OSTEOPOROSIS RISK FACTORS

"Access" (leads to) Osteoporosis


Normal bone matrix
Osteoporosis

Risk Factors for Osteoporosis

Uncontrollable Risk Factors	Controllable Risk Factors
Personal history of fracture as an adult	Current cigarette smoking
History of fracture in a first-degree relative	Low body weight (<127 lbs.)
White race	Low lifelong calcium intake
Advanced age	Alcoholism
Female sex	Impaired eyesight despite adequate correction
Dementia	Recurrent falls
Poor health/fragility	Inadequate physical activity
	Estrogen deficiency (e.g. early menopause, bilateral ovariectomy prolonged premenopausal amenorrhea)

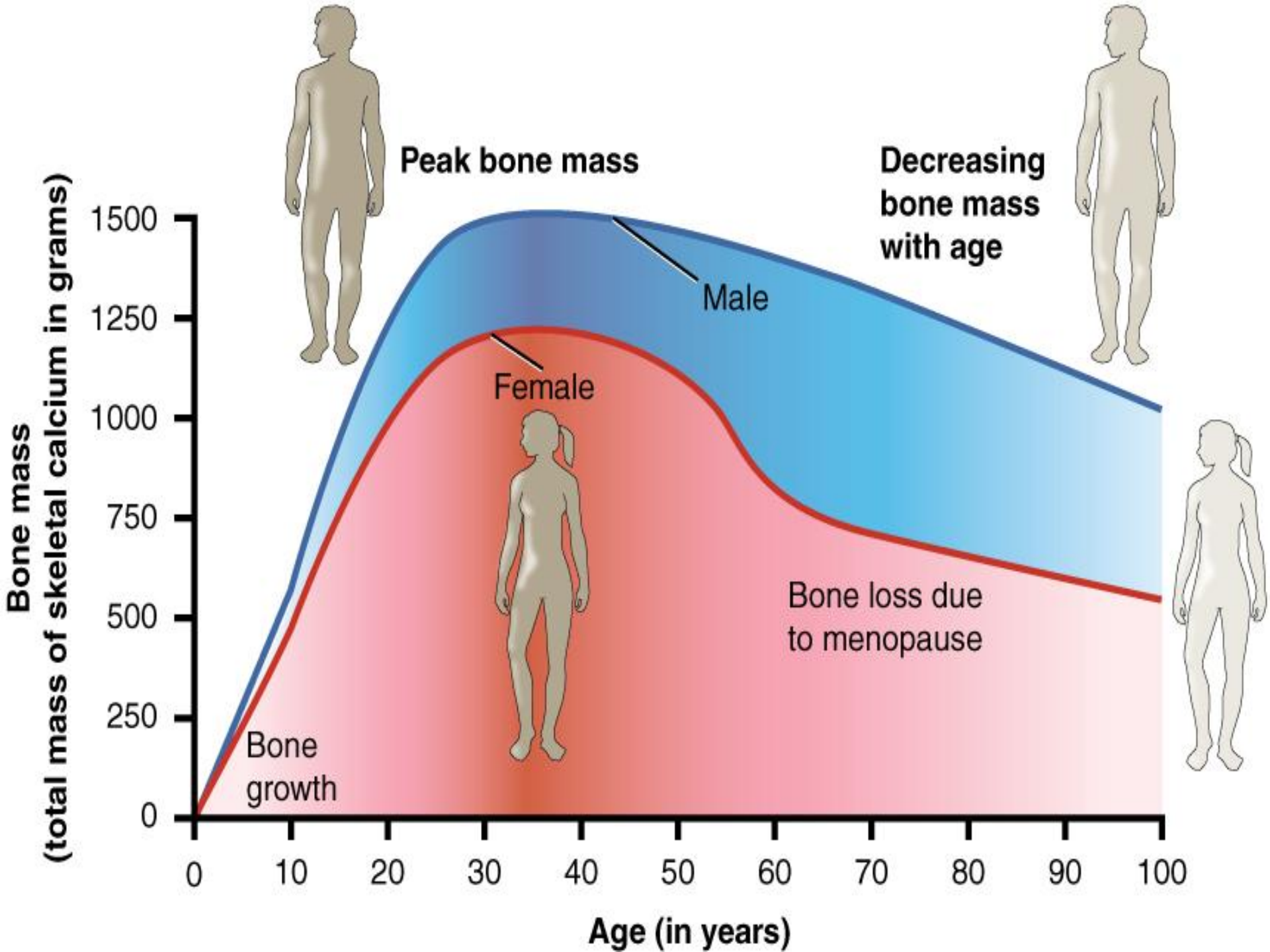
Did you know these osteoporosis facts?

