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# Lecture 4

## Contraception Evaluation

# Lecture Objectives

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

# Contraceptive Prevalence

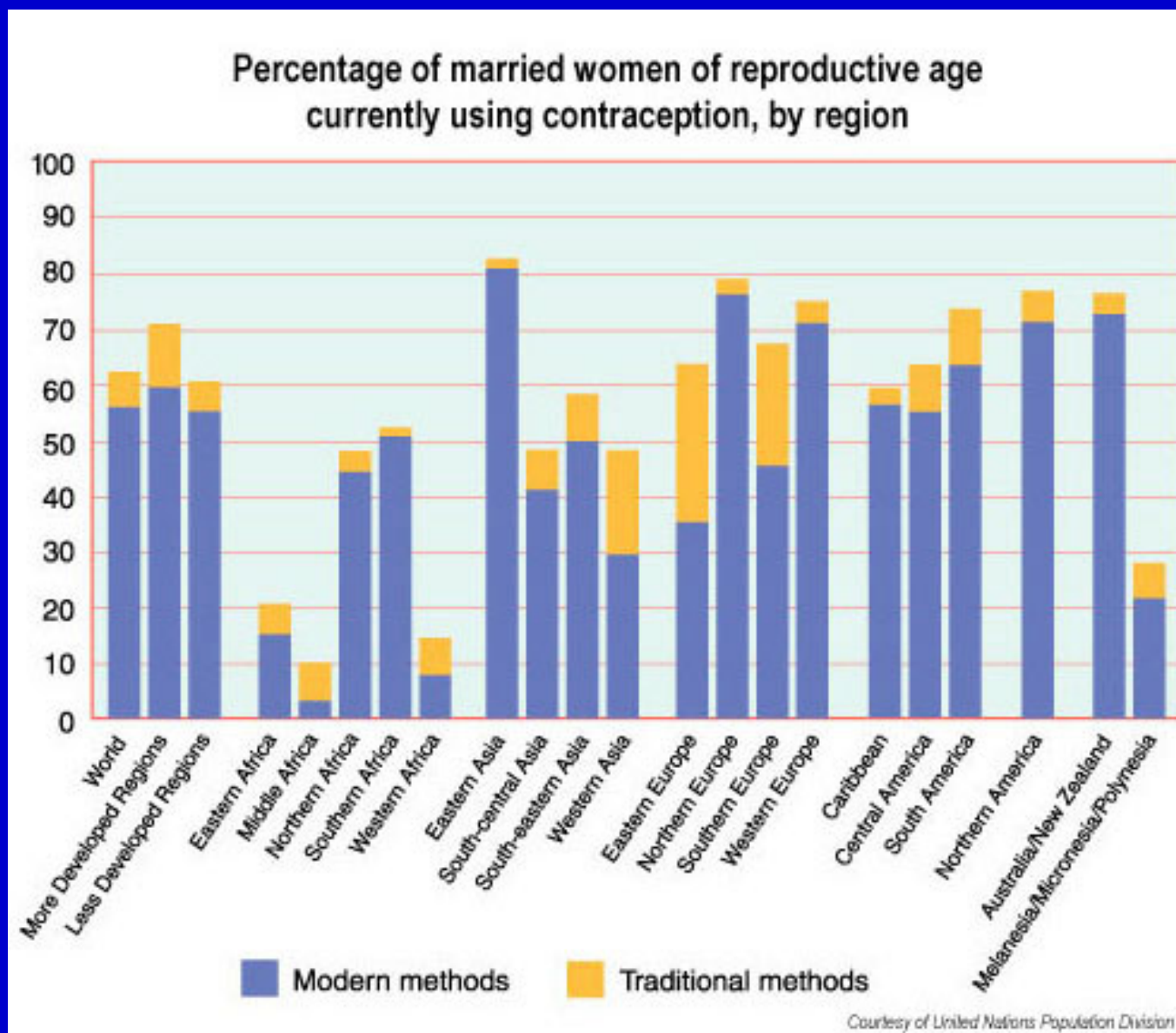
- ◆ Population-based surveys
- ◆ Provider-based data
  - Clinics
  - Pharmacy prescriptions
  - Surgical procedure surveillance (abortion, sterilization)

