Lecture 4

Contraception Evaluation
Lecture Objectives

- Measurement of contraceptive prevalence
- Estimate use-effectiveness
- Clinical trials to evaluate efficacy and safety of contraceptives
Contraceptive Prevalence

- Population-based surveys
- Provider-based data
  - Clinics
  - Pharmacy prescriptions
  - Surgical procedure surveillance (abortion, sterilization)
Population Surveys

- **International Surveys**
  - World Fertility Survey (WFS)
  - Contraceptive Prevalence Survey (CPS)
  - Demographic and Health Surveys (DHS)

- **National Surveys**
  - National Survey of Family Growth (NSFG)

- **Special Survey of Adolescents**

- Prevalence of use by method, age, and time trends
Modern contraceptive use

Percentage of married women of reproductive age currently using contraception

Contraceptive prevalence (percentage)
- 60 and over
- 40 to less than 60
- 20 to less than 40
- Less than 20
- No data

The boundaries and delineations used on this map do not imply official endorsement or acceptance by the United Nations.

Contraceptive use among married women
Type-specific contraceptive use in married women

Per cent of married women of reproductive age currently using contraception, by method

- Female sterilization
- Pill
- IUD
- Rhythm/Withdrawal
- Male sterilization
- Injectable
- Condom
- Other

World
More developed regions
Less developed regions

Total Fertility rates by region

Children Per Woman

<table>
<thead>
<tr>
<th>Region</th>
<th>1950-1955</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>6.5</td>
<td>5.0</td>
</tr>
<tr>
<td>Asia</td>
<td>6.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Latin American &amp; Caribbean</td>
<td>5.5</td>
<td>3.5</td>
</tr>
<tr>
<td>North America</td>
<td>3.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Europe</td>
<td>2.5</td>
<td>2.0</td>
</tr>
</tbody>
</table>
## Contraceptive Use in women 15-44, US 1982-2002

<table>
<thead>
<tr>
<th></th>
<th>1982 %</th>
<th>1988 %</th>
<th>1995 %</th>
<th>2002 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Using contraception</td>
<td>55.7</td>
<td>60.3</td>
<td>64.2</td>
<td>62.0</td>
</tr>
<tr>
<td>Sexually active but not using contraception</td>
<td>7.4</td>
<td>6.7</td>
<td>5.2</td>
<td>7.0</td>
</tr>
</tbody>
</table>

Piccinino & Mosher *Fam Plann Perspect* 1998;30:4, AGI 2005
# Contraceptive Use in women 15-44, by Race; US 1982-95

<table>
<thead>
<tr>
<th>Race</th>
<th>1982 %</th>
<th>1988 %</th>
<th>1995 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>57.3</td>
<td>62.9</td>
<td>66.1</td>
</tr>
<tr>
<td>Black</td>
<td>51.6</td>
<td>56.8</td>
<td>62.1</td>
</tr>
<tr>
<td>Hispanic</td>
<td>50.6</td>
<td>50.4</td>
<td>59.0</td>
</tr>
</tbody>
</table>

Piccinino & Mosher *Fam Plann Perspect* 1998;30:4
Contraceptive Prevalence US 1972-2002

National Surveys of Family Growth
Weakness of survey data

- Changing sampling frame over time (e.g., exclusion of unmarried women <1980s)

- Recall and reporting errors (e.g., omission of induced abortion, timing errors)
Abortion Underreporting

- Compare expected number of abortions from surveillance data with reported number from surveys
- U.S. underreporting $\sim 30$-$40\%$
- Underreporting of abortions
  - Embarrassment / regret
  - Reticence to admit contraceptive failure
Of abortions estimated as having occurred among U.S. women aged 15-44 in 1995, percentage reported in Cycle 5 of the NSFG, by reporting of procedure and year of abortion.
Nearly half of all pregnancies in the United States each year are unintended.
The small proportion of women who do not use contraceptives . . . account for roughly half of all unintended pregnancies.

Women at risk of unintended pregnancy, 1995 (42 million)

- Not using: 7%
- Using: 93%

Women experiencing unintended pregnancies, 1994 (3 million)

- Not using: 47%
- Using: 53%
Provider-Based Data

- Contraceptive sales and formulations from prescription surveys
- Abortion from facilities surveys
  - CDC surveillance
  - Guttmacher Institute surveillance
- Sterilization (tubal ligation, vasectomy) procedures
Provider-Based Data on Contraceptive Use
National Prescription Audit (Pharmacy based)


Oral Contraceptives in the United States: Trends In Content and Potency.


Arrow denotes change in database
Induced Abortion

- Two surveillance systems
  - Allan Gutmacher Institute (AGI)
  - CDC
  - Maintain surveillance of large samples of providers

Abortion Rate (per 1,000 women) in the U.S. 1973-1996

Converted from Henshaw, 1998
Classification of contraception

- Intercourse related methods
  - Physical barriers; condom, diaphragm, cervical cap
  - Chemical: Nonoxynol 9 (N9) spermicides
  - Periodic abstinence (Natural Family Planning NFP)

- Hormonal methods with daily compliance
  - Combined oral contraceptives (estrogen & progestin)
  - Progestin only (for breastfeeding)
Classification of contraception ctd.

