### Appendix K: Abbreviations and Glossary

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<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>1,25 OH$_3$D$_3$</td>
<td>calcitriol or 1,25 dihydroxyvitamin D$_3$</td>
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<tr>
<td>ACOG</td>
<td>American College of Obstetricians and Gynecologists</td>
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<td>AHCPR</td>
<td>Agency for Health Care Policy and Research (DHHS)</td>
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<tr>
<td>AMI</td>
<td>acute myocardial infarction</td>
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<tr>
<td>BMC</td>
<td>bone mineral content</td>
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<tr>
<td>BMD</td>
<td>bone mineral density</td>
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<tr>
<td>CEA</td>
<td>cost-effectiveness analysis</td>
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<td>CHD</td>
<td>coronary heart disease</td>
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<tr>
<td>CVA</td>
<td>cerebrovascular accident</td>
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<td>CVD</td>
<td>cardiovascular disease</td>
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<td>DES</td>
<td>diethylstilbestrol</td>
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<td>DEXA</td>
<td>dual energy x-ray absorptiometry</td>
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<td>DHHS</td>
<td>U.S. Department of Health and Human Services</td>
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<td>DPA</td>
<td>dual photon absorptiometry</td>
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<td>ERT</td>
<td>estrogen replacement therapy</td>
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<tr>
<td>FDA</td>
<td>Food and Drug Administration (DHHS)</td>
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<td>HCFA</td>
<td>Health Care Financing Administration (DHHS)</td>
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<td>HDL</td>
<td>high-density lipoprotein cholesterol</td>
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<td>HRT</td>
<td>hormone replacement therapy</td>
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<td>IHD</td>
<td>ischemic heart disease</td>
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<td>IU</td>
<td>international units</td>
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<td>IV</td>
<td>intravenous</td>
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<td>LDL</td>
<td>low-density lipoprotein cholesterol</td>
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<td>MI</td>
<td>myocardial infarction</td>
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<td>MPA</td>
<td>medroxyprogesterone acetate</td>
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<td>MRI</td>
<td>magnetic resonance imaging</td>
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<td>NCI</td>
<td>National Cancer Institute (NIH)</td>
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<td>NHLBI</td>
<td>National Heart, Lung, and Blood Institute (NIH)</td>
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<td>NIA</td>
<td>National Institute on Aging (NIH)</td>
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<td>NIAMS</td>
<td>National Institute of Arthritis, Musculoskeletal and Skin Diseases (NIH)</td>
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<td>NIDDK</td>
<td>National Institute of Diabetes and Digestive and Kidney Diseases (NIH)</td>
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<td>NIH</td>
<td>National Institutes of Health (DHHS)</td>
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<td>NOF</td>
<td>National Osteoporosis Foundation</td>
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<tr>
<td>OB-GYN</td>
<td>obstetrics and gynecology</td>
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<td>OHTA</td>
<td>Office of Health Technology Assessment (AHCPR)</td>
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<tr>
<td>OTA</td>
<td>Office of Technology Assessment</td>
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<tr>
<td>PEPI</td>
<td>Progestin Interventions Trial</td>
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<tr>
<td>PERT</td>
<td>combined estrogen/progestin replacement therapy</td>
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<td>PHS</td>
<td>Public Health Service</td>
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<tr>
<td>QALY</td>
<td>quality-adjusted life year</td>
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QCT  quantitative computed
tomography
SC   subcutaneous
SPA  single photon absorptiometry
SXA  single photon x-ray absorptiometry

19-nortestosterone
A form of progestin.

Amenorrhea
The absence or abnormal cessation of menstruation.

Anabolic steroid
Any of a group of synthetic derivatives of the androgen testosterone (a sex steroid or hormone) having pronounced anabolic properties and relatively weak androgenic properties. Anabolic steroids such as dromostanolone, ethylestrenol, nandrolone, oxandrolone, oxymetholone, and stanozolol are used clinically mainly to promote growth and repair of body tissues in senility, debilitating illness, and convalescence.

Androgen (or androgenic hormone)
Naturally occurring male sex hormones (e.g., testosterone, androsterone, and dehydroepiandrosterone) and substances that exert biological effects characteristic of these hormones (e.g., the synthetic compound methyltestosterone). Androgens inhibit bone resorption and increase calcium absorption in the intestine, but also have serious side effects.

Androgenic
Any substance, e.g., androsterone and testosterone, that stimulates male characteristics.