Approximately **10 million Americans** have osteoporosis and another **44 million** have low bone density, placing them at increased risk.

An estimated **2 million broken bones** per year. Up to **1 in 2 women** and **1 in 4 men** will break a bone due to osteoporosis.

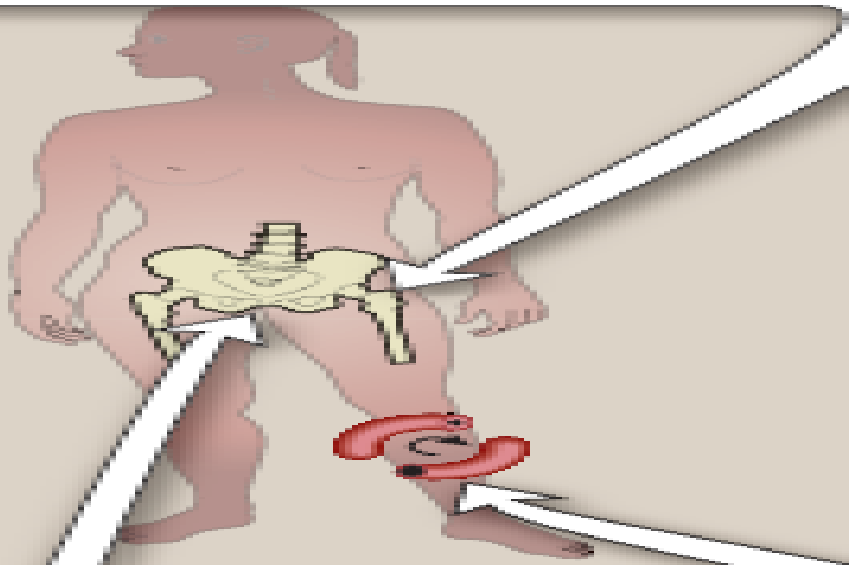
Osteoporosis-related bone breaks cost patients, their families and the healthcare system **$19 billion annually**, rising to **$25 billion** by 2025.

Risk of fracture is **equal to or greater than** risks of breast, uterine, ovarian or prostate cancer.


Peak bone mass
Decreasing bone mass with age
Male
Female
Bone loss due to menopause
Bone growth
Bone mass (total mass of skeletal calcium in grams)
1500
1250
1000
750
500
250
0
0
10
20
30
40
50
60
70
80
90
100
Age (in years)

OSTEOPOROSIS

- Estrogen decreases the resorption of bone but has no effect on bone formation.
- Estrogen decreases the frequency of hip fracture. [Note: Dietary calcium and weight-bearing exercise also slow loss of bone.]
- Estrogen replacement is not the preferred therapy for prevention of osteoporosis.



VASOMOTOR

- Estrogen treatment reestablishes feed-back on hypothalamic control of norepinephrine secretion, leading to decreased frequency of "hot flashes."

UROGENITAL TRACT

- Estrogen treatment reverses postmenopausal atrophy of the vulva, vagina, urethra, and trigone of the bladder.

- Fractures and osteoporosis are common, especially in the elderly population. Hip fractures may be devastating.
- Osteoporosis in men is greatly unrecognized and untreated.
- Treatment of osteoporosis is generally recommended in postmenopausal women and men 50 years old or older who have a bone mineral density T score of –2.5 or less, a history of previous spine or hip fracture, or a Fracture Risk Assessment Tool score indicating increased fracture risk.
- Bisphosphonates, teriparatide and denosumab have proven to reduce risk of hip, vertebral, and nonvertebral fractures. Bisphosphonates are used usually as first-line treatment in patients if no contraindications. Teriparatide reduces the risk of nonvertebral and vertebral fractures.
- Individualizing therapy is important. This includes balancing the risks and benefits of bisphosphonates in order to enact a drug holiday. For patients at lower risk for fracture, drug holidays after 5 years of alendronate therapy or 3 years of zoledronic acid therapy can be considered.