# Population Surveys

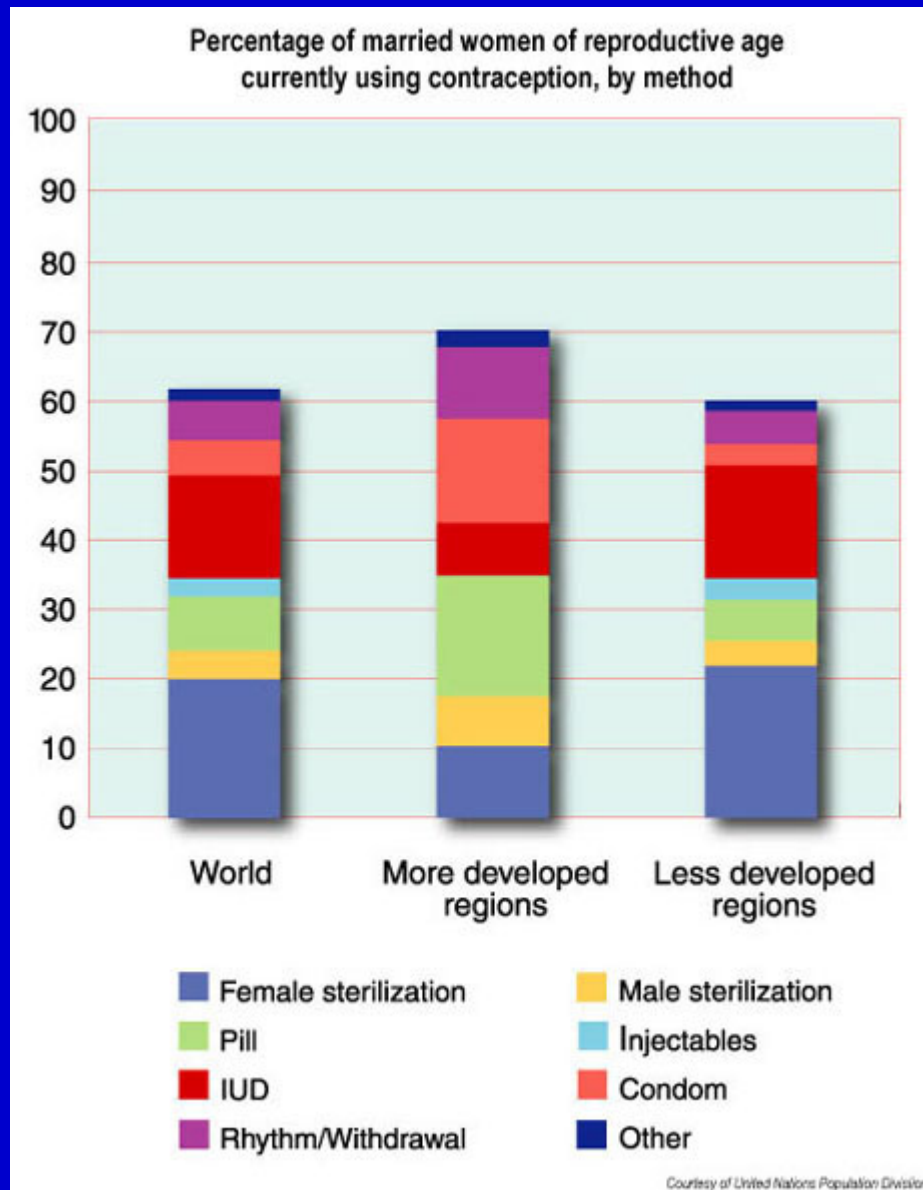
- ◆ International Surveys
  - World Fertility Survey (WFS)
  - Contraceptive Prevalence Survey (CPS)
  - Demographic and Health Surveys (DHS)
- ◆ National Surveys
  - National Survey of Family Growth (NSFG)
- ◆ Special Survey of Adolescents
- ◆ Prevalence of use by method, age, and time trends



# Contraceptive use among married women

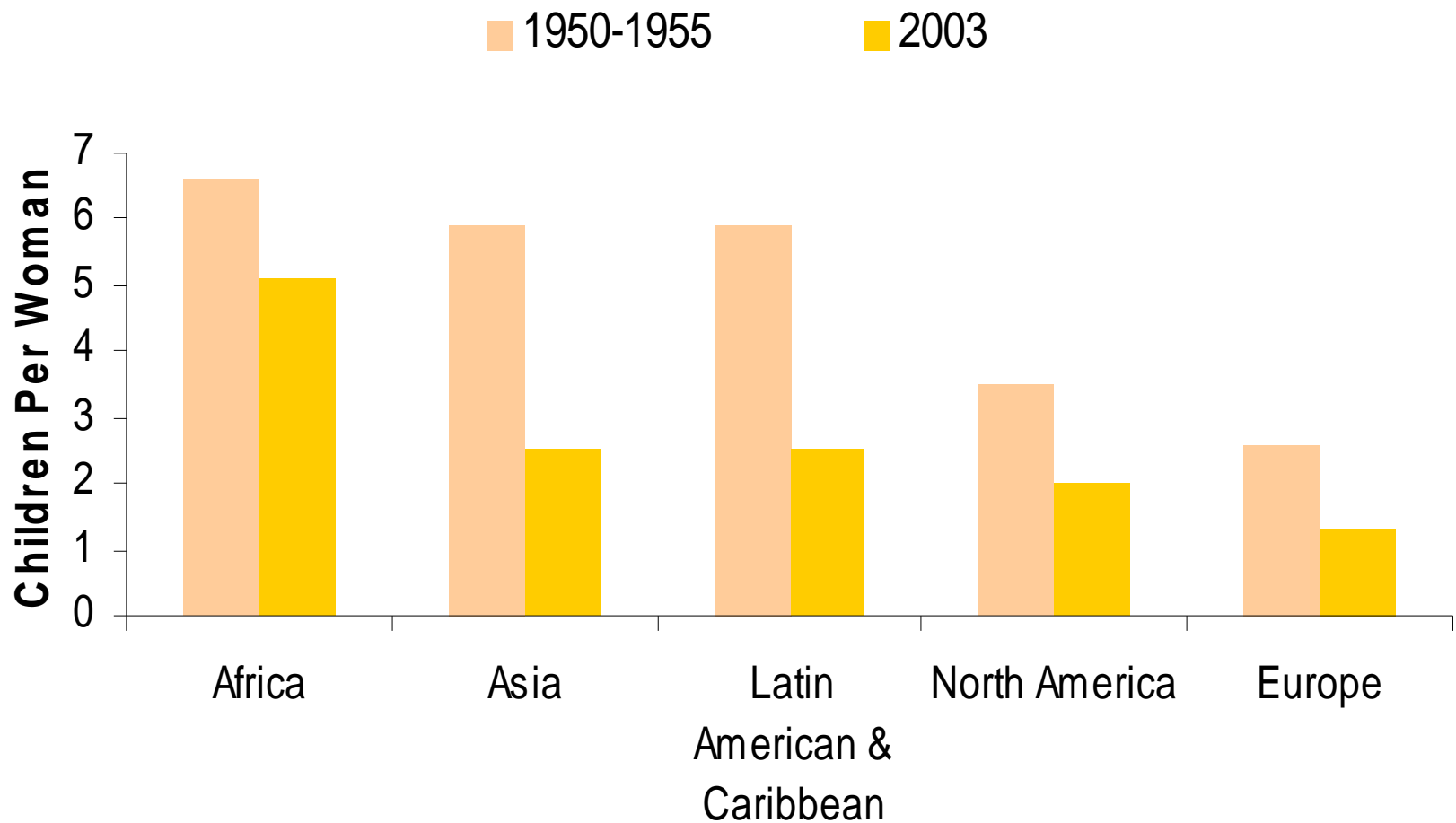


# Type-specific contraceptive use in married women





# Total Fertility rates by region



# Contraceptive Use in women 15-44, US 1982-2002

	1982 %	1988 %	1995 %	2002 %
<b>Using contraception</b>	55.7	60.3	64.2	62.0
Sexually active but not using contraception	7.4	6.7	5.2	7.0

