New Developments in Contraception: The Single-Rod Implant

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Clinical Advisory Committee

Kurt Barnhart, MD, MSCE
University of Pennsylvania
Philadelphia, PA

Barbara Clark, PA-C, MPAS
Knox OB/GYN
Galesburg, IL

Mitchell Creinin, MD (chair)
University of Pittsburgh
Pittsburgh, PA

Christina Cummings, MD, MPH
Planned Parenthood
Pasadena, CA

Wendy Grube, MSN, CRNP
University of Pennsylvania
Philadelphia, PA

Patricia Murphy, CNM, DrPH
University of Utah
Salt Lake City, UT

Lee Shulman, MD
Northwestern University
Chicago, IL

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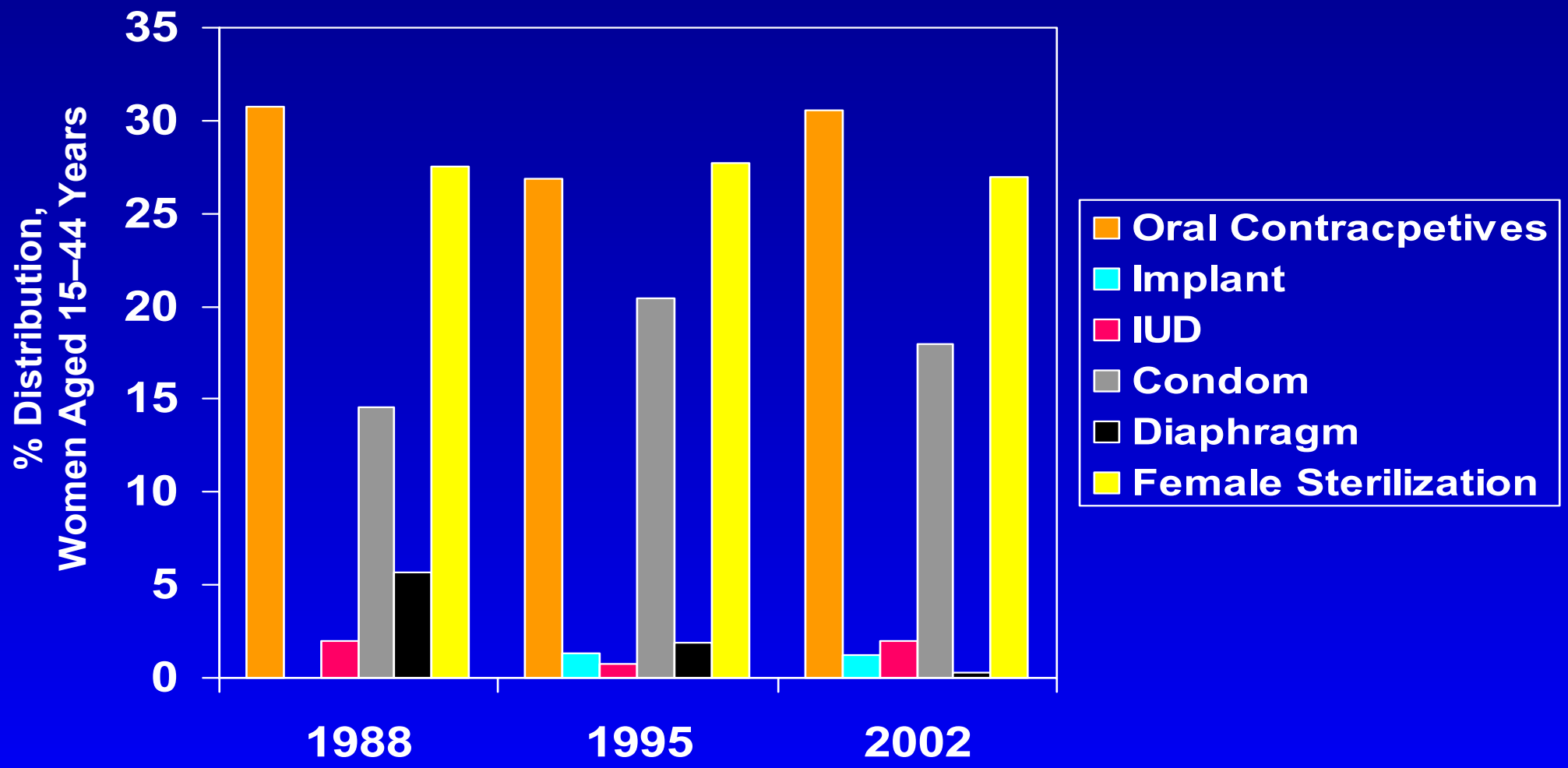
Learning Objectives

- Discuss the features of contraceptive implants
- Dispel provider myths about implants
- Discuss characteristics and clinical expectations of the single-rod implant
- Describe steps for insertion and removal
- List counseling topics for discussion with patients

Contraceptive Use, 1988–2002



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Piccinino. *Fam Plann Perspect* 1998; Mosher. *Advance Data* 2004.

Why Another Contraceptive?

- High unintended pregnancy rate
- High rates of misuse and discontinuation
- Patient interest in alternative methods
- Sterilization regret
- Greater number of safe and effective options allows for better match with individual lifestyle

Risk of Unintended Pregnancy

- Proportion of women at risk for pregnancy increased significantly between 1995 and 2002, from 5.2% to 7.4%
- This represents an increase of 1.43 million women

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Mosher. *Advance Data* No. 350 2004

High Proportion of Pregnancies Are Unintended

Age	Proportion Unintended
15–19	78.0%
20–24	58.5%
25–29	39.7%
30–34	33.1%
35–39	40.8%
>40	50.7%
Total	49.2%

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Henshaw. *Fam Plann Perspect* 1998

High Rate of Contraceptive Misuse

- 1 million pregnancies/year are due to misuse or discontinuation of oral contraceptives (OCs)—the most common reversible contraceptive used in the United States today
- > 50% of all OC users miss more than 2 pills by the 3rd cycle
- Based on 2002 data from the NSFG, it appears that teen use of injectable contraceptives has contributed to the decrease in rate of unintended pregnancy

Rosenberg. *J Reprod Med* 1995
Potter. *Fam Plann Perspect* 1996
Mosher. *Advance Data* No. 350 2004

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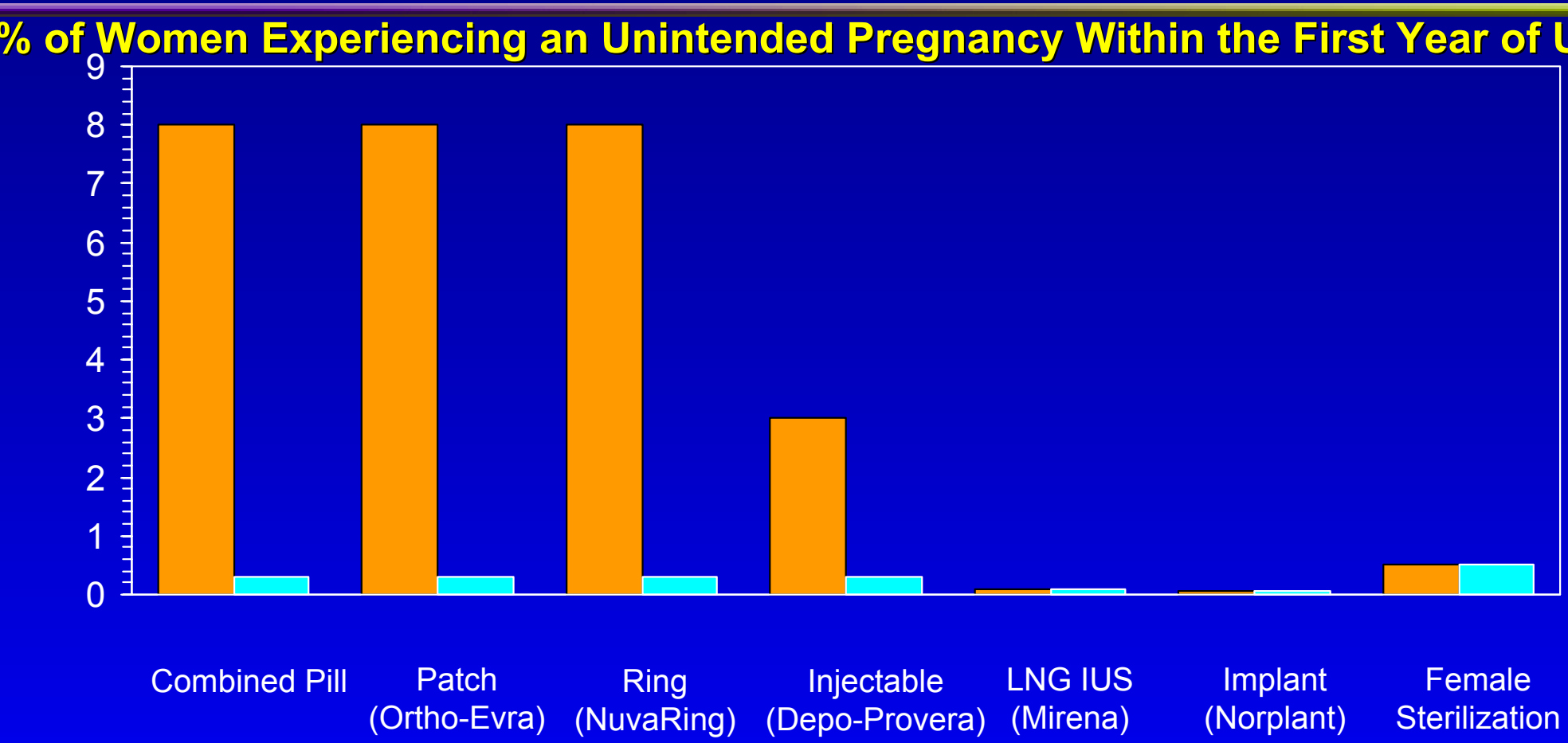
Typical Use Versus Perfect Use