BISPHOSPHONATE	FORMULATION	DOSING FREQUENCY
Alendronate	Oral tablet	Daily or weekly
Ibandronate	Oral tablet Intravenous	Daily or monthly Every 3 months
Risedronate	Oral tablet Oral delayed-release tablet	Daily or weekly Twice monthly or monthly
Zoledronic acid	Intravenous	Yearly

DOSING INSTRUCTIONS FOR ORAL BISPHOSPHONATES

- Take with 6 to 8 ounces of plain water only

  [Note: Take *risedronate* delayed-release tablet with at least 4 ounces of plain water]

- Take at least 30 minutes (60 minutes for *ibandronate*) BEFORE other food, drink, or medications

  [Note: Take *risedronate* delayed-release tablet immediately AFTER breakfast]

- Remain upright and do not lie down or recline for at least 30 minutes (60 minutes for *ibandronate*) after taking

TABLE

PHARMACOLOGICAL TREATMENT FOR OSTEOPOROSIS

Generic Drug (Brand Name)	Indications and Dosing	Contraindications	Comments
Alendronate (Fosamax®)	Prevention: 5 mg per day or 35 mg per week; treatment: 10 mg per day or 70 mg per week	Delayed esophageal emptying, inability to sit or stand upright for 30 minutes, hypocalcemia, creatinine clearance <35 mL per minute, hypersensitivity	Firstline treatment option; significantly reduces vertebral and nonvertebral fractures
Risedronate (Actonel®)	Prevention and treatment: 5 mg per day, 35 mg per week, or 75 mg twice monthly	Delayed esophageal emptying, inability to sit or stand upright for 30 minutes, hypocalcemia, creatinine clearance <35 mL per minute, hypersensitivity	Firstline treatment option; significantly reduces vertebral and nonvertebral fractures
Ibandronate (Boniva®)	Prevention and treatment: 2.5 mg per day or 150 mg per month	Delayed esophageal emptying, inability to sit or stand upright for 60 minutes, hypocalcemia, creatinine clearance <35 mL per minute, hypersensitivity	Secondline treatment option; significantly reduces vertebral fractures
Zoledronic acid (Reclast®)	Prevention and treatment: 5 mg (100 mL) infusion once yearly	Hypocalcemia, creatinine clearance <35 mL per minute, hypersensitivity	Firstline treatment option; significantly reduces vertebral and nonvertebral fractures
Calcitonin (Miacalcin®)	Treatment: 200 IU nasal spray per day	Hypersensitivity	Lastline treatment option; significantly reduces vertebral fractures
Raloxifene (Evista®)	Prevention and treatment: 60 mg per day	Past or current history of venous thromboembolic events, pregnancy, hypersensitivity	Second- or thirdline treatment option; significantly reduces vertebral fractures
Teriparatide (Forteo®)	Treatment: 20 micrograms per day subcutaneous injection	Risk of osteosarcoma, hypersensitivity	Significantly reduces vertebral and nonvertebral fractures; use in severe cases and/or if other agents cannot be used/have failed
Denosumab (Prolia®)	Treatment: 60 mg subcutaneous injection every 6 months	Hypocalcemia, immunosuppression, creatinine clearance <30 mL per minute	Firstline treatment option; significantly reduces vertebral and nonvertebral fractures

Treatment

Reclast®
(zoledronic acid) injection
5 mg/100 mL for infusion

- A novel approach for the treatment of osteoporosis has just been approved by the FDA: **Reclast (Zoledronic acid)**
- This IV medication is a **once a year, 15 minute infusion,** which will allow the easiest available intake of an osteoporosis medication, with excellent efficacy, and a good safety profile
- Serum creatinine (renal function) should be measured before each Reclast dose