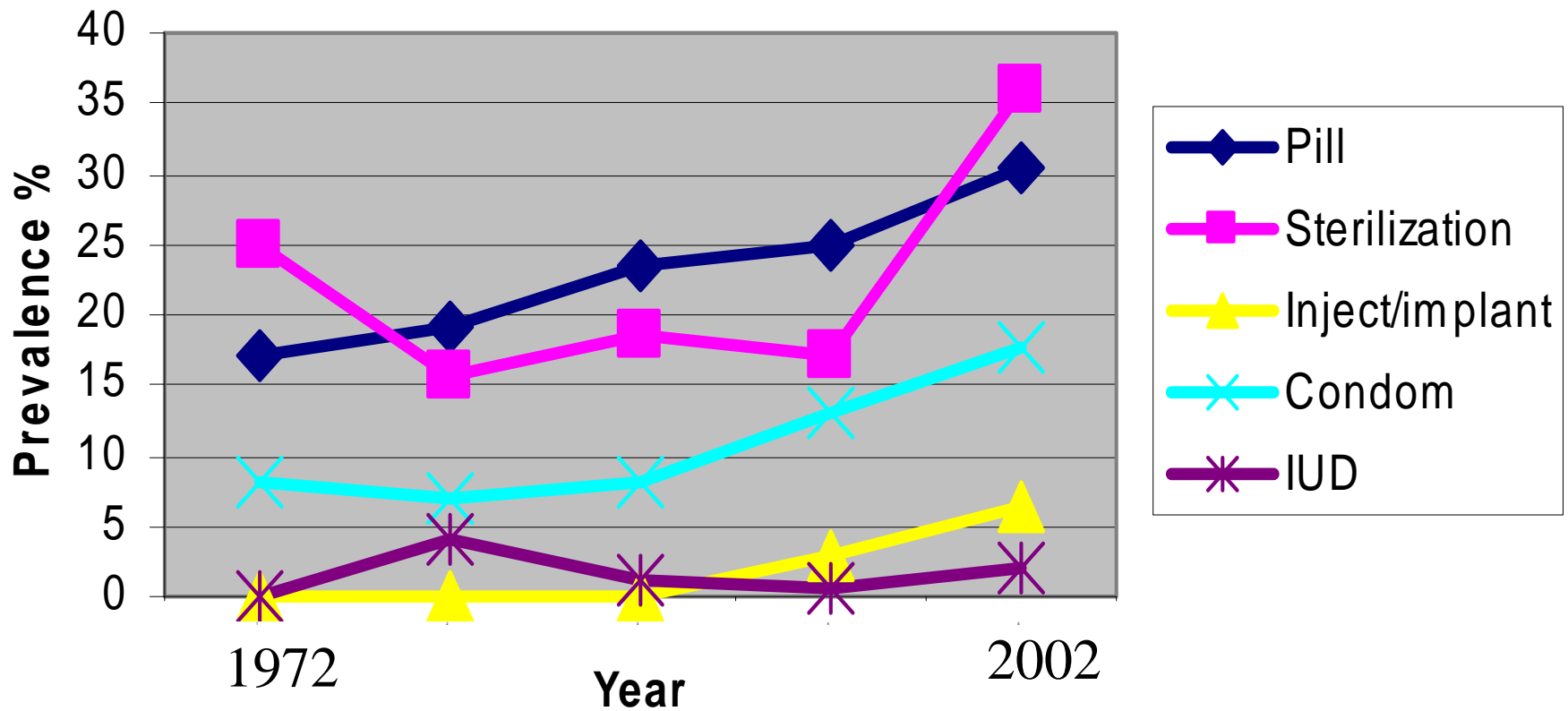
Piccinino & Mosher *Fam Plann Perspect* 1998;30:4, AGI 2005

# Contraceptive Use in women 15-44, by Race; US 1982-95

	1982 %	1988 %	1995 %
Caucasian	57.3	62.9	66.1
Black	51.6	56.8	62.1
Hispanic	50.6	50.4	59.0