Orange = typical use
Blue = perfect use

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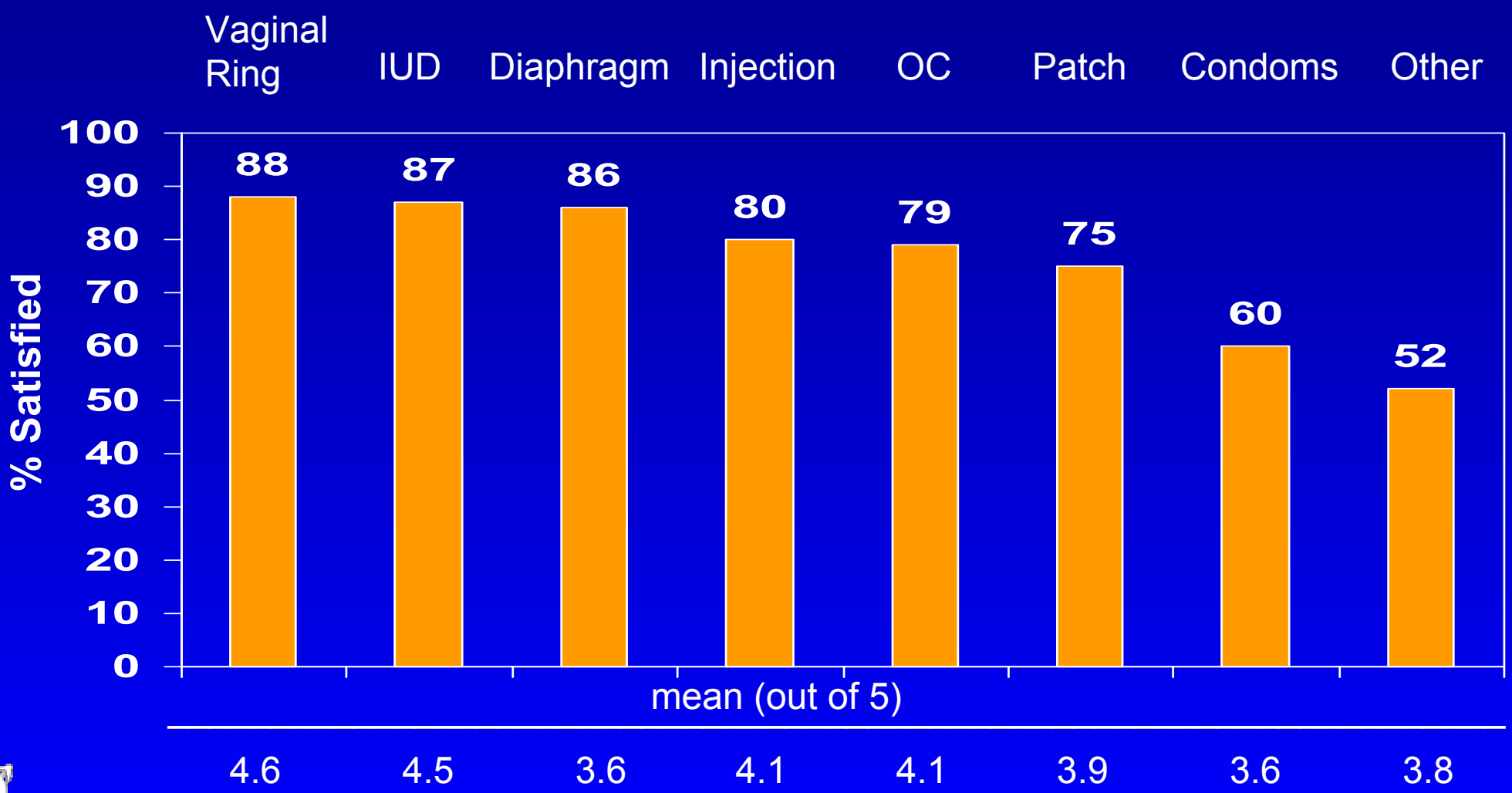
Hatcher R. *Contraceptive Technology* 2004.

High Rate of OC Discontinuation

- Of 1,657 women initiating or switching to a new OC, 18% discontinued by 6 months
- Reasons:
  - Side effects (46%)
  - No need for contraception (23%)
  - Method-related problems (14%)
  - Other, unspecified (17%)

Rosenberg. *Am J Obstet Gynecol* 1998

Interest in Contraceptive Methods



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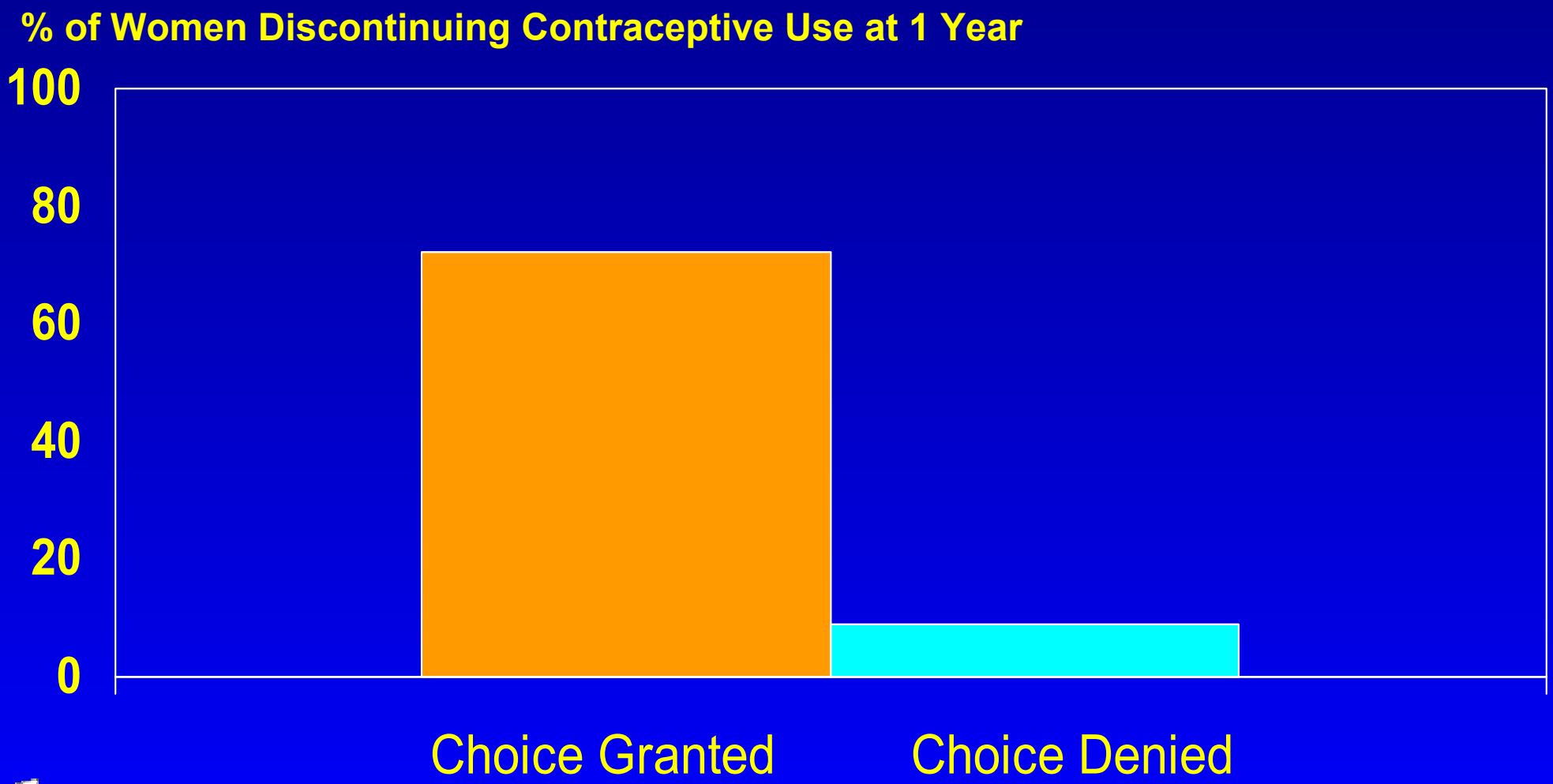
Harris Interactive Poll 2004