Angina
Any spasmodic, choking, or suffocating pain. The term is often used to denote angina pectoris—a condition characterized by severe, transient chest pain, accompanied by a feeling of suffocation, is due to a deficiency in blood supply to the heart.

Angiography
See arteriography.

Anovulation
The absence of ovulation (development and release of an ovum from the ovary).

Appendicular skeleton
The bones of the extremities, including all of the bones of the limb girdles.

Arteriography
A diagnostic procedure that allows blood vessels to be seen on X-ray film after the injection of contrast material into the bloodstream; used to detect abnormalities such as obstructions, aneurysms, clots, tumors, and injured organs.

Arteriosclerosis
A general term that describes thickened and hardened arteries, the condition that leads to most cases of heart disease and a significant proportion of cerebrovascular disease in the United States.

Atherogenesis
The formulation of patchy plaques of fatty or lipid material on the inner lining of the arteries, restricting blood flow and encouraging the development of blood clots; can result in sudden stoppage of blood flow to the heart.

Atherosclerosis
A descriptive term for thickened and hardened lipid-rich lesions of the medium and large muscular arteries; classified into two forms: early lesions, consisting of fatty streaks, and advanced lesions, consisting of fibrous plaques; commonly occurs in arteriosclerosis, in which deposits of fibrous and cellular tissue, cholesterol, and fat accumulate in large and medium-sized arteries, impeding blood flow; responsible for the majority of cases of myocardial and cerebral infarction.

Axial skeleton
The spine, ribs, sternum, and skull.
Bilateral oophorectomy
Surgical removal of both ovaries.

Bioavailability
The degree to which a drug or other substance becomes available to the target tissue after administration.

Bioequivalence
The requirement that a generic product include the same therapeutic ingredient, and that its rate and extent of absorption be the same as the innovative product.

Bisphosphonates
Chemical compounds developed during the past 20 years for treatment of various bone diseases. Basically, they are carbon-substituted analogues of pyrophosphate (an endogenous physiologic inhibitor of bone mineralization).

Several bisphosphonates are under investigation as therapeutic agents for osteoporosis, among them etidronate, clodronate, tiludronate, pamidronate, risedronate, and alendronate. Bisphosphonates are considered experimental (investigational) in the prevention and treatment of osteoporosis in the United States.

Blinding
A technique used in a randomized clinical trial (RCT) to prevent bias by preventing the patients and/or investigators involved in the trial from knowing which participants are receiving which treatment. In a single-blind RCT, the patients in the trial are “blind” as to which individuals in the study are receiving the experimental or control treatment. In a double-blind RCT, both the investigators and the patients are “blind” as to which individuals in the study are receiving the experimental treatment and which are receiving control treatment. Additional layers of blinding can be added, as, for example, when a third individual (usually the evaluator of outcomes, the individual analyzing the data) also is unaware of treatment assignments.

Body mass index (BMI)
Weight in kilograms divided by height in meters squared. A measure used to define normal ranges of body weight.

Bone
A specialized connective tissue in which a matrix consisting of collagen fibers, a large variety of other proteins and ground substances is impregnated with a solid mineral. Bone is the dynamic and complex tissue of which the bones in the adult skeleton of humans and other vertebrates is largely composed. The skeleton is composed of two kinds of bone: an outer, dense shell of cortical (or compact or haversian) bone and an inner, open, sponge-like region of cancellous (or trabecular) bone. About 80 percent of the mass of the skeleton is cortical bone, and 20 percent is cancellous bone.

Bone densitometry
A term used to refer to a range of noninvasive techniques that use a densitometer to measure the density of bone (e.g., SPA, DEXA, DPA, SXA) and is used to detect osteoporosis.

Bone density
The mass of bone substance per unit volume (g/cm³).

Bone mineral content (BMC)
The mass of bone divided by the one dimensional length of bone measured expressed as grams per cm.

Bone mineral density (BMD)
The mass of bone divided by the two dimensional projected area of the bone measured, expressed as mass per unit area (g/cm²).

Calcaneus
The heel bone.

Calcitonin, human
One of the three calcium-regulating hormones in humans, the others being human parathyroid hormone (hPTH) and calcitriol.

Calcitriol (1,25 OH,D₃, 1,25-dihydroxyvitamin D₃, or 1,25-dihydroxycholecalciferol)
One of several vitamin D metabolizes.