Piccinino & Mosher *Fam Plann Perspect* 1998;30:4

# Contraceptive Prevalence US 1972-2002



National Surveys of Family Growth

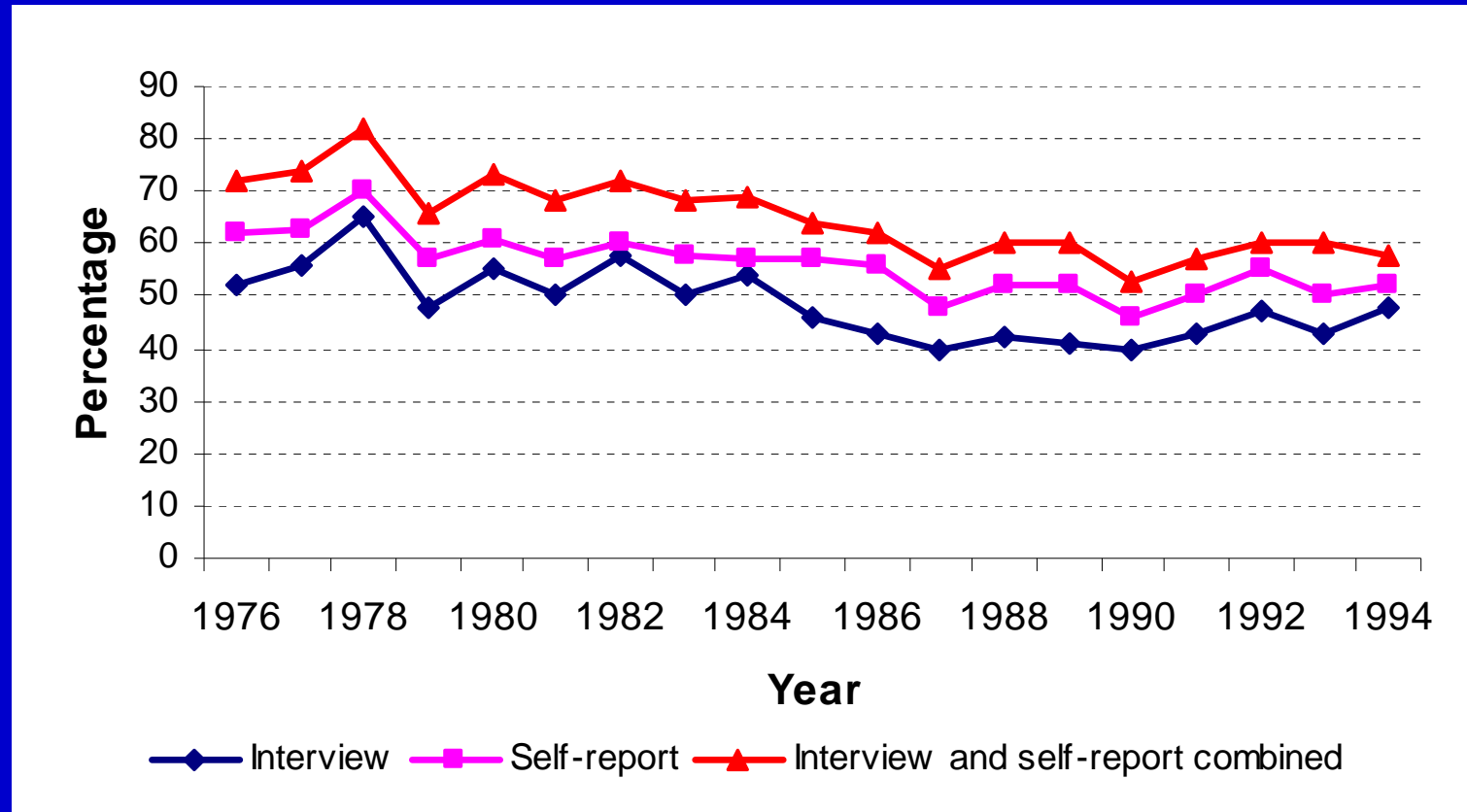
# Weakness of survey data

- ◆ 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

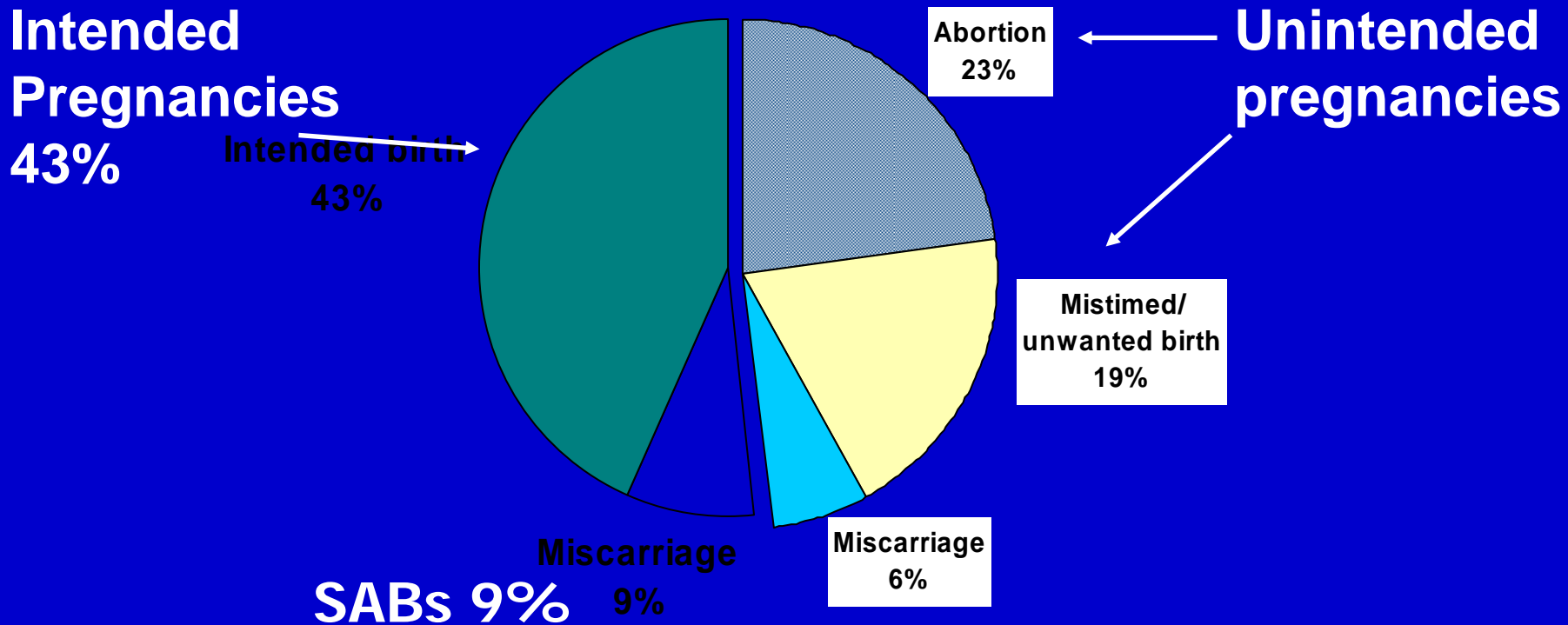
- ◆ Compare expected number of abortions from surveillance data with reported number from surveys
- ◆ U.S. underreporting ~ 30-40%
- ◆ Underreporting of abortions
  - Embarrassment / regret
  - Reticence to admit contraceptive failure