- **Long acting methods**
  - Injectable: Depot Provera (3 months), NET (2 mths), monthly combined Est & Progestin
  - Norplant, Jadelle
  - IUD (copper and hormonal devices)
Implants (Brache et al Contraception 2006;73:364)

- **Norplant:** Levonorgestrel 6 rods implanted under the skin. Effective for 7 years
- Problems
  - Local irritation
  - Difficult to remove

- **Jadelle:** Levonorgestrel 2 rods, effective 5 years
- Advantages
  - Less local irritation
  - Easier removal
Permanent methods

- **Female Tubal ligation**
  - Surgical (reversible, irreversible), chemical

- **Male vasectomy**
  - Surgical (reversible, irreversible), chemical
Contraceptive Use Effectiveness

Definition:
- Measurement of the cumulative incidence of events (e.g. pregnancy rates), and continuity of use (continuation rates)

Sources of data:
- Retrospective data from surveys used for population based estimates
- Prospective data from clinical trials used for comparative effectiveness estimates
Data for Use-Effectiveness

- Date of first and last use, or date of withdrawal or last observation
- Reason for termination (exclusive definition varies by method)
- Sociodemographic characteristics
  - Age, parity, marital status
  - Fertility intention (spacing/limiting)
Measurement of Use-Effectiveness

- **Pearl Pregnancy Rate:**

  Pregnancy per 100 woman years = total accidental pregnancies / total years of exposure x 100

  - Problem of interpretation due to time bias (combines months of use into an aggregate total and assumes constant risk)
  
  - One woman using for 12 months, same as 12 women using for one month
Measurement of Use-Effectiveness

- *Multiple decrement Life table Rates:*

- Estimates of cumulative continuation rates and cumulative non-competing risk discontinuation rates for specific events
Estimation of Use-Effectiveness

- Population Surveys

- Objectives: To compare pregnancy and continuation rates between different types of contraceptives in the general population

- Methods: Population sample surveys using retrospective interviews
Survey Estimation of Use-Effectiveness

- **Advantages**: Allows comparison between methods in general use, shorter study time and lower costs.

- **Limitations**: Recall errors, underestimation of induced abortion, self-selection affect comparisons between methods. Need to adjust for age, parity, SES and fertility intention.
Effectiveness
By burden of compliance

Comparing Typical Effectiveness of Contraceptive Methods

<table>
<thead>
<tr>
<th>Most effective</th>
<th>How to make your method more effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generally 1 or fewer pregnancies per 100 women in one year</td>
<td>One-time procedures; nothing to do or remember</td>
</tr>
<tr>
<td>Implants</td>
<td>Female Sterilisation</td>
</tr>
<tr>
<td>Injectables</td>
<td>Need repeat injections every 1, 2 or 3 months</td>
</tr>
<tr>
<td>Pills</td>
<td>Patch</td>
</tr>
<tr>
<td>Must take a pill or wear a patch or ring every day</td>
<td></td>
</tr>
<tr>
<td>Lactational Amenorrhea Method (LAM)</td>
<td>Must follow LAM instructions</td>
</tr>
<tr>
<td>Male condoms</td>
<td>Must use every time you have sex; requires partner’s cooperation</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>Must use every time you have sex</td>
</tr>
<tr>
<td>Cervical Cap</td>
<td>Sponge</td>
</tr>
<tr>
<td>Must use every time you have sex</td>
<td></td>
</tr>
<tr>
<td>Withdrawal</td>
<td>Fertility Awareness-Based Methods (selected)</td>
</tr>
<tr>
<td>Require partner’s cooperation; for FABs must abstain or use condoms on fertile days</td>
<td>Must use every time you have sex</td>
</tr>
</tbody>
</table>

About 30 pregnancies per 100 women in one year

Least effective

Source: WHO 2006
Contraceptive Failure

- **Method of contraception**
  - Failure rates higher with intercourse related methods (barriers, NFP)
  - Intermediate with non-intercourse related, interval methods (e.g. Pill, injection, implant, IUD)
  - Lowest with permanent methods (e.g. sterilization)
Factors Associated with Contraceptive Failure

- **Sociodemographic Characteristics**
  - Age
  - Parity
  - Marital status
  - Education / SES

- **Motivation / Sensitivity**
  - Spacing vs. terminating reproduction
  - Underreporting of unplanned pregnancy
  - Underreporting of induced abortion
# Relative Risk of Contraceptive Failure