Calcium
The most abundant mineral element in the human body. In humans, calcium is an essential nutrient not only for the normal mineralization of bones
and teeth but also for regulating intracellular events in most, if not all body tissues.

**Cancellous (or trabecular) bone**
The inner, open, sponge-like region of bone prevalent in the vertebrae and in the pelvis, the main sites of osteoporotic fractures. About 20 percent of the mass of the skeleton is cancellous bone. Compare *cortical bone*.

**Carcinogen**
An agent that causes cancer (e.g., certain chemicals, ionizing radiation, tobacco smoke, asbestos fibers, and estrogen).

**Carcinoma**
A cancer arising from epithelial cells, including the external epitheliums (mainly skin and linings of the gastrointestinal tract, lungs, and cervix) and the internal epitheliums that lines various glands (e.g., breast, pancreas, uterus, and thyroid).

**Cardiac arrhythmias**
Variations from the normal rate or rhythm of heart beats.

**Cardiac catheterization**
Passage of a small catheter through a vein or artery into the heart for the purpose of securing blood samples, determining intracardiac pressures, and detecting cardiac anomalies.

**Cardiovascular disease (CVD)**
Any of a diverse group of diseases affecting the heart, blood vessels, and/or blood circulation. CVD includes diseases of the heart muscle itself, ischemic heart disease, hypertension, cerebrovascular diseases, and various other conditions.

**Case-control study**
A type of observational study, where the frequency of a suspected causative factor, such as estrogen use, is compared in a group of people who have a disease (cases) and those who do not (controls). If this factor is found with greater frequency in those with disease, a causal association may be suspected. Results of the comparison may be expressed as the relative risk. See *relative risk*.

**Cerebral infarction**
An area of dead tissue in the cerebrum caused by an interruption of blood circulation due to functional constriction or actual obstruction of a blood vessel, hemorrhage, etc. Also known as a stroke or cerebrovascular accident (CVA).

**Cerebrovascular disease**
Any disease of the blood vessels supplying blood to the brain or of the brain’s covering membranes (meninges), characterized by rupture of the blood vessels or inadequacy of blood to the brain. Common causes include atheroma, hypertension, cerebral thrombosis, or embolism.

**Cholecystectomy**
Surgical removal of the gall bladder.

**Cholesterol**
A sterol present in animal tissues (e.g., cell membranes, blood plasma, and lipoproteins), involved in physiological processes, such as the manufacture of bile acids, sex hormones, and adrenocorticotoid hormones; also involved in the development of pathological processes such as atherosclerosis. See also *high-density lipoprotein cholesterol* and *low-density lipoprotein cholesterol*.

**Climacteric**
The syndrome of endocrine, somatic, and psychic changes occurring at the end of the female reproductive period (menopause).

**Clinical trial (also called therapeutic trial)**
A research activity that involves the administration of an experimental prophylactic, diagnostic, or therapeutic agent, device, regimen, procedure, etc. to humans to evaluate its safety and effectiveness. The term is subject to wide variation in usage, from the first use in humans without any control treatment to a rigorously designed and executed experiment involving test and control treatments and randomization. See also *randomized clinical trial (RCT)*.

**Coagulation**
The process of certain particles joining together to form larger masses.
Coagulation proteins
Proteins found in the plasma that aid in the coagulation process of blood (e.g., Factor VIII, Factor IX, antihemophilic factor, or prothrombin). Also called “clotting factors.”

Cohort study
A type of observational study, where the investigator begins with a group of subjects (the “cohort”), some or all of whom are exposed to a suspected causative factor, and follows this cohort over time for development of a disease. Comparison is made with a control group composed of unexposed members of the cohort (internal controls), or to subjects outside the cohort who are similar to members of the cohort, but who have not been exposed to the suspect factor (population, community, or external controls).

Cones fracture
Fracture of the wrist.

Compact bone
See cortical bone

Comparison group
In a cohort study, the group of unexposed members to which the exposed members are compared. In case-control studies, the group of subjects without disease to which the subjects with disease (the cases) are compared.

Confidence interval
Conventionally, a 95-percent confidence interval is used, which implies that there is a 95-percent chance that the true relative risk being measured falls within the interval, and a 5-percent risk that it does not.

Confounding variables
Variables related to both the disease and the exposure under study that can explain or alter all or part of an observed association.