ESTROGENS

Estradiol USED IN MANY COMBINATIONS
Estrone MENEST
Ethinyl estradiol USED IN MANY COMBINATIONS
Mestranol (w/norethindrone) NECON 1/50, NORINYL 1+50

SELECTIVE ESTROGEN-RECEPTOR MODULATORS (SERMs)

Clomiphene CLOMID, SEROPHENE
Ospemifene OSPHENA
Raloxifene EVISTA
Tamoxifen TAMOXIFEN, NOLVADEX
Toremifene FARESTON

PROGESTOGENS

Desogestrel USED IN MANY COMBINATIONS
Dienogest (w/estradiol valerate) NATAZIA
Drospirenone (w/ethinyl estradiol) BEYAZ, YAZ, YASMIN
Etonogestrel (w/ethinyl estradiol) NUVA RING
Etonogestrel (subdermal) IMPLANON, NEXPLANON
Levonorgestrel MIRENA, NEXT CHOICE, PLAN B ONE-STEP
Medroxyprogesterone PROVERA
Norelgestromin (w/ethinyl estradiol) ORTHO EVRA
Norethindrone NOR-QD, ORTHO MICRONOR
Norethindrone acetate AYGESTIN
Norgestimate USED IN MANY COMBINATIONS
Norgestrel (w/ethinyl estradiol) LO/OVRAL
Progesterone USED IN MANY COMBINATIONS