# Reporting of Abortion in US



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

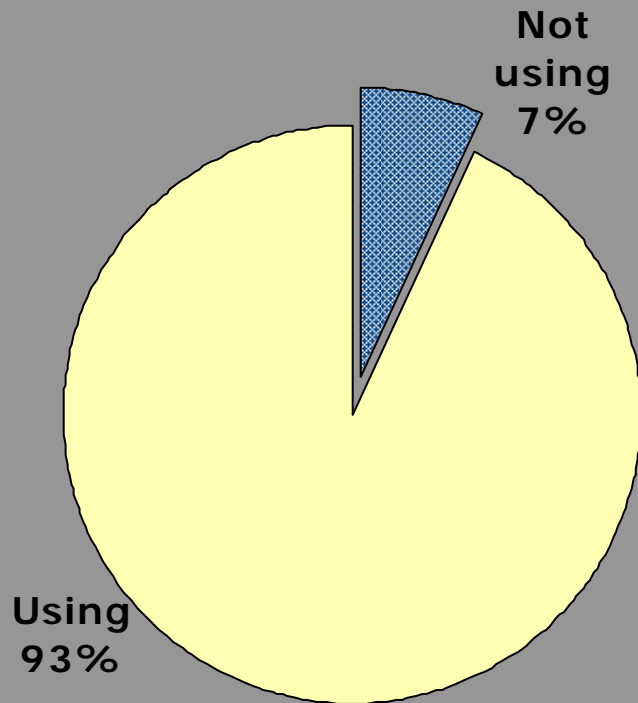


Pregnancies, 1994  
(6.3 million)

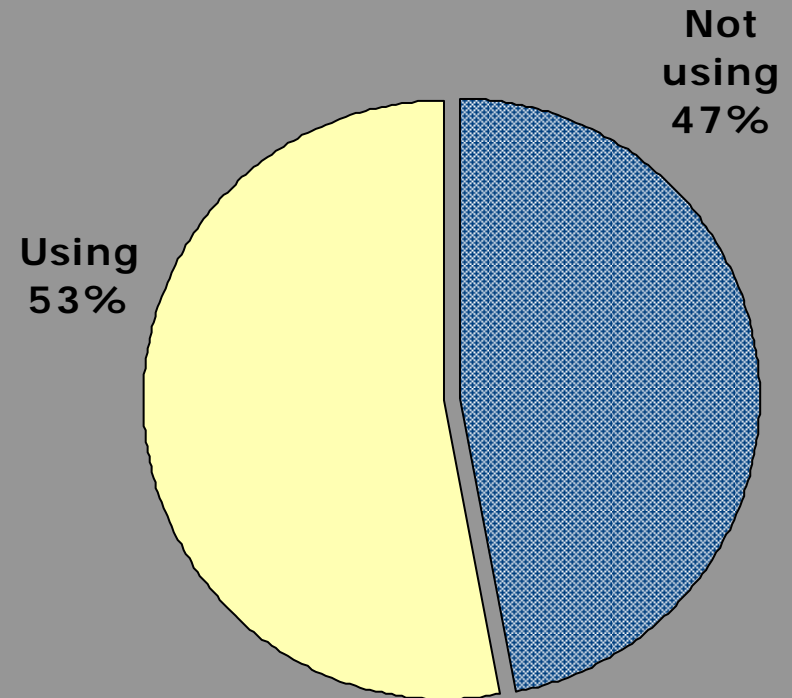


The small proportion of women who do not use contraceptives . . .

. . . account for roughly half of all unintended pregnancies



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



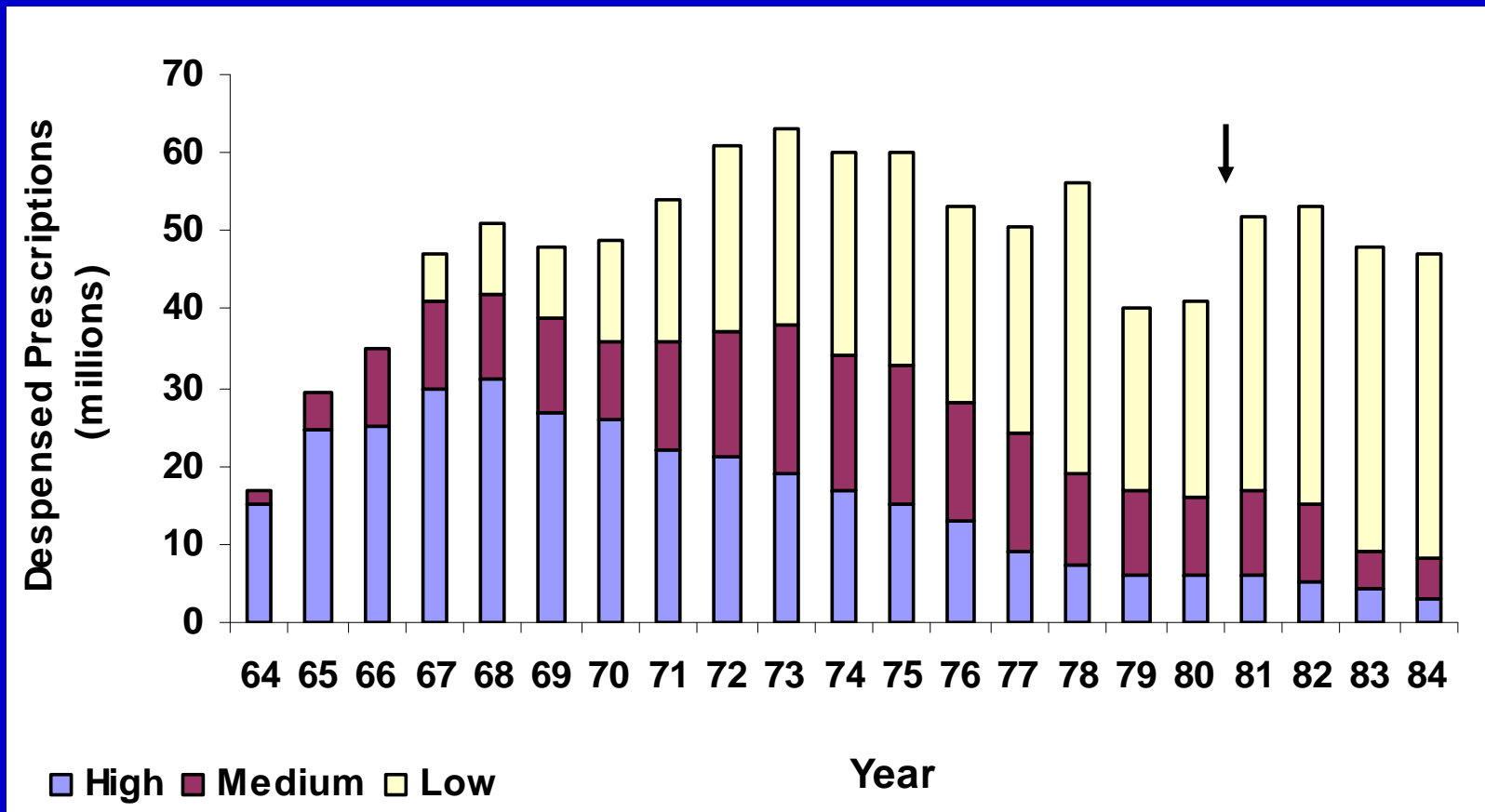
**Women experiencing unintended pregnancies, 1994 (3 million)**