Conjugated estrogens
An amorphous preparation of naturally occurring, water-soluble, conjugated forms of mixed estrogens, chiefly sodium estrone sulfate, extracted from the urine of pregnant mares; suitable for parenteral, oral, and topical administration and used in estrogen hormone therapy. The conjugated estrogens have pharmacologic effects similar to those of endogenous estrogens.

Consensus conference
A meeting of scientists, medical practitioners, and informed lay people to review scientific information about biomedical technologies and to develop a consensus statement on the clinical application of current medical findings.

Coronary artery bypass graft (CABG) surgery
A surgical procedure in which a vein or an artery is used to bypass a constricted portion of one or more coronary arteries. This procedure has become the primary surgical approach to the treatment of coronary artery disease.

Coronary artery disease (CAD)
Narrowing or blockage of the coronary arteries, which usually results in reduced blood flow to the heart muscle.

Coronary perfusion
The pumping of a fluid through the heart by way of an artery.

Cortical (or compact or haversian) bone
The dense outer shell of bone. One of the two general structural categories of the bone tissue making up the skeleton, cortical bone consists of tightly packed layers of bone. It forms the outer shell of all bones and is prevalent in the shafts of the long bones of the arms and legs. About 80 percent of the mass of the skeleton is cortical bone. Compare cancellous bone.

Cost-effectiveness analysis (CEA)
An analytical technique that compares the costs of a project or of alternative projects to the resultant benefits, with costs and benefits/effectiveness expressed by different measures. Costs are usually expressed in dollars, but benefits/effectiveness are ordinarily expressed in terms such as “lives saved,” “disability avoided,” “quality-adjusted life-years saved,” or any other relevant objectives.

Cross-sectional study
In epidemiology, an observational study that examines the relationship between diseases (or other health-related characteristics) and other variables
of interest as they exist in a defined population at one particular time. The temporal sequence of cause and effect cannot necessarily be determined in a cross-sectional study.

**Cyclic regimen**
Interrupted episodes with ongoing medication. In cyclic regimens of estrogen and progestin, estrogen is usually given for 21 days each month, and a progestin is given with estrogen for the last 7 to 14 days of those 21 days.

**Densitometry**
See bone densitometry

**Diethylstilbestrol (DES)**
A synthetic estrogenic compound used to treat menopausal symptoms, vaginitis, and suppressed lactation.

**Discounting**
A procedure used in economic analysis to express as “present values” those costs and benefits that will occur in future years. Discounting is based on two premises: 1) individuals prefer to receive benefits today rather than in the future; and 2) resources invested today in alternative programs could earn a return over time.

**Double blind**
See randomized clinical trial (RCT) and blinding.

**Dual energy x-ray absorptiometry (DEXA)**
A bone densitometry technique similar to DPA but uses an x-ray machine rather than a radioactive material to produce a dual-energy radiation beam. Different manufacturers use different terms for this technology (e.g., quantitative digital radiography (QDR), dual-energy radiography (DER), dual energy radiographic absorptiometry (DRA), and dual x-ray absorptiometry (DXA).

**Dual photon absorptiometry (DPA)**
A bone densitometry technique that uses a dual-energy radioactive material (usually gadolinium-153) as the source of a dual-energy radiation beam; the dual-energy beam allows measurement of bone and soft tissue without the necessity of encausement in water required in SPA or SXA. The site of measurement for DPA is typically the hip or spine. DPA is sometimes used to measure bone mass in the whole body and can be used to measure bone mass in the forearm, distal radius (wrist), and calcaneus (heel).

**Duration of exposure**
The length of time a person or test animal is exposed to a chemical.

**Dysmenorrhea**
Difficult and painful menstruation.

**Dyspareunia**
Difficult or painful coitus/intercourse in women.

**Dysuria**
Painful or difficult urination.

**Effectiveness**
The same as efficacy (see below) except that it refers to “... average or actual conditions of use.”

**Efficacy**
The probability of benefit to individuals in a defined population from a medical technology applied for a given medical problem under ideal conditions of use. Efficacy is generally evaluated in controlled trials of an experimental therapy and a control condition. Compare to effectiveness.

**Endogenous**
Produced within or caused by factors within the organism.

**Endometrial biopsy**
The microscopic examination of a sample of cells, obtained from the lining of the uterus, in order to evaluate ovulatory function and/or to detect the presence of hyperplasia, dysplasia, or cancer.

**Endometrium**
The tissue lining the inner uterus, the thickness and structure of which vary with the phase of the menstrual cycle.