PROGESTERONE AGONIST/ANTAGONIST

Ulipristal acetate ELLA

PROGESTERONE ANTAGONIST

Mifepristone MIFEPREX

ANDROGENS

Danazol DANOCRINE

Fluoxymesterone ANDROXY

Methyltestosterone ANDROID, TESTRED, METHITEST

Oxandrolone OXANDRIN

Oxymetholone ANADROL

Testosterone ANDRODERM, ANDROGEL, AXIRON, FORTESTA, STRIANT, TESTIM, TESTOPEL

Testosterone cypionate DEPO-TESTOSTERONE

Testosterone enanthate DELATESTRYL

ANTIANDROGENS

Bicalutamide CASODEX

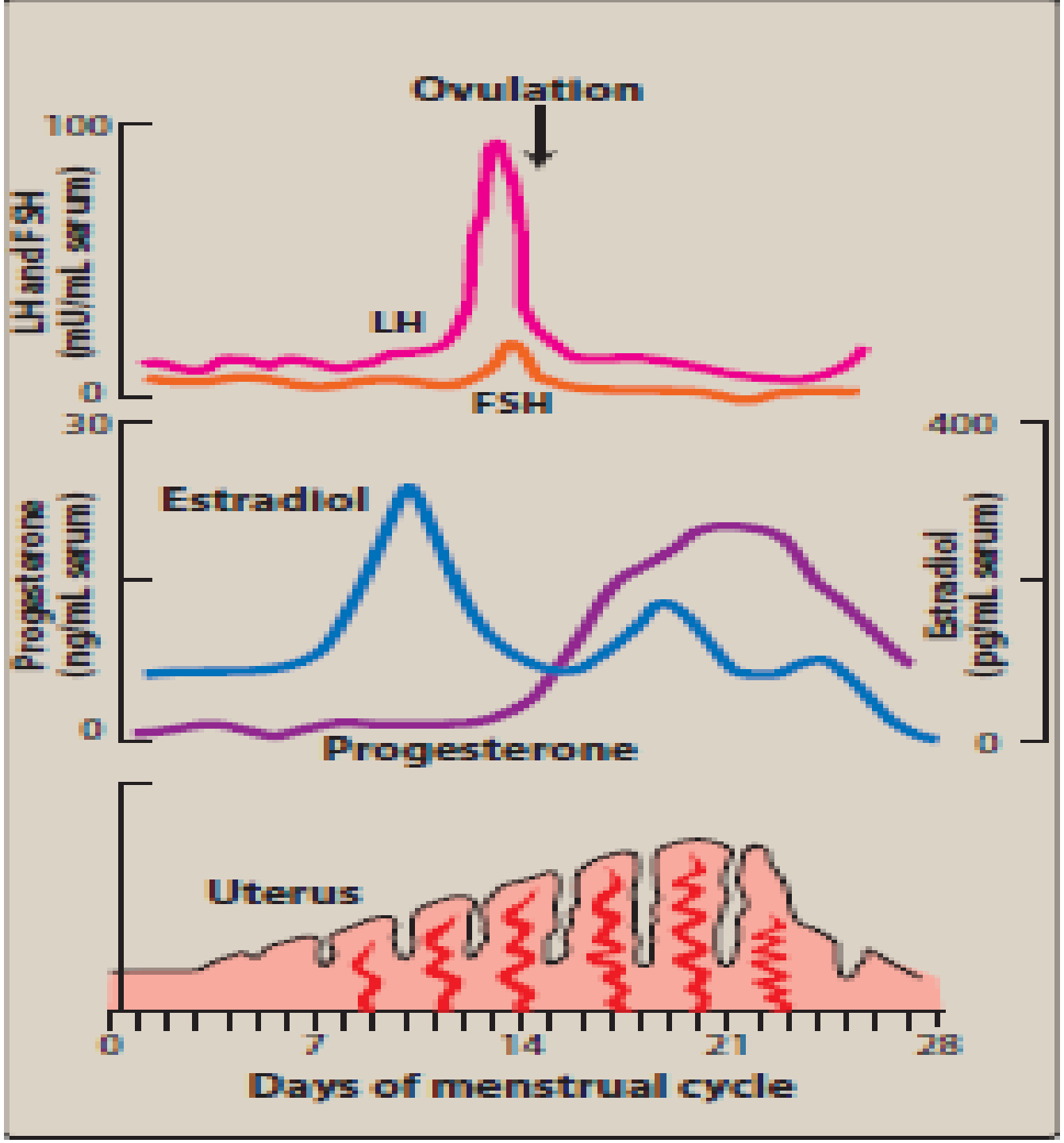
Dutasteride AVODART

Enzalutamide XTANDI

Finasteride PROPECIA, PROSCAR

Flutamide EULEXIN

Nilutamide NILANDRON


Ovulation
100
0
LH and FSH (mU/mL serum)
LH
FSH
30
0
Progesterone (ng/mL serum)
Estradiol
Progesterone
400
0
Estradiol (pg/mL serum)
Uterus
0
7
14
21
28
Days of menstrual cycle

Most effective

Less than 1 pregnancy per 100 women in a year

Implant
0.05%
Effective for 3 years

IUD
0.2–0.8%
Hormonal (two types) or copper; effective for up to 3, 5, and 10 years

Sterilization
0.15–0.5%
Available for women and men

6–12 pregnancies per 100 women in a year

Injection
6%
Get a shot on time every 3 months

Pill
9%
Take a pill on time each day

Patch
9%
Change patch every week

Vaginal Ring
9%
Change ring every month

Diaphragm
12%
Use each time you have sex; must be refitted after childbirth

18 or more pregnancies per 100 women in a year

Male Condom
18%
Use each time you have sex; protects against HIV and other STIs

Female Condom
21%
Use each time you have sex; protects against HIV and other STIs