Sterilization Regret

- 20% of women who select sterilization at age 30 years or younger later express regret
- Most common reasons for regret—desire for more children (33%) and divorce/remarriage (24%)
- Reversible methods can be as effective as sterilization

Hillis S. *Obstet Gynecol* 1999

Impact of Choice



Pariani. *Stud Fam Plann* 1991

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Unmet Need

For a contraceptive method that is

- Highly effective
- Safe
- Not a daily method
- Rapidly reversible

Worldwide History of Contraceptive Implant Use

1950s Norplant (6 rods) developed

1960s First used for contraception

1990 Approved in United States

1994 Used by almost 1 million American women

2002 Manufacture discontinued

Today

- Norplant is registered in more than 60 countries
- Norplant II (2 rods) is registered in Europe
- Implanon (single rod) likely to be approved by FDA soon

Planned Parenthood. 2004

Glasier. *Contraception* 2002

Features of Contraceptive Implants

- Highly effective and rapidly reversible
- Discreet
- Require no daily or coitus-related action
- Provide non-fluctuating hormone levels and extended contraceptive protection
- Contain no estrogen
- Can be used during lactation

Reinprayoon. *Contraception* 2000
Diaz. *Contraception* 2000

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Features of Contraceptive Implants
(continued)

- Cause unscheduled vaginal bleeding
- Require clinician visits for insertion and removal

Dispelling Provider Myths About Contraceptive Implants

- Insertion and removal are neither time-consuming nor difficult to learn
- Implants are not associated with higher risk of ectopic pregnancy
- Implants are not associated with high litigation risk for providers

Insertion and Removal Are Neither Time-Consuming nor Difficult

	Single-rod implant	Multiple-rod implant	*P* value
Insertion time (minutes)	0.61	3.90	<0.001
Removal time (minutes)	2.18	11.25	<0.001

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Zheng. *Contraception* 1999

No Increased Risk of Ectopic Pregnancy

- No pregnancies (intrauterine or ectopic) reported during 4,103 woman-years of use for single-rod implant in 13 clinical trials
- Multiple-rod implant associated with ectopic rate of 0.3 to 0.6 per 1,000 woman-years
- US baseline ectopic rate is 19.7 per 1,000 pregnancies

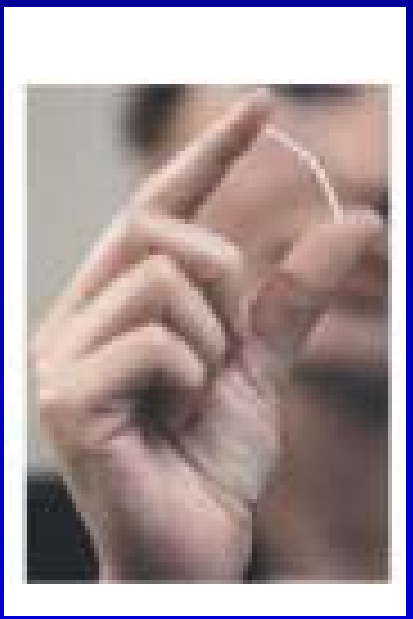
Glasier. *Contraception* 2002
CDC. *MMWR* 1995

Not Associated with High Litigation Risk for Providers

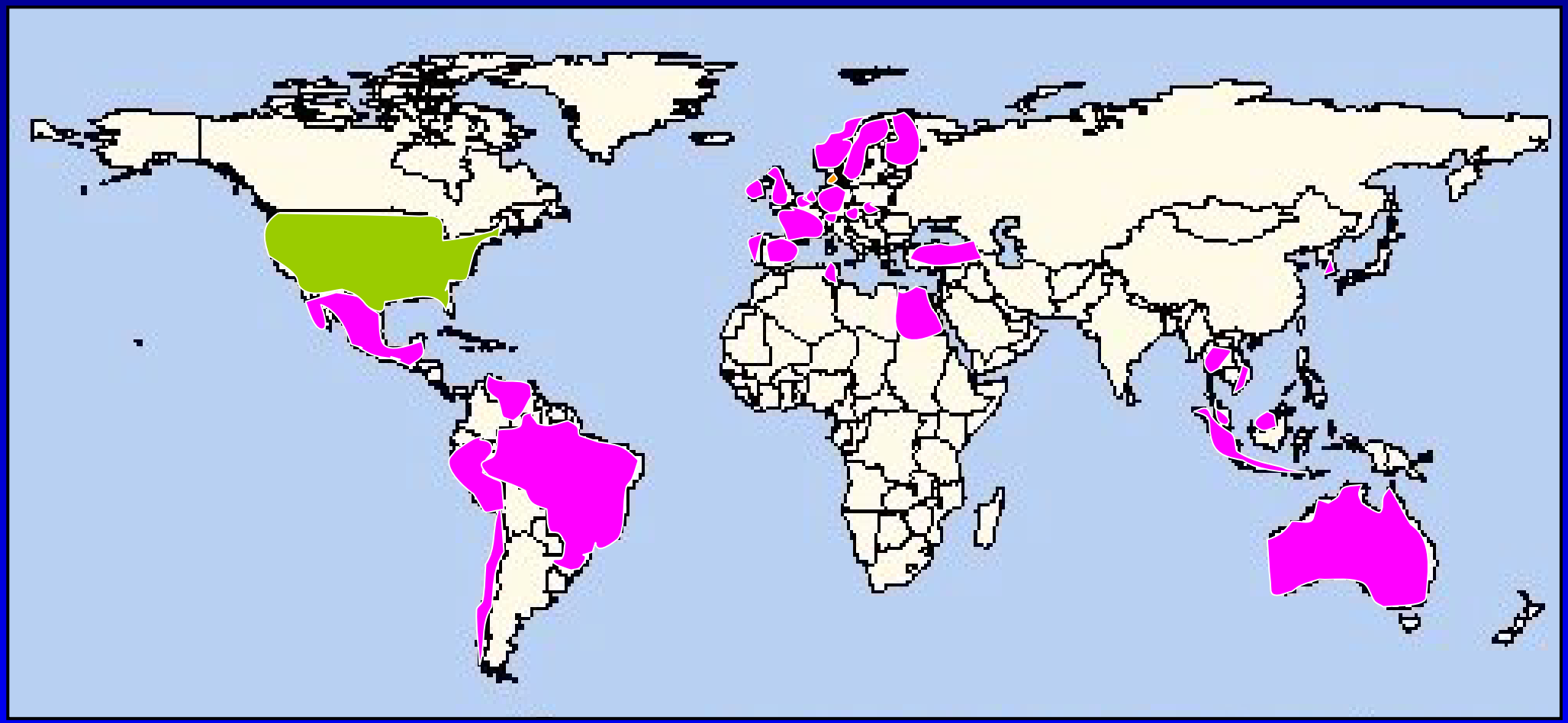
- How many lawsuits lost by Norplant manufacturer?
  - Zero
- How many implants withdrawn from market by regulatory agency?
  - Zero

Single-Rod Implant

- Trade name: Implanon®
- One rod 40 mm x 2 mm
- Core:
  - 40% ethylene vinyl acetate (EVA)
  - 60% etonogestrel (68 mg)
- Rate-controlling membrane: 100% EVA