**Endothelium**
The layer of epithelial cells that lines the cavities of the heart and of the blood and lymph vessels, and the serious cavities of the body.

**Epidemiological studies**
Studies concerned with the relationships of various factors determining the frequency and dis-
tribution of specific diseases in a human community.

**Epidemiology**
The scientific study of the distribution and occurrence of human diseases and health conditions, and their determinants.

**Equine estrogen**
Estrogen pertaining to, characteristic of, or derived from the horse. See *conjugated estrogens*.

**Erythema**
Redness of skin due to congestion of the capillaries.

**Esterified estrogen**
A mixture of the sodium salts of sulfate esters of estrogenic substances; used for oral estrogen therapy.

**Estradiol**
The most potent naturally occurring estrogen in humans.

**Estrogen**
A generic term for estrus-producing compounds; the naturally occurring female sex hormones, including estradiol, estriol, and estrone. The term also refers to substances occurring in plants or made synthetically (as benzestrol or diethylstilbestrol) that have biologic activity similar to that of estrogens produced in the ovaries of female mammals.

**Estrogen replacement therapy (ERT)**
The use of estrogen for the relief of menopausal symptoms, e.g., hot flashes, the prevention of heart disease, and the prevention of osteoporosis.

**Estrone**
An estrogen isolated from pregnancy urine, the human placenta, and palm kernel oil, and also prepared synthetically.

**Etidronate**
A bisphosphonate (C$_{17}$H$_{26}$Na$_2$O$_7$P$_2$) that was patented as a therapeutic agent for calcium disorders in 1972 by Procter&Gamble, parent company of Norwich Eaton Pharmaceuticals, Inc. Oral etidronate is indicated for the treatment of Paget’s disease and some other conditions, but it has not been approved by FDA for osteoporosis. As of 1995, etidronate was the only bisphosphonate available on the U.S. market. Neither etidronate nor any other bisphosphonates have been approved by FDA for indications related to osteoporosis.

**Etiology**
The cause or origin of disease.

**Exogenous estrogen**
Estrogen that is not produced within the body but is provided by other means, e.g., tablets, injection, cream.

**External controls**
In a cohort study, individuals not part of the cohort and who have not been exposed, with which the exposed members of the cohort are compared. In a clinical trial, individuals not formally enrolled in the trial who have had an alternative treatment, with which the experimentally treated group is compared. External controls may be historical or concurrent.

**External validity**
A measure of the extent to which study results can be generalized to the population that is represented by individuals in the study, assuming that the characteristics of that population are accurately specified.

**Femur**
The thigh bone, the bone that extends from the hip to the knee. It is the longest and largest bone in the body.

**Fibrin**
A white insoluble protein formed at the site of an injury from fibrinogen that becomes the foundation of a blood clot.

**Fibrinogen**
A soluble plasma protein synthesized in the liver, which is involved in blood coagulation as the precursor of fibrin. Also called “Factor I.”

**Fibroblast**
A connective tissue cell, found in the skin.

**First-pass hepatic effect**
See hepatic effect.
**Functional impairment**
A deficit in an individual’s ability to function independently. Functional impairments in elderly people are often described in terms of deficits in activities of daily living (ADLs) and instrumental activities of daily living (IADLs).

**Grade**
The histological appearance of a cancer cell. In oncology, the classification of cancer according to the degree of differentiation of the cancer cell. More differentiated cell types are generally less malignant.

**Haversian bone**
See cortical bone.

**Healthy user effect**
A phenomenon in epidemiologic studies in which subject participants exhibit lower incidence of morbidity or mortality than the general population because they are generally in good health while the less healthy either choose not to participate in the study or are excluded.

**Hemostatic**
The arrest of bleeding, whether by the physiological properties of vasoconstriction and coagulation or by surgical means.

**Hepatic effect**
Pertaining to the liver, the metabolism of estrogen by the liver.

**Hepatobiliary**
Related to the gallbladder.

**High-density lipoprotein cholesterol (HDL)**
A class of cholesterol; low levels of HDL are associated with an increased risk of heart attack.

**Histology**
Microscopic anatomy. The study of the minute anatomical structure, composition, and function of the tissues.

