sort this out . . . ?
Syria Tracker, Number of Reports, May 28, 2012
14,887 documented killings, 3/18/11—5/18/12
How do we Mitigate Risk?

- Chronic diseases: CHD, cancer, stroke, ...

- Infectious Diseases: mode of transmission
  - Airborne
  - Physical contact
  - Sexual contact
  - Blood and blood products
  - Hygiene (food and water-borne)
  - Transcutaneous
  - Congenital or maternal-fetal
How do we Mitigate Risk?

• Chronic diseases: CHD, cancer, stroke, accidents, suicide, . . .  Treatment, diet, environmental protection, screening, genetic testing (most voluntary but some through regulation)

• Infectious Diseases: mode of transmission
  • Airborne (treatment, quarantine, immunization, . . .)
  • Physical contact (quarantine, immunization, . . .)
  • Sexual contact (education, safe sex practices including condoms, immunization, case tracking and treatment, circumcision, . . .)
  • Blood and blood products (testing donors, heat treatment, immunization, . . .)
  • Hygiene--food and water-borne (sanitation, food supply regulations, animal and food control, immunization, . . .)
  • Transcutaneous (pesticides, bed nets, animal interventions, environmental control of water and sewage, education, occupational controls, immunization, . . .)
  • Congenital or maternal-fetal (treatment, testing, immunization, . . .)
How do we Mitigate Risk?

• For infectious disease in particular, surveillance and case tracking are crucial. Many infectious diseases are thus *reportable*. Ethical issue/privacy?

• For infectious diseases particularly, there are population impacts that go beyond individual considerations

• Eradication? (cost of eradicating smallpox was approximately $112M; worldwide savings are estimated at $1B+ annually).
Greatest Health Advances of 20th Century

Life expectancy changed from 47 in 1900 to 78 (2011)

- Vaccines and Immunizations *
- Antibiotics
- Surgical Anesthetic and antisepsis
- Clean water and improved sanitation *
- Family Planning *
- Childbirth advancements *
- Cardiac care
- Organ transplants
- Randomized controlled trials
- Radiologic imaging
- Motor vehicle safety *
- Workplace safety *
- Food safety *
- Tobacco risk education
- Decline in deaths from coronary heart disease and stroke *
- Fluoridation of drinking water *
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Societal Risks & The Law

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March 21, 2013
October 2009 Swine Flu

The Greeks had two gods of health. Aesculapius and Hygiea, therapy and prevention, respectively. Medicine in the twentieth century retains those two concepts, and vaccination is a powerful means of prevention.

Vaccines


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### TABLE 4.4 Annual Incidence of Selected Vaccine-Preventable Infectious Diseases in Rates per 100,000 Population, Selected Years, United States, 1950–2004

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>3.8</td>
<td>0.5</td>
<td>0.2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pertussis</td>
<td>79.8</td>
<td>8.2</td>
<td>2.1</td>
<td>0.8</td>
<td>1.8</td>
<td>2.9</td>
<td>8.9</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>22.0</td>
<td>1.8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Measles</td>
<td>211.0</td>
<td>245.4</td>
<td>23.2</td>
<td>6.0</td>
<td>11.2</td>
<td>0.03</td>
<td>0.04</td>
</tr>
<tr>
<td>Mumps</td>
<td>na</td>
<td>na</td>
<td>55.6</td>
<td>3.9</td>
<td>2.2</td>
<td>0.08</td>
<td>0.09</td>
</tr>
<tr>
<td>Rubella</td>
<td>na</td>
<td>na</td>
<td>27.8</td>
<td>1.7</td>
<td>0.5</td>
<td>0.06</td>
<td>0</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>na</td>
<td>na</td>
<td>27.8</td>
<td>12.3</td>
<td>12.6</td>
<td>4.9</td>
<td>2.0</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>na</td>
<td>na</td>
<td>4.1</td>
<td>8.4</td>
<td>8.5</td>
<td>3.0</td>
<td>2.1</td>
</tr>
</tbody>
</table>

*Note: na = not available
Source: Health United States, 1998, 2006*
### Introduction of first generation of vaccines for use in humans