Single-Rod Implant Study Worldwide



Green = not yet available
Pink = available for use

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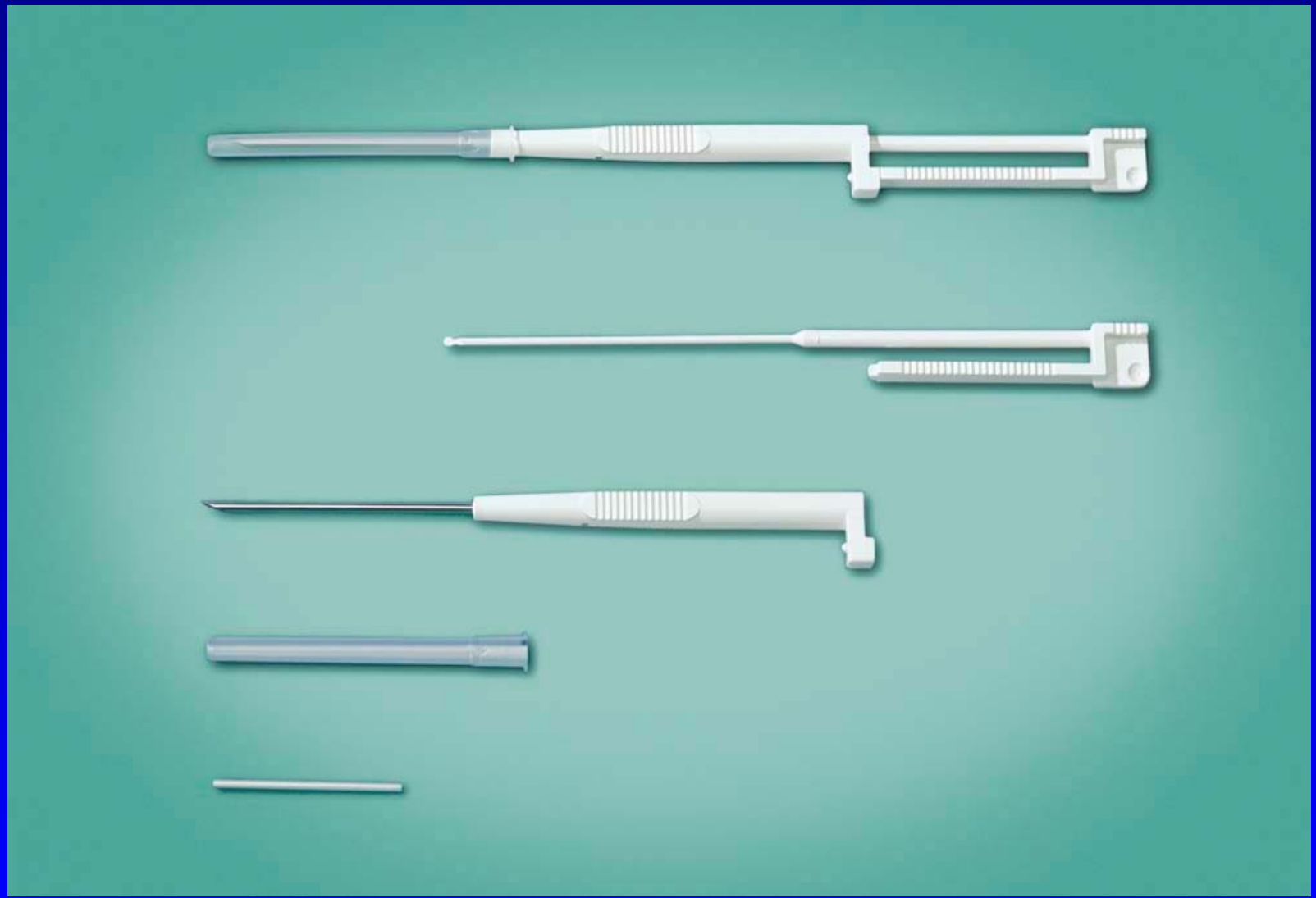
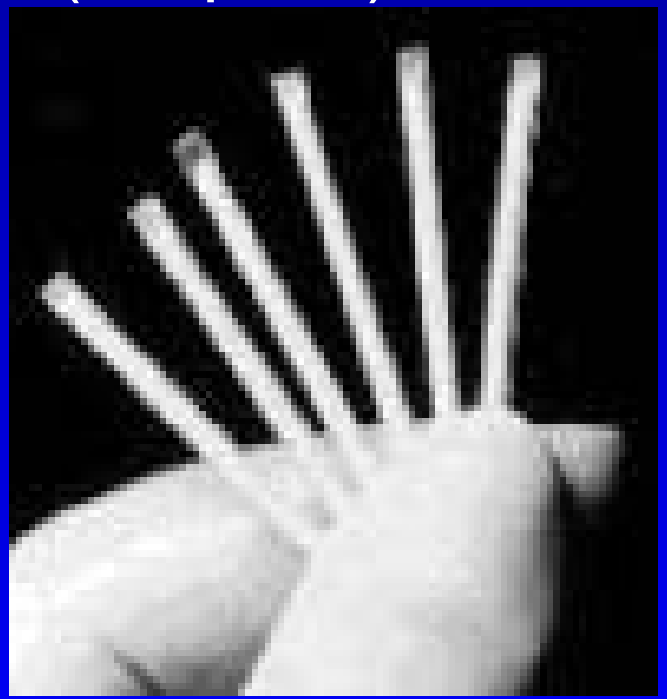
Components of the Single-Rod Implant Insertion System



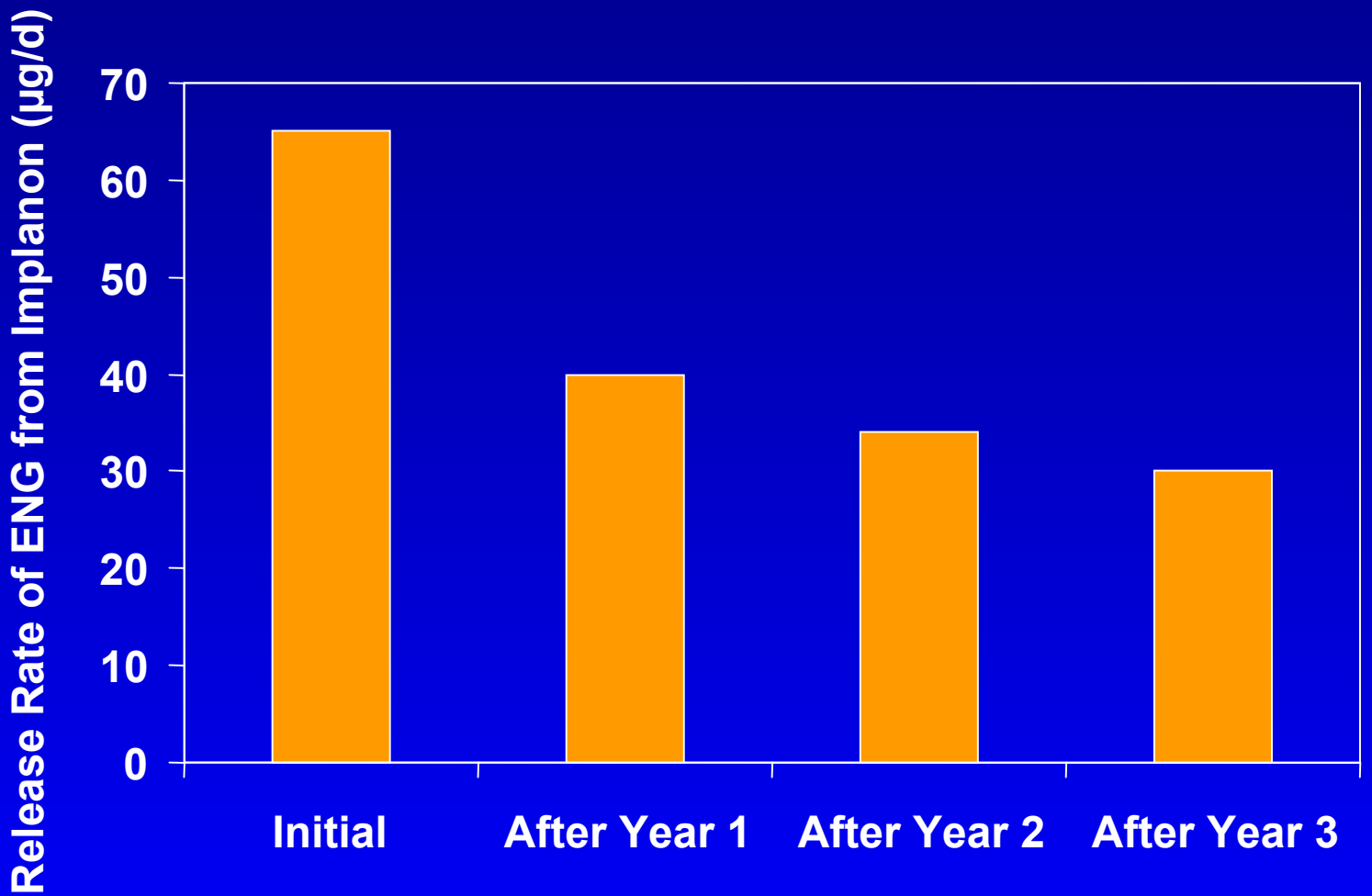
Other Implant Systems

- 6-Rod Implant (Norplant)