(US 1995)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic</td>
<td>1.25 (1.02-1.54)</td>
</tr>
<tr>
<td>Low-income</td>
<td>1.54 (1.28-1.85)</td>
</tr>
<tr>
<td>First use of any method</td>
<td>0.60 (0.48-0.76)</td>
</tr>
<tr>
<td>Higher education</td>
<td>0.64 (0.44-0.2)</td>
</tr>
<tr>
<td>Desire for a child in the future</td>
<td>1.77 (1.46-2.150)</td>
</tr>
</tbody>
</table>

Trussell and Vaughan Fam Plann Perspect 1999;31:64
Semen exposure with Condom failures

- 830 couples, women collect postcoital vaginal sample for PSA and sperm detection
- No condom 97% PSA+, 79% sperm
- Condom breaks 65% PSA+, sperm 38%
- Condom slip 45% PSA+, sperm 0%

- Walsh *Contraception* 2003, 67:139
Contraceptive Clinical Trials

- **Phase 1**: Short-term pharmacokinetics and pharmacodynamics, acute toxicity and dose finding
- **Phase 2**: Estimate of use-effectiveness in non-comparative trial, determine clinical regimen
- **Phase 3**: Large-scale comparative, randomized trials to establish use-effectiveness relative to standard treatment
Randomized Clinical Trials

- **Objectives**: Comparison of use-effectiveness between two or more methods of the same type of contraceptive (e.g. IUDs, pills)

- **Methods**: Random allocation within method and prospective follow-up study, preferably double blind
Randomized Clinical Trials

- **Advantages**: Unbiased comparison, comparability of treatment groups, good internal validity

- **Limitations**: Selected clinic population may affect external validity. Prolonged study and high costs. Cannot compare across type of contraceptive (e.g. IUD vs. Pill)
Multiple Decrement Life Table Analysis

- Multiple reasons for terminating contraception, requires multiple decrement life table
- **Competing risk rates**: estimated for each termination type, adjusted for losses to follow-up and censoring.
  - Estimates the relative frequency of different terminations, rates are additive
Life Table Analysis

- **Non-Competing Risk Rates**: Estimated for each reason for termination, treating all other reasons for termination as censoring.
  - Provides unbiased estimate of termination rates for each reason separately, rates are not additive.
  - Estimates are higher than for competing risks
  - Best estates for clinical trials
**Competing Risk Rates**

\[ q_x = \frac{E_x}{N_x^*} \]

- Where \( q_x \) is the conditional probability of termination during the interval \((x, x+1)\), \( E \) the number of terminations and \( N^* \) is the adjusted population at risk

- \( N_x^* = N_x - \frac{W_x}{2} \), where \( W_x \) are the withdrawals due to losses or censoring in the interval \((x, x+1)\)
Non-Competing Risk Rates

$q_x = \frac{E_x}{N_x^{**}}$

- Where $q_x$ is the non-competing risk probability of terminating in the interval, the $N^{**}$ the population at risk after adjusting for withdrawals ($W_x$) and all other reasons for termination ($T_x$)

- $N_x^{**} = N_x - (W + T_x /2)$
Cumulative Rates of Continuation and Termination

- **Cumulative rates of continuation**, $P(0, x+1)$ are estimated from the product of the interval retention rates ($p_x$), where:
  - $p_x = 1 - q_x$
  - $P(0, x+1) = p_1 \times p_2 \times p_3 \ldots \times p_x$

- **Cumulative termination rates are**:
  - $Q(0, x+1) = 1 - P(0, x+1)$
# IUD Trials: Events per 100 person years

<table>
<thead>
<tr>
<th></th>
<th>Pregnancy %</th>
<th>Expulsion %</th>
<th>Removal Bleeding / pain %</th>
<th>Continuation %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper T</td>
<td>0.5</td>
<td>3.7</td>
<td>2.2</td>
<td>76.3</td>
</tr>
<tr>
<td>Lippes Loop</td>
<td>1.9*</td>
<td>7.8*</td>
<td>4.5*</td>
<td>68.8*</td>
</tr>
</tbody>
</table>

WHO Contraception 1982;26:1-26
Post-coital Emergency Contraception

- Combination of estrogen + progestin (e.g., COC) Plan B
- Levonorgestrel
- Low dose mifepristone (RU486)
- Taken <72 hrs after unprotected intercourse
Evaluation of Post-Coital Emergency Contraception

- Expected probability of pregnancy ~ 25% cycle
- Emergency contraception ~1.5- 3% pregnancy rate/cycle
- 8 studies suggest effectiveness ~81% with intercourse on or before -1 day before ovulation and 17% if intercourse occurred later

(Trussel Contraception 2003; 67: 167)
Access to post-coital contraception

- Timing of use <72 hours critical
- **France**
  - Access without prescription and no fees
  - Via pharmacies, school nurses etc
  - 1.5 mill prescriptions since 1999, 97% without prescription
- **US.** Requires physician prescription, restrictions on OTC by age, limits access and causes delays