# Provider-Based Data

- ◆ Contraceptive sales and formulations from prescription surveys
- ◆ Abortion from facilities surveys
  - CDC surveillance
  - Guttmacher Institute surveillance
- ◆ Sterilization (tubal ligation, vasectomy) procedures

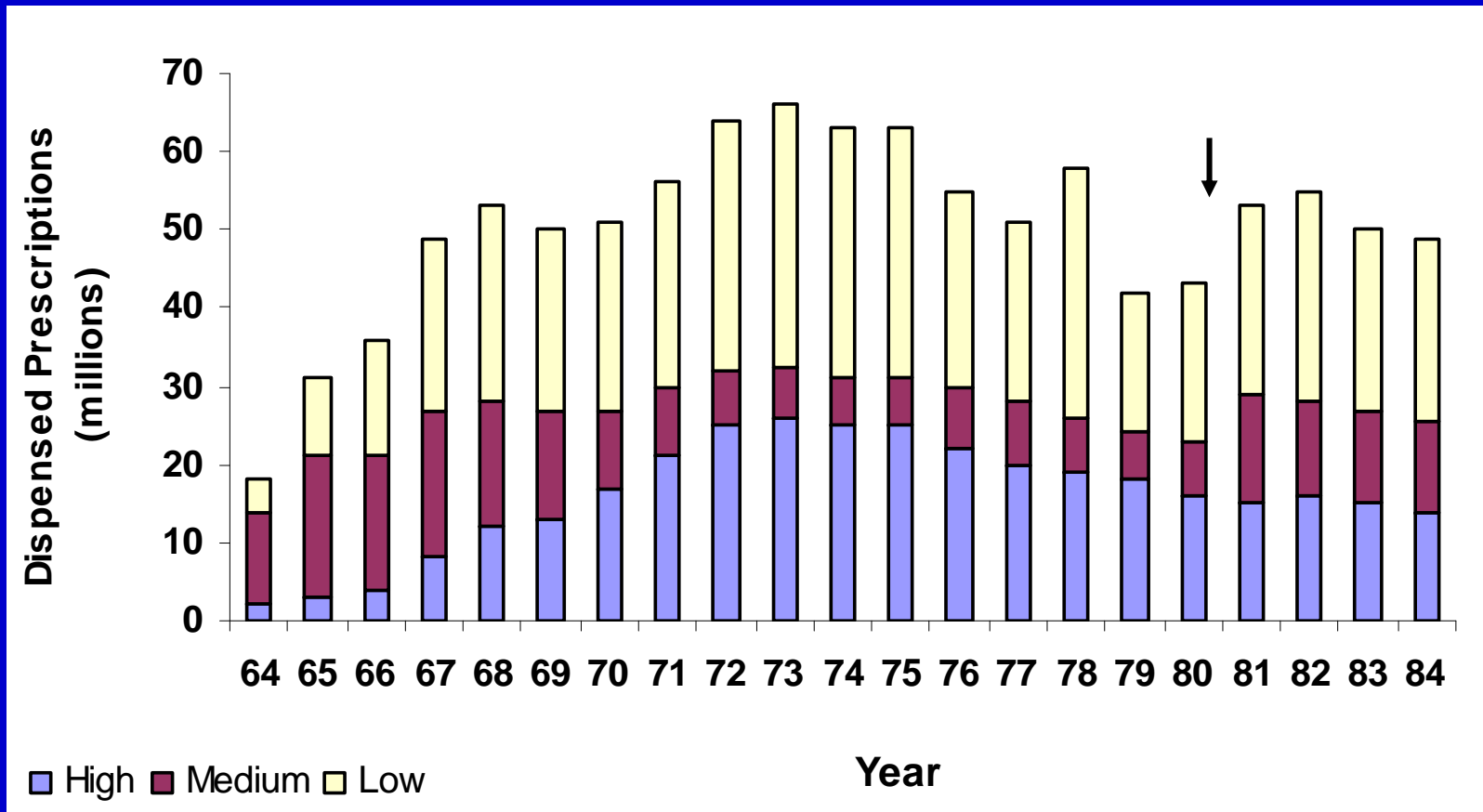
# Provider-Based Data on Contraceptive Use National Prescription Audit (Pharmacy based)

Dispensed retail prescriptions of oral contraceptives by oestrogen potency.  
United States, 1964-84. National Prescription Audit Data.



Data Source: Piper JM and DL Kennedy. *Internatl J Epi.* 16(2): 215-221, 1987.