- 2-Rod Implant (Jadelle)

Release Rate of 3-Ketodesogestrel (ENG)



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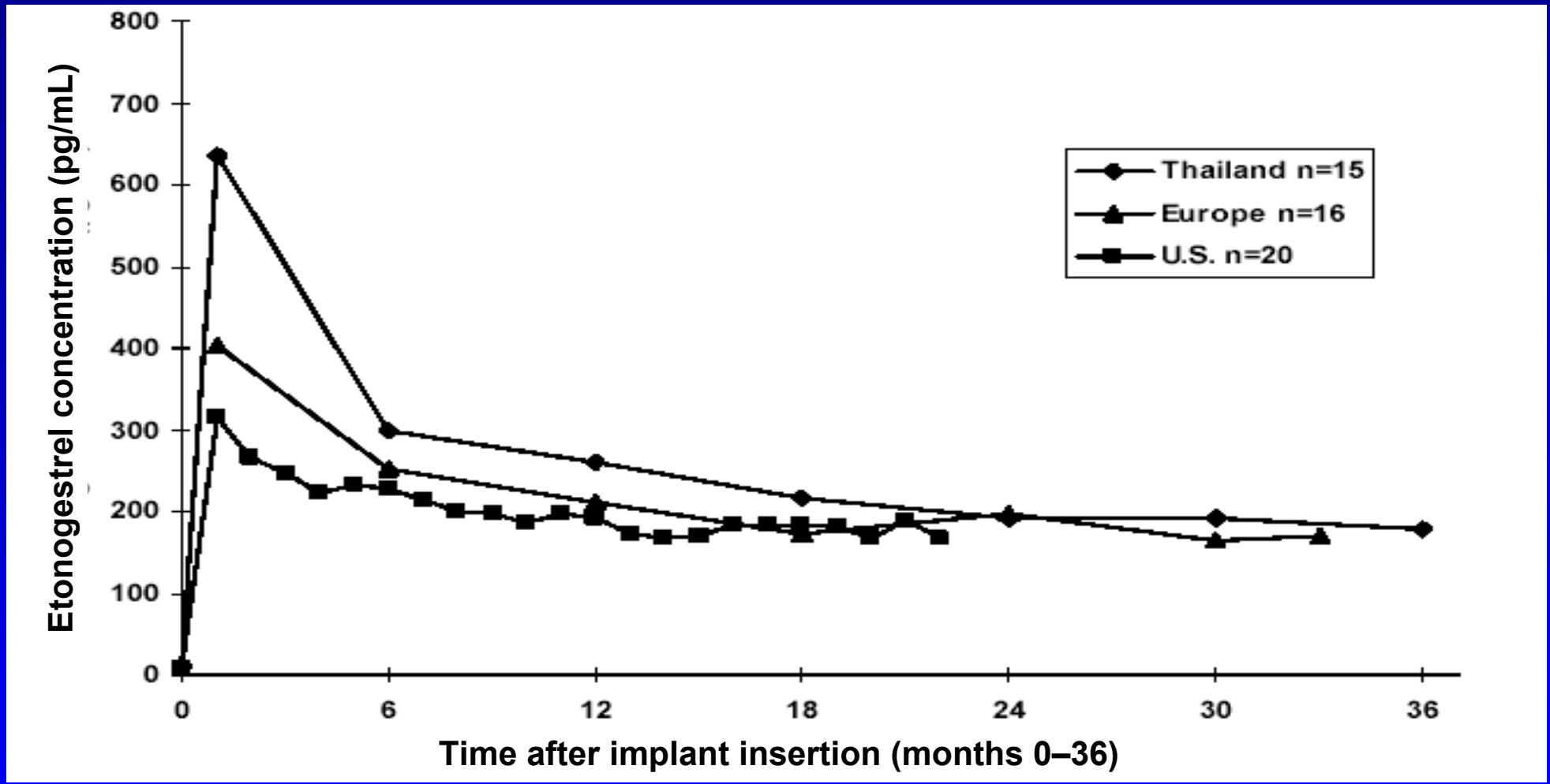
Huber. *Contraception* 1998

Pharmacokinetics



Organon Data on File

Mechanism of Action

- Inhibits ovulation
  - No ovulation was observed for 30 months in clinical trials
    - Only 2 out of 31 (6.5%) subjects ovulated in Year 3, with no resulting pregnancies
- Increases viscosity of cervical mucus

Organon Data on File;
Implanon™ [package insert]

Efficacy

	Subjects with Ovulation		Cycles with Ovulation		Subjects with Pregnancy
Year	No.	%	No.	%	No.
1	0/47	0	0/177	0	0
2	0/39	0	0/103	0	0
3	2/31	6.5	4/86	4.7	0

Organon Data on File

Efficacy from Multiple Sources

No. of Women	1,117
No. of Cycles	26,787
No. of Pregnancies	**0**

Body Weight Distribution and Efficacy

	≤1 Yr (n)	1–2 Yrs (n)	2–3 Yrs (n)	Pregnancies (n)
< 50 kg	182	157	127	0
50–60 kg	539	423	292	0
60–70 kg	442	344	239	0
70–80 kg	201	151	109	0
80–90 kg	42	35	21	0
>90 kg	5	2	1	0

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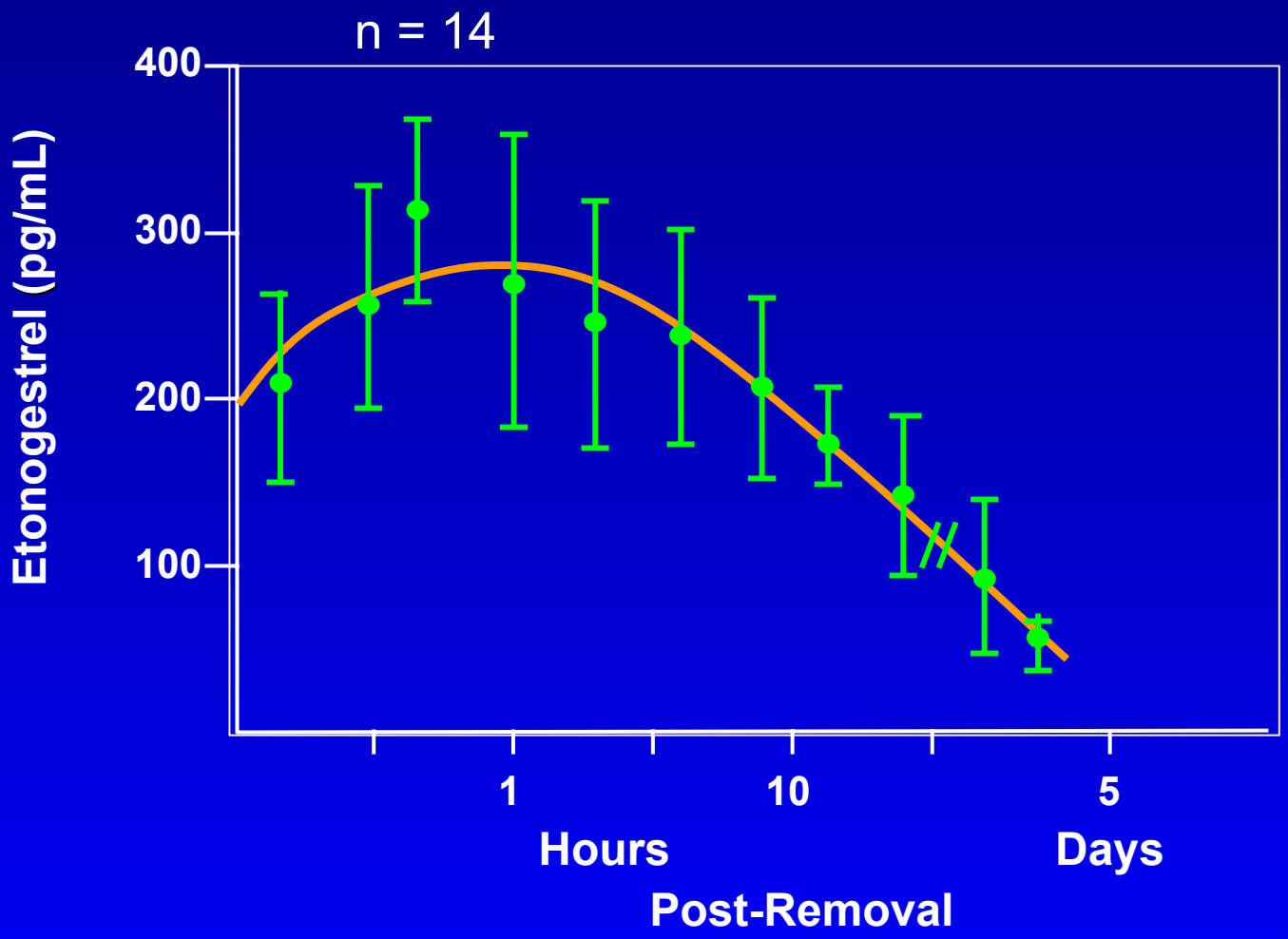
Total n = 3,312