Cervical Cap
17–23%
Use each time you have sex

Sponge
12–24%
Use each time you have sex

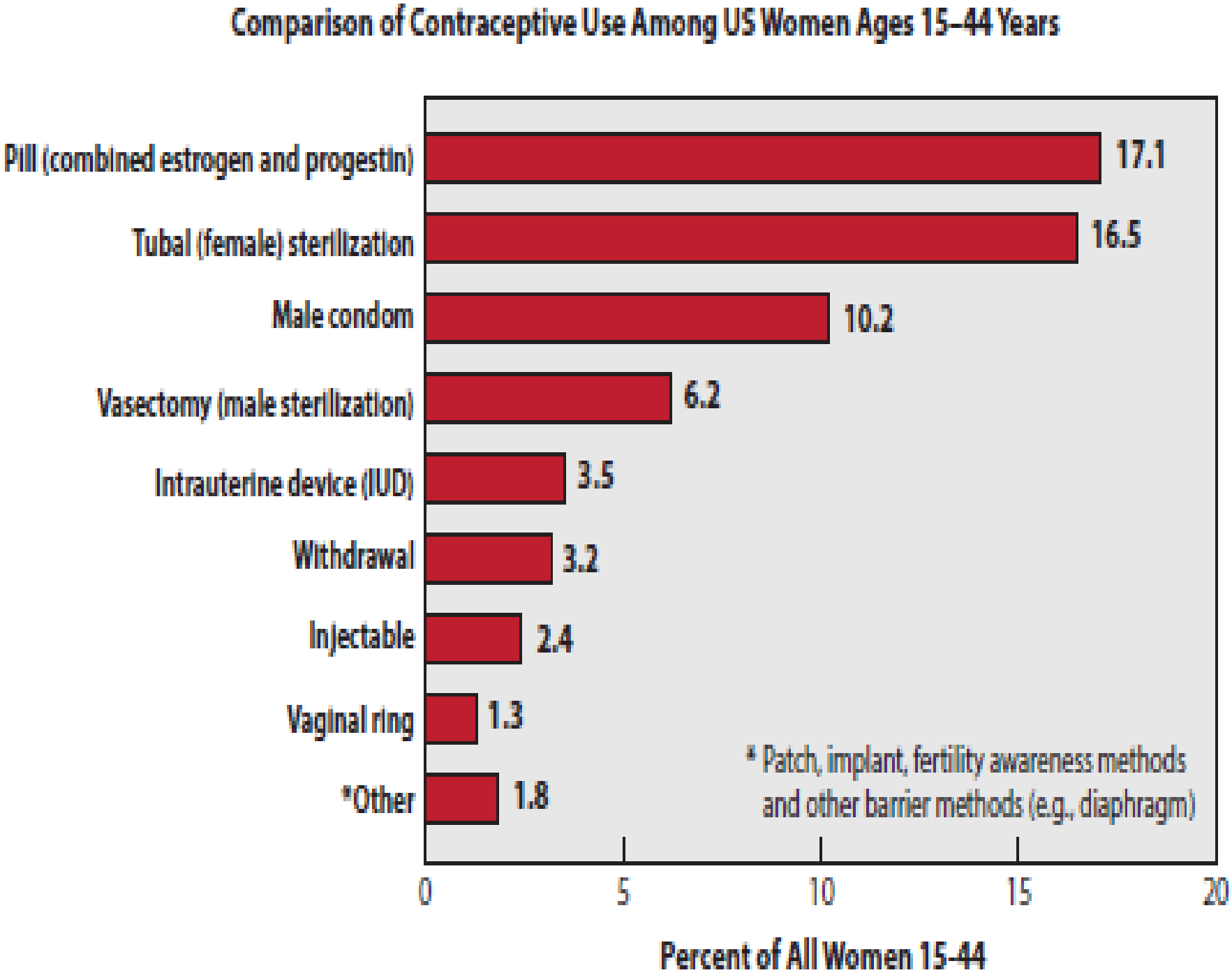
Fertility Awareness-Based Methods
24%
Requires training; use a barrier method or abstain from sex periodically