**Historical controls**
In nonrandomized clinical trials, individuals treated with a “control treatment” outside the study proper, at some time previous to the trial, against which the experimentally treated individ-

**Hormone**
A specific organic product of living cells that, transported by body fluids, produces a specific effect on the activity of cells remote from its point of origin (e.g., metabolism, growth, and the development of secondary sex characteristics, such as breasts and facial hair). Examples of such hormones include insulin, estrogen, progestin, testosterone, adrenaline, and thyroxine. Also a synthetic substance that resembles a naturally occurring hormone in producing a specific biological effect.

**Hormone replacement therapy (HRT)**
This term describes either estrogen replacement therapy or combined estrogen and progestin replacement therapy when a distinction is not necessary.

**Hospital-based case-control studies**
In this type of study, all cases diagnosed with the disease under study in one or more hospitals are compared with patients in the same hospitals who do not have the disease.

**Hot flash**
Sudden sensations of heat and flushing of the face and torso, associated with menopause.

**Hypermenorrhea**
Excessive menstrual bleeding, but occurring at regular intervals and being of usual duration.

**Hyperplasia**
Abnormal increase in the number of normal cells in normal arrangement in an organ or tissue, which increases its volume.

**Hypertension**
Elevated pressure, usually referring to high blood pressure—a common and significant cardiovascular disorder characterized by persistently high arterial blood pressure, usually greater that 140mm Hg systolic and 90mm Hg diastolic pressure.
Hypertriglyceridemia
An excess of triglycerides in the blood.

Hysterectomy
Surgical removal of the uterus, in some cases also including the cervix, ovaries, oviducts, and pelvic lymph nodes.

In vitro
Literally “in glass”; pertaining to a biological process or reaction taking place in an artificial environment, usually a laboratory.

In vivo
Literally “in the living”; pertaining to a biological process or reaction taking place in a living cell or organism.

Incidence
In epidemiology, the number of new cases of disease, infection, or some other event having their onset during a prescribed period of time in relation to the unit of population in which they occur. The incidence rate is the number of new cases of specified disease divided by the number of people in a population over a specified period of time, usually 1 year.

Infarction
Necrosis (death) of tissue, resulting from the interruption of blood supply (e.g., as in a heart attack (myocardial infarction)).

Internal controls
A control group composed of unexposed members of a cohort. See cohort study.

Internal validity
A measure of the extent to which study results reflect the true relationship of a “risk factor” (e.g., treatment or technology) to the outcome of interest in study subjects.

Ischemia
Insufficient blood supply to meet the full physiologic needs of the tissue for oxygen (but short of the degree of ischemia that results in necrosis), usually due to atherosclerosis, but also due to injury to blood vessels, muscle spasm, or inefficient pumping of the heart.

Ischemic heart disease (IHD)
A spectrum of conditions caused by insufficient oxygen supply to the heart muscle, and the leading cause of death in the United States. The most common manifestations of IHD are angina, acute myocardial infarction (heart attack), and sudden death.

Latency
Time since first exposure to a suspected causative factor.

Latent effect
A reaction to a substance that is not immediately evident but that appears later in life; also referred to as a silent effect.

Life expectancy
An expected number of years of life based on statistical probability.

Lipids
A group of organic compounds, classified into complex lipids (e.g., fatty acids, phospholipids, cholesterol) and simple lipids (e.g., steroids). Lipids are central to a wide variety of metabolic and structural functions in the body, such as energy storage, formation of hormones and bile acids, and structure of cell membranes.

Lipoprotein
Compounds consisting of lipids (fatty substances such as cholesterol) and proteins, the form in which lipids are transported in the blood and lymph fluid. Lipoproteins form the main structural components of cell membranes and cell organelles. They are classified as very low-density (VLDL), low-density (LDL), and high-density (HDL) lipoprotein cholesterol.

Low-density lipoprotein cholesterol (LDL)
A class of cholesterol; high levels of LDL are associated with a greater risk of heart attack.

Magnetic resonance imaging (MRI)
A diagnostic technique that produces cross-sectional images of organs and structures in the body by measuring the reaction of nuclei (typically of hydrogen protons) in magnetic fields to radio fre-
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Frequency waves. MRI has also been used to measure bone density.

Matching
A method of minimizing the impact of confounding factors. Controls may be matched to cases to try to minimize other differences between groups. Matching may be done with groups of subjects (stratification) or with individuals, and may be done with highly specific characteristics, such as age, age at menopause, family history of the disease, etc.