Organon Data on File

Return to Fertility



- **ENG Levels undetectable within 1 week**

Davies. *Contraception* 1993
Croxatto. *Contraception* 1998
Lahteenmaki. *Fertil Steril* 1980

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Clinical Management Issues

- No anemia
- No reduction in bone mineral density
- No increased risk of deep vein thrombosis
- Little pain at site
- Associated non-contraceptive benefits
- Changes in bleeding pattern
- Minor weight change
- Mild side effects:
  - Breast pain
  - Headache

Changes in Bleeding Pattern

- "Irregularly irregular" cycles
- Amenorrhea more common
- Patterns include:
  - Frequent irregular bleeding
  - Heavy menstrual flow
  - Prolonged bleeding
  - Amenorrhea
  - Spotting
  - Unpredictability of bleeding pattern over time

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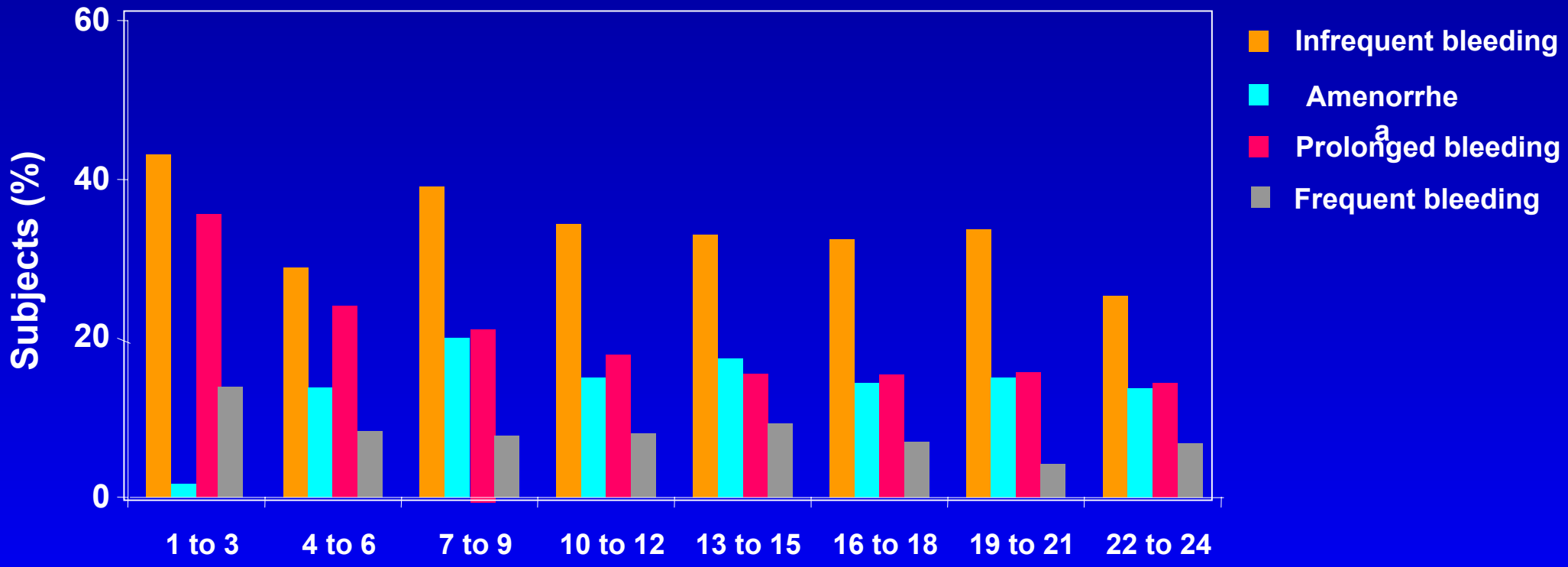
Affandi B. *Contraception* 1998
Zheng SR. *Contraception* 1999

Bleeding Patterns

US Data
n=330



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Funk. (in press) *Contraception*

Bleeding Pattern Comparison

	Single Rod n=432	Multiple Rod n=430
No. Bleeding-spotting days per 90 days	7.7	10.2
No. Bleeding days per 90 days	3.3	4.6
No. Bleeding-spotting episodes per 90 days	1.5	1.9

Affandi. *Contraception* 1998

Bleeding Pattern Comparison (continued)

	Single Rod n=432	Multiple Rod n=430
Amenorrhea	40.6%	29.4%
Infrequent bleeding-spotting	32.2%	33.5%
Frequent bleeding-spotting	2.5%	3.6%
Prolonged bleeding-spotting	3.4%	4.5%

Affandi. *Contraception* 1998

Management of Bleeding

- Few data available
- Considerations:
  - Oral estrogen
  - NSAIDs
  - Combination OCs
  - Watchful waiting

Bleeding Does Not Result in Anemia

	Mean Hgb (g/dL)
Baseline	11.8
24 mo	12.2
36 mo	12.4

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Affandi. *Contraception* 1998

Minor Weight Change

- Small but steady weight increases seen
- In a comparative analysis, weight increase seen in 21% of women but reported as drug-related in only 6.4%
- A comparative study found mean increase similar to that seen with non-medicated IUD

Urbancsek J. *Contraception* 1998

Little Pain at Insertion Site

N = 1,409

Condition	n	%
Swelling	5	0.4
Redness	6	0.4
Pain	48	3.4
Hematoma	4	0.3
Expulsion	0	0.0

Organon Data on File

Mild Side Effects

- Breast pain (9%)
- Headache (8.5%)

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Urbancsek. *Contraception* 1998

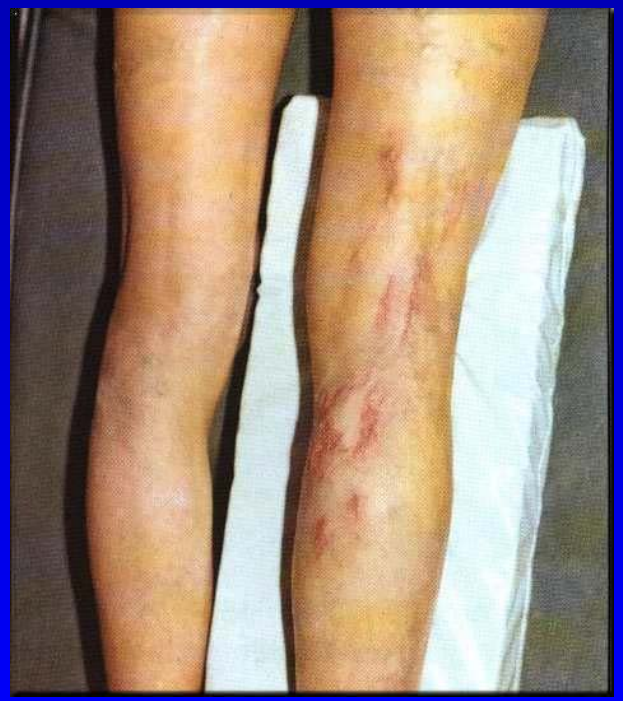
No Reduction in Bone Mineral Density

- Open, prospective comparison 2-year study of 44 women with single-rod implant and 29 with non-medicated IUD
- Changes in bone mineral density similar

Beerthuizen. *Hum Reprod* 2000

No Increased Risk of Deep Vein Thrombosis (DVT)