<table>
<thead>
<tr>
<th>Originals</th>
<th>After World War II</th>
</tr>
</thead>
<tbody>
<tr>
<td>1798 Smallpox</td>
<td>1955 Injectable Polio Vaccine (IPV)</td>
</tr>
<tr>
<td>1885 Rabies</td>
<td>1962 Oral Polio Vaccine (OPV)</td>
</tr>
<tr>
<td>1897 Plague</td>
<td>1964 Measles</td>
</tr>
<tr>
<td>1923 Diphtheria</td>
<td>1967 Mumps</td>
</tr>
<tr>
<td>1926 Pertussis</td>
<td>1970 Rubella</td>
</tr>
<tr>
<td>1927 Tuberculosis (BCG)</td>
<td>1981 Hepatitis B</td>
</tr>
<tr>
<td>1927 Tetanus</td>
<td></td>
</tr>
<tr>
<td>1935 Yellow Fever</td>
<td></td>
</tr>
</tbody>
</table>

Plotkin SA, Mortimer EA
## Licensed Vaccines in Routine Use in the United States, 1980 and 2008

**Table 1.** Licensed Vaccines in Routine Use in the United States, 1980 and 2008

<table>
<thead>
<tr>
<th>FDA-licensed vaccines in routine use in 1980</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
</tr>
<tr>
<td>Tetanus</td>
</tr>
<tr>
<td>Pertussis</td>
</tr>
<tr>
<td>Polio</td>
</tr>
<tr>
<td>Measles</td>
</tr>
<tr>
<td>Mumps</td>
</tr>
<tr>
<td>Rubella</td>
</tr>
<tr>
<td>Influenza</td>
</tr>
<tr>
<td>Pneumococcal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FDA-licensed vaccines in routine use in 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
</tr>
<tr>
<td>Tetanus</td>
</tr>
<tr>
<td>Pertussis</td>
</tr>
<tr>
<td>Polio</td>
</tr>
<tr>
<td>Measles</td>
</tr>
<tr>
<td>Mumps</td>
</tr>
<tr>
<td>Rubella</td>
</tr>
<tr>
<td>Influenza</td>
</tr>
<tr>
<td>Pneumococcal</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em> type b</td>
</tr>
<tr>
<td>Hepatitis A</td>
</tr>
<tr>
<td>Hepatitis B</td>
</tr>
<tr>
<td>Herpes zoster (shingles)</td>
</tr>
<tr>
<td>Human papillomavirus</td>
</tr>
<tr>
<td>Meningococcal</td>
</tr>
<tr>
<td>Rotavirus</td>
</tr>
<tr>
<td>Varicella</td>
</tr>
</tbody>
</table>

*FDA = U.S. Food and Drug Administration.*

• Priorities in PH interventions
• VPD deaths can be averted if existing vaccines used at full potential
• 2002 deaths from diseases for which vaccines are WHO recommended
  – <1,000 children <5 died from polio;
  – 4,000 children died from diphtheria;
  – 15,000 children died from yellow fever;
  – 198,000 children died from tetanus;
  – 294,000 children died from pertussis;
  – 386,000 children died from (Hib) *Hemophilus influenzae* type b);
  – 540,000 children died from measles
FIGURE 1. Percentage of deaths from vaccine-preventable diseases (VPDs)* among children aged <5 years, by disease — worldwide, 2002

- Pneumococcal diseases: 28%
- Pertussis: 11%
- Hemophilus influenzae type B: 15%
- Rotavirus: 16%
- Measles: 21%
- Tetanus: 8%
- Other VPDs: 1%

*An estimated 2.5 million deaths worldwide (of a total of 10.5 million for this age group) are caused by diseases for which vaccines are currently available.
†Diphtheria, hepatitis B, Japanese encephalitis, meningococcal disease, poliomyelitis, and yellow fever. (In older age groups, approximately 600,000 hepatitis B deaths are preventable by routine immunization.)
Rubella incidence per 100000

Countries included in the graph:
- Denmark
- Israel
- Russian Federation
- United Kingdom
- Uzbekistan
Viral hepatitis B incidence per 100000

- Finland
- Israel
- Russian Federation
- United Kingdom

Russia
Hospital discharges, infectious and parasitic diseases per 100000

- Finland
- Israel
- Russian Federation
- United Kingdom
Clinically diagnosed AIDS incidence per 100000