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



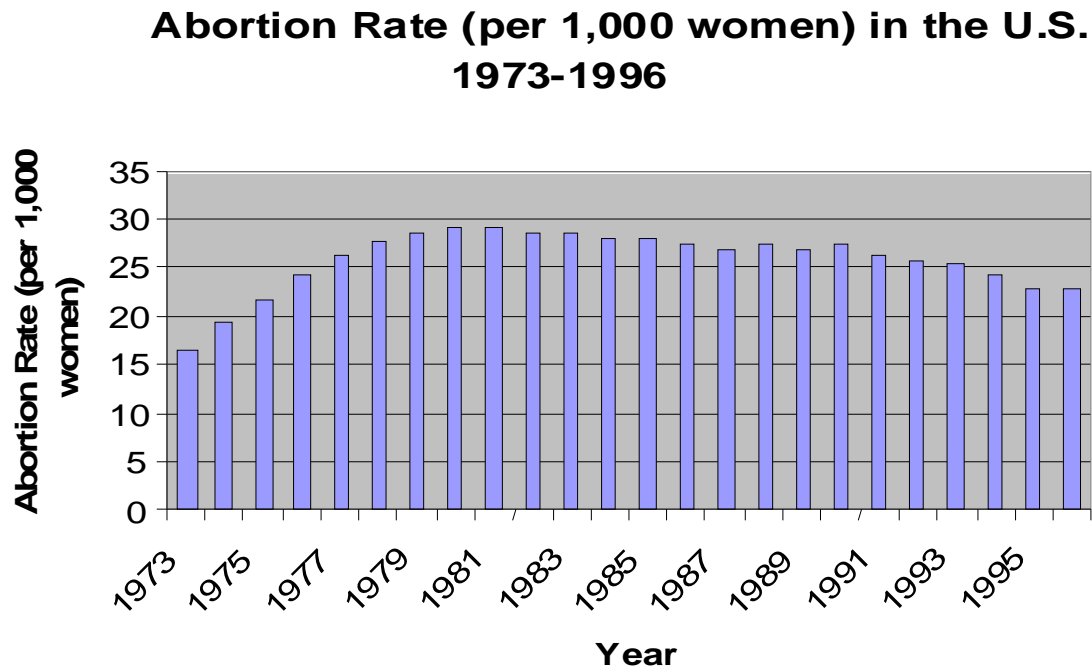
Data Source: Piper JM and DL Kennedy. *Internatl J Epi.* 16(2): 215-221, 1987.

Arrow denotes change in database

# Induced Abortion

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

# U.S. Abortion Rates 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 =  $\frac{\text{total accidental pregnancies}}{\text{total years of exposure}} \times 100$ 
  - 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

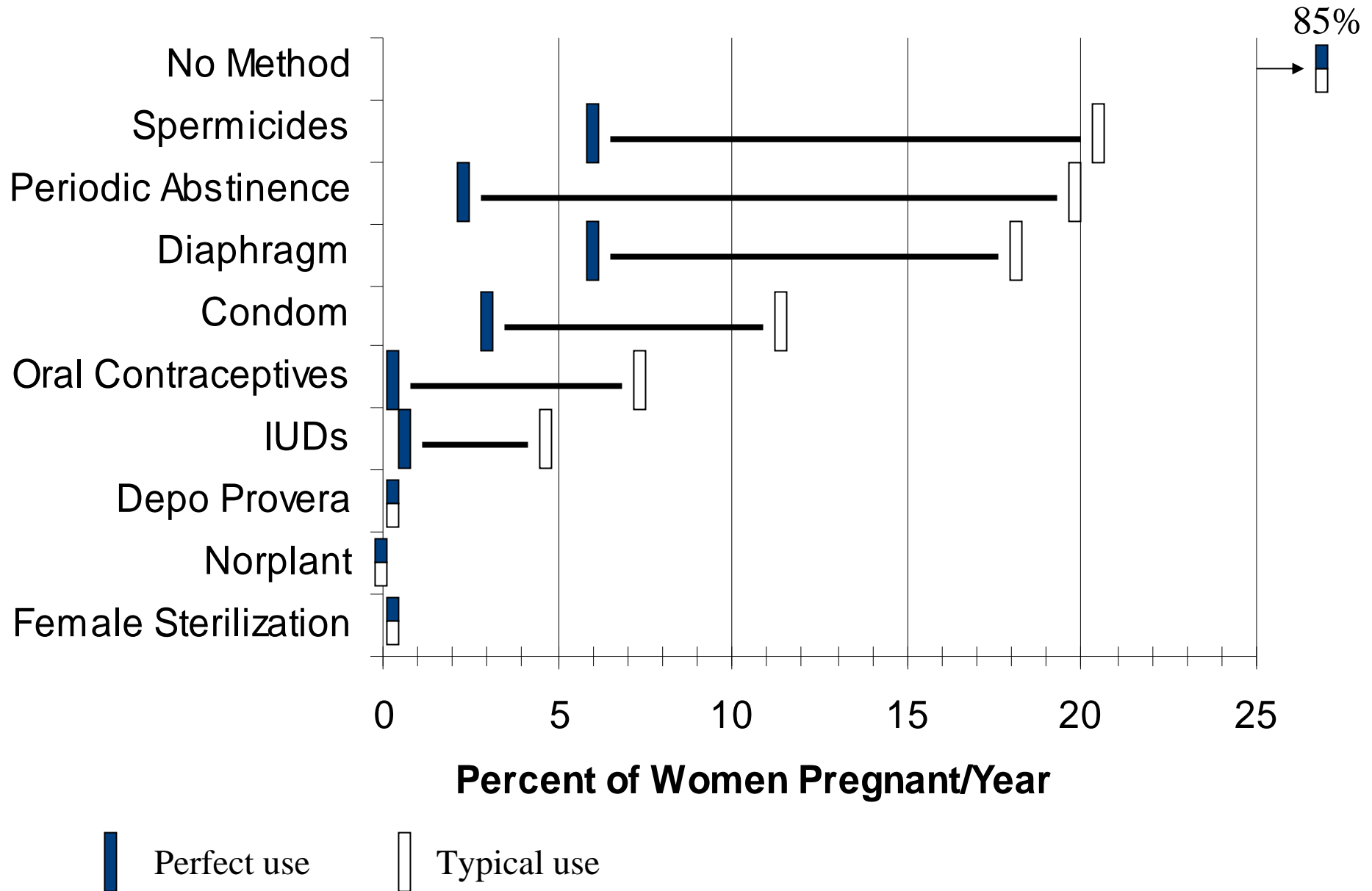
- ◆ **Population Surveys**
- ◆ *Objectives:* To compare pregnancy and continuation rates between different types of contraceptives in the general population
- ◆ *Methods:* Population sample surveys using retrospective interviews