- No DVT in 13 clinical trials
- Total of 4,103 woman-years of exposure



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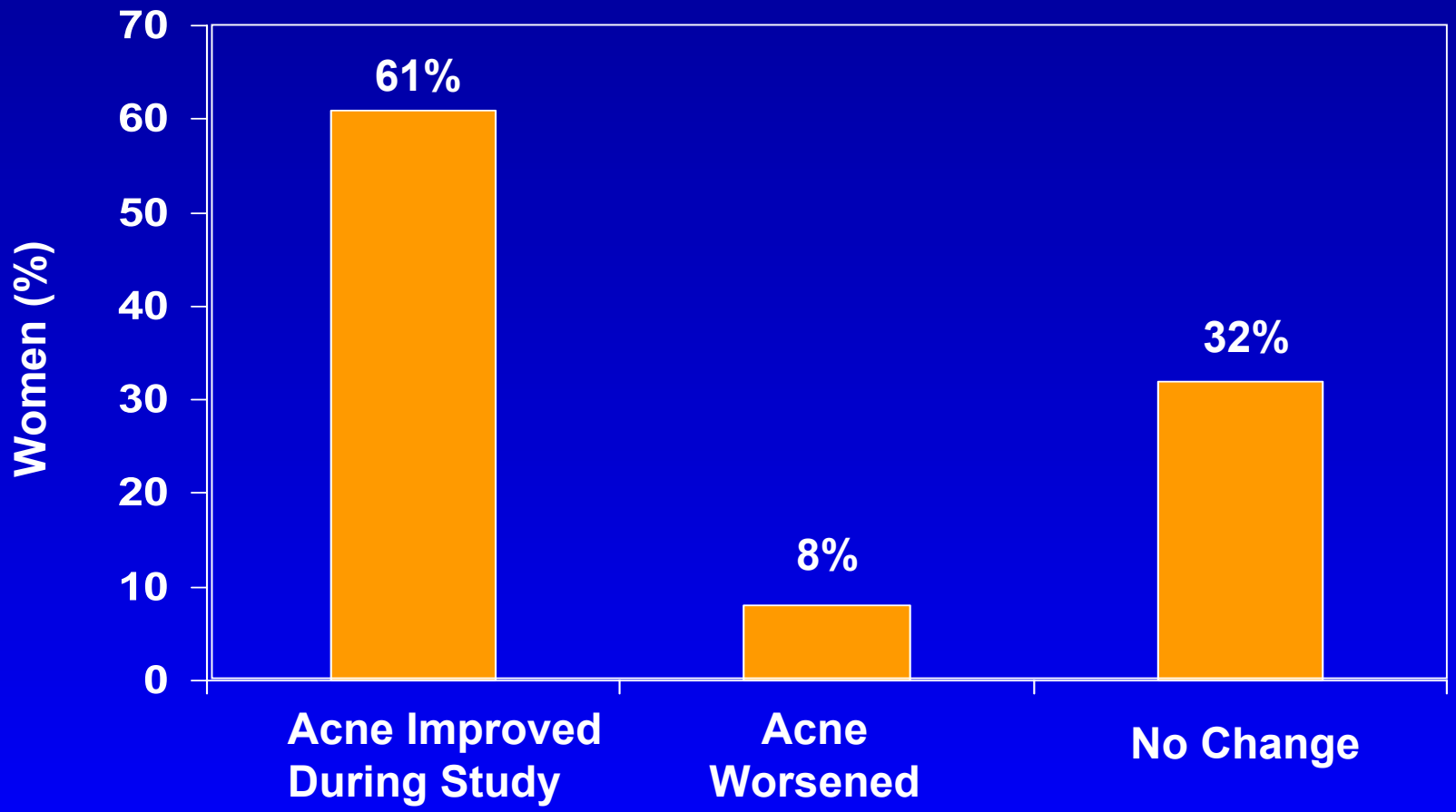
Urbancsek. *Contraception* 1998

Non-Contraceptive Benefit: Acne Improvement



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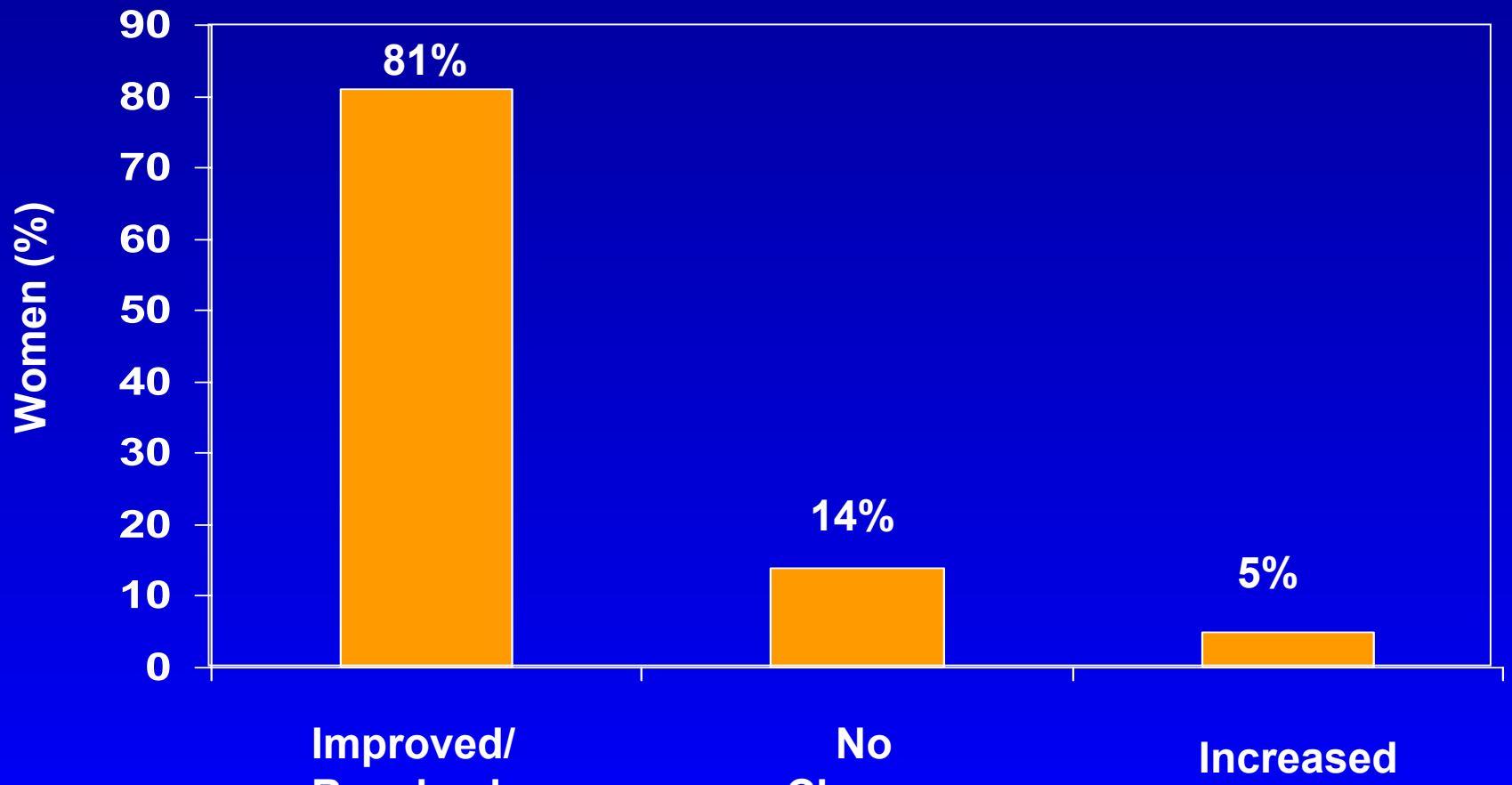
Funk. (in press) *Contraception*