- Finland
- Israel
- Russian Federation
- United Kingdom
Vaccination Issues

- Political support
- Professional recognition
- Financing
- Expanding vaccine capability
- Organization, delivery, follow up
- Reporting “up and down and sideways” (UDS)
- Program content

- Strategies
- Select target groups
- Coverage
- Herd immunity
- Cold chain and logistics
- Continuous up-dating
- International and “gold standards”
- Infectious and chronic diseases
New Vaccines-New Issues

- Pneumococcus
- Rotavirus
- Human Papilloma Virus
- HIV
- Malaria
- Dengue
- Salmonella
- Eschericia coli

- Lyme disease
- Western Equine Encephalitis
- Ebola virus
- Leishmaniasis
- Helicobacter pylori
- Many others
2010: A global view of HIV infection

33.3 million people [31.4 – 35.3 million] living with HIV, 2009
CONTAGION
Potential for spread of an infection

- The *basic reproduction number* $R_0$ (“R nought”) = key quantity in infectious disease epidemiology:

  $$R_0 = \text{average number of new infectious cases generated by one primary case during its entire period of infectiousness in a totally susceptible population.}$$

- $R_0 < 1 \rightarrow$ No invasion of the infection within the population; only small epidemics.

- $R_0 > 1 \rightarrow$ Endemic infection; the bigger the value of $R_0$ the bigger the potential for spread of the infection within the population.
Evaluation of the potential for spread of an infection

- Vaccination reduces the proportion of susceptibles in the population.

- The minimal immunization coverage needed to eliminate an infection in the population, \( p_c \), is related to \( R_0 \) by the relation
  \[
  p_c = 1 - \left( \frac{1}{R_0} \right)
  \]
Evaluation of the potential for spread of an infection

$R_0 = 4$
with whole population susceptible

$R_0 = 4$
with 75% population immune
(25% susceptible)
Values of $R_0$ of Various infectious diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Mode of Transmission</th>
<th>$R_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>Airborne</td>
<td>12-18</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Airborne droplet</td>
<td>12-17</td>
</tr>
<tr>
<td>Diptheria</td>
<td>Saliva</td>
<td>6-7</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Social contact</td>
<td>3</td>
</tr>
<tr>
<td>Polio</td>
<td>Fecal-oral route</td>
<td>5-7</td>
</tr>
<tr>
<td>Rubella</td>
<td>Airborne droplet</td>
<td>5-7</td>
</tr>
<tr>
<td>Mumps</td>
<td>Airborne droplet</td>
<td>5-7</td>
</tr>
<tr>
<td>HIV</td>
<td>Sexual contact</td>
<td>2-5</td>
</tr>
<tr>
<td>SARS</td>
<td>Airborne droplet</td>
<td>2-5</td>
</tr>
<tr>
<td>Influenza (1918)</td>
<td>Airborne droplet</td>
<td>2-3</td>
</tr>
</tbody>
</table>
Evaluation of the potential for spread of an infection

<table>
<thead>
<tr>
<th>Infection</th>
<th>$p_c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>90% - 95%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>90% - 95%</td>
</tr>
<tr>
<td>H. parvovirus</td>
<td>90% - 95%</td>
</tr>
<tr>
<td>Chicken pox</td>
<td>85% - 90%</td>
</tr>
<tr>
<td>Mumps</td>
<td>85% - 90%</td>
</tr>
<tr>
<td>Rubella</td>
<td>82% - 87%</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>82% - 87%</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>82% - 87%</td>
</tr>
<tr>
<td>Scarlet fever</td>
<td>82% - 87%</td>
</tr>
<tr>
<td>Smallpox</td>
<td>70% - 80%</td>
</tr>
</tbody>
</table>

“Infectious Diseases in Humans”
Anderson, May
How Do We Estimate $R_0$ (early in an epidemic)?

- At equilibrium (endemic rather than epidemic), we can use the fraction of the population that remains susceptible to provide an estimate

- Average age at infection

- Final size of an epidemic

- Initial rate of growth of epidemic (doubling time)
Measuring a Vaccine’s Effectiveness

- Various measures of efficacy
  - Efficacy for susceptibility: compare risk of infection in vaccinated people to unvaccinated people (condition on exposure?)
    - Double blind randomized trials (efficacy or effectiveness?)