# Survey Estimation of Use-Effectiveness

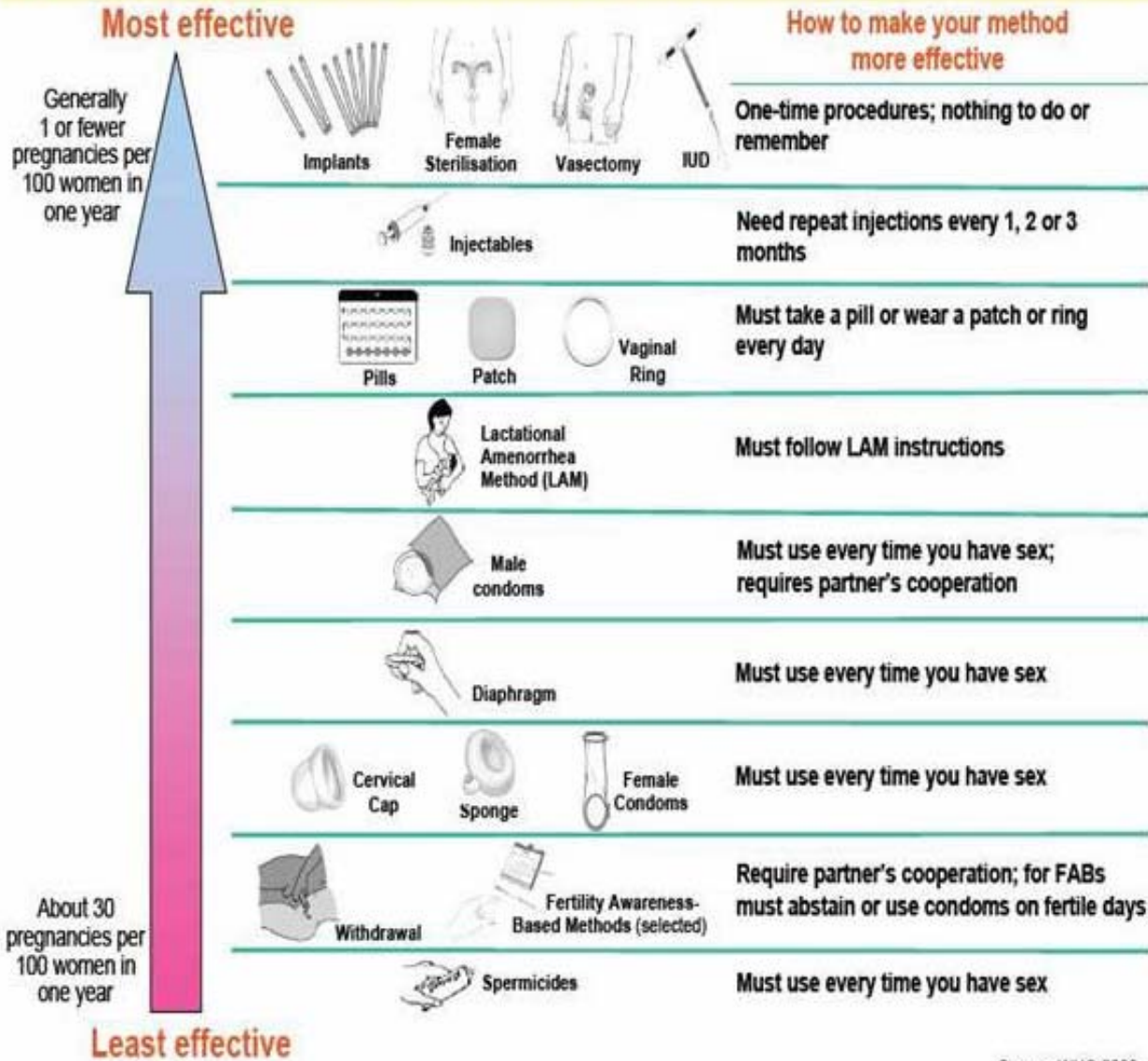
- ◆ *Advantages:* Allows comparison between methods in general use, shorter study time and lower costs.
- ◆ *Limitations:* Recall errors, underestimation of induced abortion, self-selection affect comparisons between methods. Need to adjust for age, parity, SES and fertility intention



# Pregnancy rates with perfect and typical use, by method



# Comparing Typical Effectiveness of Contraceptive Methods



Source: WHO 2006

Effectiveness  
By burden of  
compliance

# 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)

Characteristic	RR (95%CI)
Hispanic	1.25 (1.02-1.54)
Low-income	1.54 (1.28-1.85)
First use of any method	0.60 (0.48-0.76)
Higher education	0.64 (0.44-0.92)
Desire for a child in the future	1.77 (1.46-2.150)

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 estimates for clinical trials

# Competing Risk Rates

$$q_x = E_x / N_x^*$$

- 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
- $N_x^* = N_x - W_x / 2$ , where  $W_x$  are the withdrawals due to losses or censoring in the interval  $(x, x+1)$

# Non-Competing Risk Rates

$$q_x = E_x / N_x^{**}$$

- 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:
  - $p_x = 1 - q_x$
  - $P(0, x+1) = p_1 \times p_2 \times p_3 \dots p_x$
- ◆ Cumulative termination rates are:
  - $Q(0, x+1) = 1 - P(0, x+1)$

# IUD Trials: Events per 100 person years

	Pregnancy %	Expulsion %	Removal Bleeding /pain %	Continuation %
Copper T	0.5	3.7	2.2	76.3
Lippes Loop	1.9*	7.8*	4.5*	68.8*

WHO Contraception 1982;26:1-26

# Post-coital Emergency Contraception

- ◆ Combination of estrogen + progestin (e.g., COC) Plan B
- ◆ Levonorgesterel
- ◆ 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