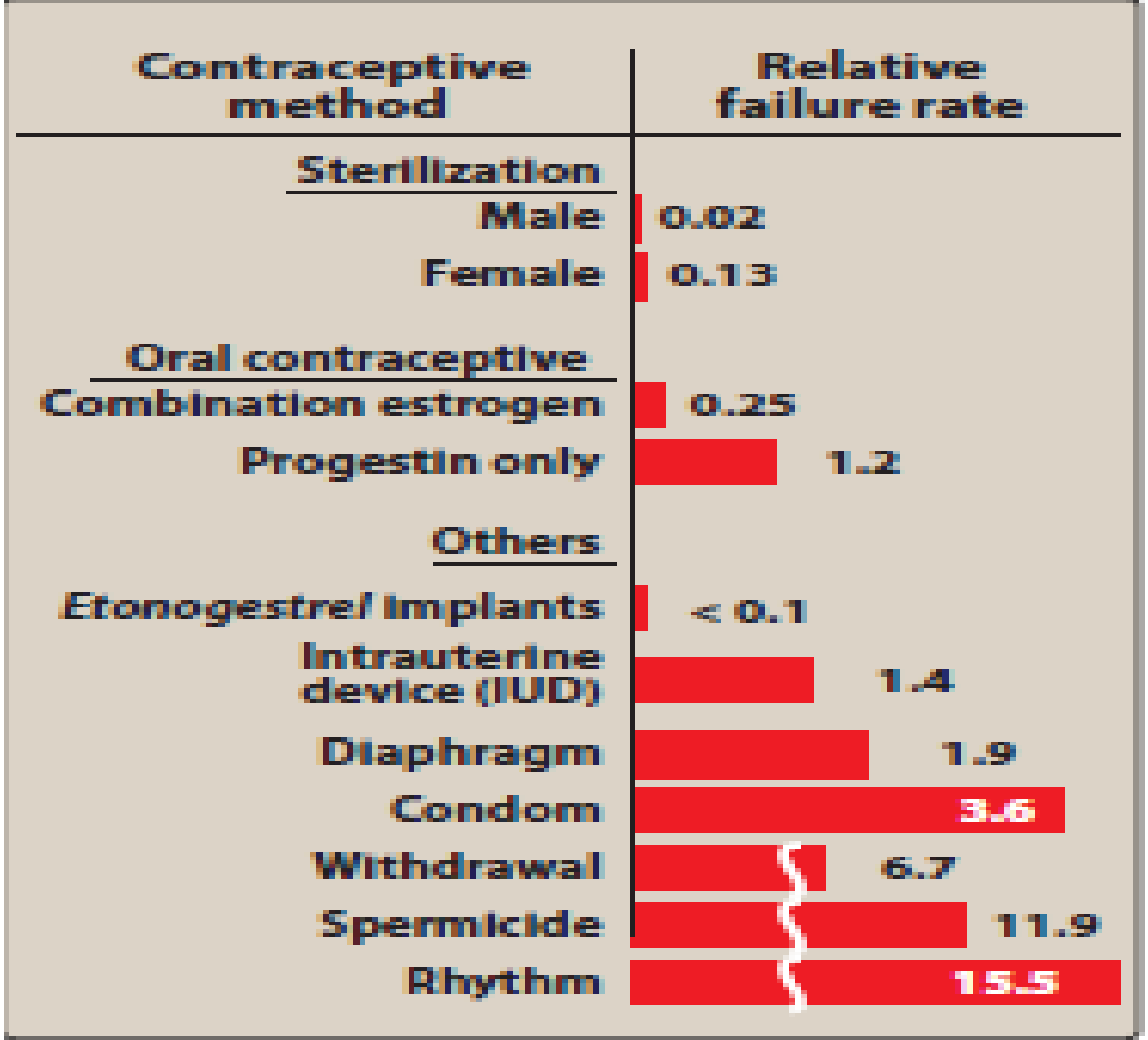
Spermicide
28%
Use each time you have sex

Least effective

Other methods of birth control

Lactational amenorrhea method: This is a temporary method of birth control that can be used for the first 6 months after giving birth by women who are exclusively breastfeeding.
Emergency contraception: Emergency contraceptive pills taken or a copper IUD inserted within 5 days of unprotected sex can reduce the risk of pregnancy.
Withdrawal: The man withdraws his penis from the vagina before ejaculating; 22 out of 100 women using this method will become pregnant in the first year.


Comparison of Contraceptive Use Among US Women Ages 15–44 Years
Pill (combined estrogen and progestin)
17.1
Tubal (female) sterilization
16.5
Male condom
10.2
Vasectomy (male sterilization)
6.2
Intrauterine device (IUD)
3.5
Withdrawal
3.2
Injectable
2.4
Vaginal ring
1.3
*Other
1.8
* Patch, implant, fertility awareness methods and other barrier methods (e.g., diaphragm)
0
5
10
15
20
Percent of All Women 15-44


Contraceptive method
Relative failure rate
Sterilization
Male
0.02
Female
0.13
Oral contraceptive
Combination estrogen
0.25
Progestin only
1.2
Others
Etonogestrel implants
< 0.1
Intrauterine device (IUD)
1.4
Diaphragm
1.9
Condom
3.6
Withdrawal
6.7
Spermicide
11.9
Rhythm
15.5