---

Kendrick and Eldering (1939): pertussis vaccine

<table>
<thead>
<tr>
<th>Classification according to history of exposure</th>
<th>No history of exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite in own household</td>
<td>Definite in other household</td>
</tr>
<tr>
<td>Both groups</td>
<td>243</td>
</tr>
<tr>
<td>No. of exposures</td>
<td>172</td>
</tr>
<tr>
<td>Per cent</td>
<td>70.8</td>
</tr>
</tbody>
</table>

Vaccine group

<table>
<thead>
<tr>
<th>Classification according to history of exposure</th>
<th>No history of exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite in own household</td>
<td>Definite in other household</td>
</tr>
<tr>
<td>No. of exposures</td>
<td>83</td>
</tr>
<tr>
<td>No. of exposures</td>
<td>29</td>
</tr>
<tr>
<td>Per cent</td>
<td>34.9</td>
</tr>
</tbody>
</table>

Control group

<table>
<thead>
<tr>
<th>Classification according to history of exposure</th>
<th>No history of exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite in own household</td>
<td>Definite in other household</td>
</tr>
<tr>
<td>No. of exposures</td>
<td>160</td>
</tr>
<tr>
<td>No. of exposures</td>
<td>143</td>
</tr>
<tr>
<td>Per cent</td>
<td>89.4</td>
</tr>
</tbody>
</table>

PEARL KENDRICK AND GRACE ELDERING
Measuring a Vaccine’s Effectiveness

• Various measures of efficacy

  – Efficacy for susceptibility: compare risk of infection in vaccinated people to unvaccinated people (condition on exposure?)

• Double blind randomized trials (efficacy or effectiveness?)

\[ \text{Kendrick and Eldering (1939): pertussis vaccine} \]

<table>
<thead>
<tr>
<th></th>
<th>Vaccinated</th>
<th>Unvaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attacks</td>
<td>29</td>
<td>143</td>
</tr>
<tr>
<td>Exposures</td>
<td>83</td>
<td>160</td>
</tr>
</tbody>
</table>

\[ VE_{S,p} = 1 - \frac{.349}{.894} = 0.61. \]
Measuring a Vaccine’s Effectiveness

• Various measures of efficacy
  – Efficacy for susceptibility: compare risk of infection in vaccinated people to unvaccinated people (condition on exposure?)
    • Double blind randomized trials (efficacy or effectiveness?)
  – Efficacy for infectiousness: transmission rates for infected vaccinated individuals compared to infected unvaccinated
  – Efficacy for disease progression
Measuring a Vaccine’s Effectiveness

- Various measures of efficacy
  - Efficacy for susceptibility: compare risk of infection in vaccinated people to unvaccinated people (condition on exposure?)
    - Double blind randomized trials (efficacy or effectiveness?)
  - Efficacy for infectiousness: transmission rates for infected vaccinated individuals compared to infected unvaccinated
  - Efficacy for disease progression
  - Direct and indirect effects (herd immunity)

*Figure: Halloran and Struchiner (1991)*
Figure: Comparison of two populations.
• $\text{VE}_{\text{direct}} = 1 - \frac{70}{700} = 1 - \frac{0.1}{0.3} = 0.66$

• $\text{VE}_{\text{indirect}} = 1 - \frac{90}{300} = 1 - \frac{0.3}{0.85} = 0.65$

• $\text{VE}_{\text{total}} = 1 - \frac{70}{850} = 1 - \frac{0.1}{0.85} = 0.88$

• $\text{VE}_{\text{overall}} = 1 - \frac{160}{1000} = 1 - \frac{0.16}{0.85} = 0.81$
Adverse Side Effects

• 1950s: Thalidomide & birth defects (> 10K)
  – Sherry Finkbine
• 2000s: Vioxx and heart attacks (80M patients, > 100K Mis)
• 200s: Avandia ($2.2B per year at height, lawsuits cost perhaps $1-6B)
• Rare events
• Meta-analysis (combining information from different sources)