Non-Contraceptive Benefit: Dysmenorrhea Improvement



Funk. (in press) *Contraception*

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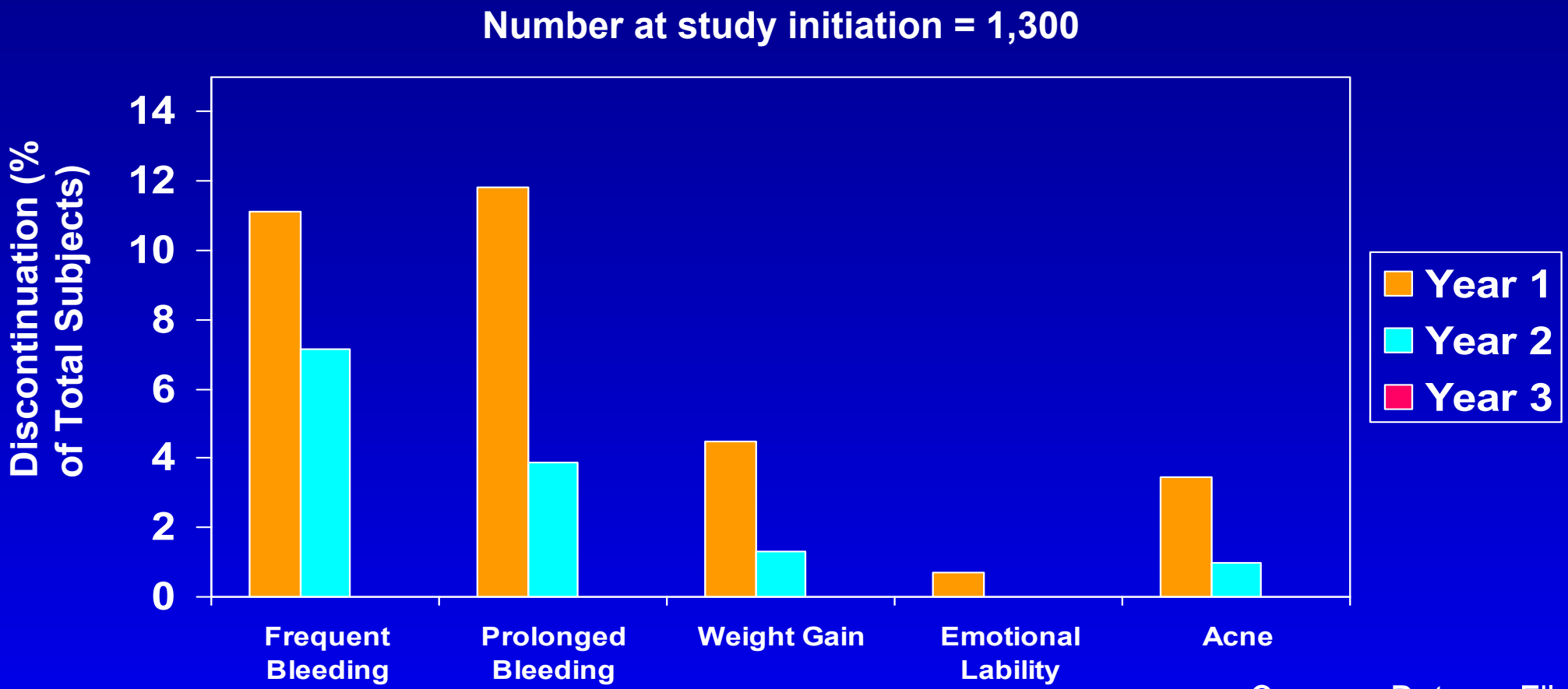
Reasons for Discontinuation



Organon Data on File

Croxatto. *Hum Reprod* 1999

Zheng. *Contraception* 1999

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Patient Selection

Women who desire:

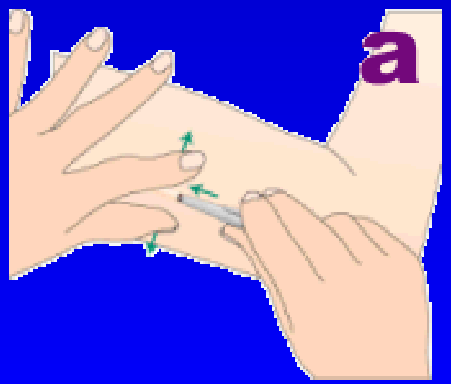
- Long-term contraception
- High effectiveness
- Rapid reversibility
- Estrogen-free contraception

Contraindications

- Known or suspected pregnancy
- Active thrombosis or thromboembolic disorders
- Hepatic tumor or active liver disease
- Undiagnosed abnormal genital bleeding
- Known or suspected carcinoma of the breast or history of breast cancer
- Progestogen-dependent tumor
- Hypersensitivity to the components of the implant

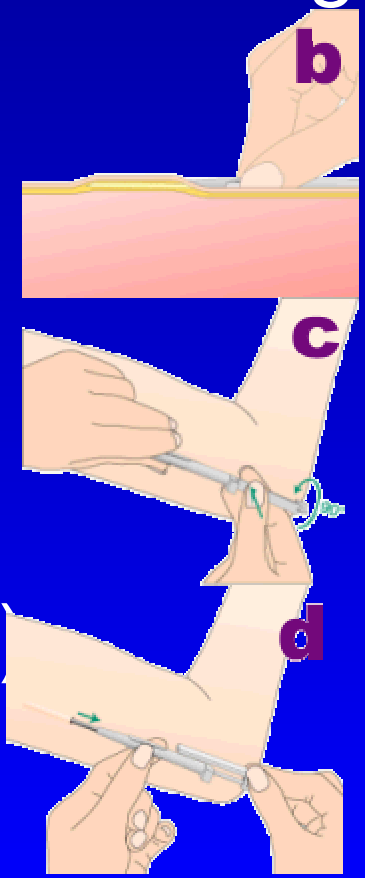
Insertion Steps Overview

1. Mark site and sterilize.
2. Inject 1% lidocaine just under skin.
3. Remove applicator from pack, maintaining sterility.
4. Verify implant is within needle of applicator.
5. Remove needle cover.
6. Stretch skin at insertion site. (a)



Insertion Steps Overview (continued)

7. Lift or tent skin with needle tip while inserting and insert needle to full length. (b)
8. Press the obturator support to break seal of applicator.
9. Turn obturator 90 degrees and fix with one hand. (c)
10. With other hand, pull needle out. (d)
11. Palpate to verify correct insertion.



Insertion Timing

- Standard start-up
  - Insertion within 5 days of initiation of menses
- Switching from combined OC
  - Insertion within 7 days of last active tablet
- Switching from progestin-only method
  - Insertion any day with progestin only-pill
  - Same day as IUD or implant removal
  - On due date for next contraceptive injection

Insertion Timing (continued)

- After abortion
  - Within 5 days of 1st trimester abortion
  - Within 6 weeks of 2nd trimester abortion
- After childbirth
  - Within 6 weeks
  - Considered safe with lactation after 6 weeks
  - Clinical study: low concentrations present in milk; no associated adverse events

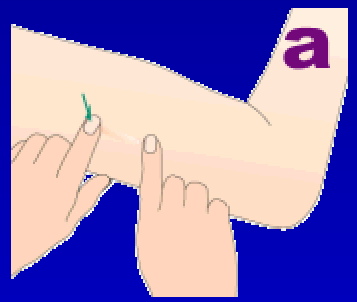
Implanon package labeling
Reinprayoon. *Contraception* 2000
Diaz. *Contraception* 2002

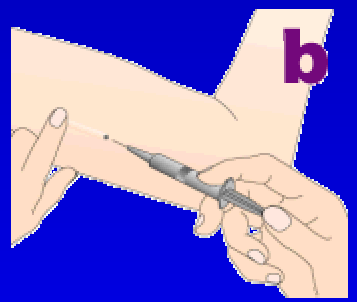
‘Quick Start’ Method

- Single-rod implant is inserted at any time during menstrual cycle
- Provider should recommend use of back-up barrier contraception for 7 days
- If Quick Start method is used with emergency contraception, provider should obtain urine pregnancy test in 4 weeks

Removal Steps Overview

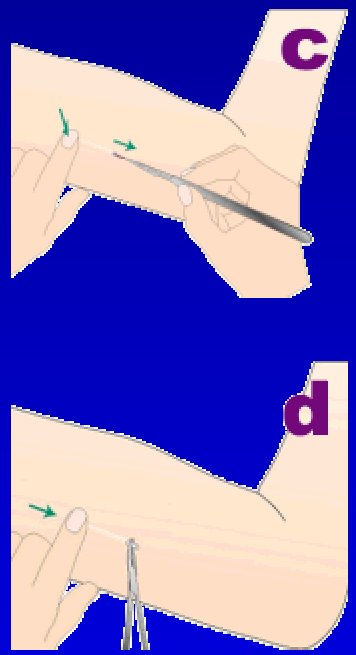
1. Locate rod and mark site. (a)
2. Sterilize site.
3. Inject 1% lidocaine *under* distal end of rod. (b)
4. Press down on proximal end of rod.





Removal Steps Overview (continued)

5. Use scalpel to make 2–3 mm incision over distal end. (c)
6. Gently push rod toward incision, then grasp with mosquito forceps. (d).
7. Close with butterfly closure.



Patient Counseling

- Important for all women needing contraception
- May include written materials
- Should be sensitive to literacy level and language requirements
- Must include informed consent

Patient Counseling Topics

- Description of implant
- Efficacy
- Return to fertility
- Bleeding patterns
- Potential side effects
- Tips for dealing with bleeding patterns and other side effects
- Overview of insertion and removal
- Follow-up

Dispelling Common Myths About Contraceptive Implants

- Virtually invisible
- No hair loss or excessive growth
- No breakage or movement in arm
- Insertion not painful
- Infection rare
- No long-term health problems
- No health problems in children conceived after removal
- No effect on libido

Meirik. *Obstet Gynecol* 2001
Zheng. *Contraception* 1999
Croxatto. *Hum Reprod* 1999
Brache. *Contraception* 2002

The Single Rod Implant

- New method for women that fulfills unmet need
- Advancement in contraceptive options
- Offers women another choice in safe, effective contraception

Resources

- Information: 1-877-IMPLANON, www.implanon.com

Summary

- Contraceptive implants widely used worldwide
- Implants are safe, highly effective, and rapidly reversible
- Majority of reproductive-age women are candidates
- New option for women that fulfills unmet need