Medicare
A nationwide, Federally administered health insurance program authorized by Title XVIII of the Social Security Act in 1965 to cover the cost of hospitalization, medical care, and some related services for eligible persons over age 65, persons receiving Social Security Disability Insurance payments for 2 years, and persons with end-stage renal disease. Medicare consists of two separate but coordinated programs—hospital insurance (Part A) and supplementary medical insurance (Part B). Health insurance protection is available to insured persons without regard to income.

MEDLINE database
The original, largest, and most utilized database in the National Library of Medicine’s computerized retrieval and technical processing system. MEDLINE contains references to biomedical and other literature relevant to health and health services.

Medroxyprogesterone acetate (MPA)
A form of progestin. Also known as Provera (Wyeth-Ayerst). In the United States, MPA is the most commonly used progestin in combined estrogen/progestin replacement therapy.

Membership bias
Bias introduced when the group or cohort being studied is unrepresentative of the population at large, so that comparisons and extrapolations to the population group are unjustified.

Menarche
The onset of menses at puberty.

Menopausal syndrome
Symptoms associated with menopause, e.g., hot flashes, vaginal dryness, osteoporosis.

Menopause
Cessation of menstruation; the immediate postproductive phase of a woman’s life, when menstrual function ceases due to failure to form ovarian follicles and ova. Menopause occurs naturally around the age of 50. Menopause is also a secondary consequence of surgical removal of the ovaries, and of certain illnesses (e.g., premature ovarian failure).

Menorrhagia
Excessive menstruation.

Menses
The monthly flow of blood from the female genital tract.

Meta-analysis
A statistical process used to pool results from a number of studies (e.g., from many small randomized clinical trials) to enable the demonstration of statistically significant differences when the results are combined.

Metastasis
The process by which malignant cells spread to distant body sites via the lymphatic circulation of the bloodstream; also, a secondary malignant tumor.

Metrorrhagia
Uterine bleeding, usually of normal amount, occurring at completely irregular intervals, the period of flow sometimes being prolonged.

Morbidity
The condition of being ill or otherwise afflicted with an unhealthful condition.

Morbidity rate
The rate of illness in a population, calculated as the number of people ill during a time period divided by the number of people in the total population; used to refer to incidence or prevalence rates of disease.

Mortality rate
The death rate, often made explicit for a particular characteristic; e.g., age, sex, or specific cause of
death. A mortality rate contains three essential elements: 1) the number of people in a population group exposed to the risk of death (the denominator); 2) a time factor; and 3) the number of deaths occurring in the exposed population during a certain time period (the numerator).

**Myocardial infarction (MI)**
Heart attack. Sudden necrosis (death) of tissue in the myocardium (heart muscle) characterized by severe, unremitting chest pain, leading to arrhythmias and/or heart failure; in most cases, caused by coronary atherosclerosis (obstruction of coronary vessels, leading to insufficient blood supply to the heart muscle).

**Myocardium**
Muscle of the heart.

**Natural estrogen**
An estrogen derived from natural sources, (i.e., not synthetic), such as conjugated equine estrogens, estradiol, or estriol.

**Natural menopause**
Menopause that occurs as a natural part of the aging process; not surgically induced.

**Naturally occurring estrogenic hormones**
Female sex hormones produced by the ovaries, the placenta, testes, and possibly the adrenal cortex.

**Neoplasm**
Uncontrolled and progressive growth of tissue, either benign or malignant; a tumor.

**Nested case-control studies**
Case-control studies conducted, or “nested,” within a cohort group.

**Nonischemic heart disease**
Heart disease from causes other than coronary artery disease (e.g., congenital heart disease, myocardial infarction).

**Norethidrone acetate**
A progestational agent similar in action to progesterone.

**Observational study**
An epidemiologic study in which the experiences of the groups being compared are simply observed (e.g., case-control studies, cross-sectional studies, and cohort studies). Such studies are the traditional source of information on suggestive associations in epidemiology.

**Oclusion**
In the context of the vascular system, the blocking off or obstruction of blood flow through a vessel.

**Odds ratio**
A measure of association closely related to relative risk; the ratio of the odds of a disease occurring in individuals exposed to the risk compared to those unexposed. For large samples, the odds ratio is essentially equal to the relative risk.

**Oligomenorrhea**
Abnormally infrequent menstruation.

**Oophorectomy**
Excision of one or both ovaries.

**Opposed estrogen**
Estrogen used in conjunction with progestin.

**Osteoblast**
A cell arising from a fibroblast, which, as it matures, is associated with bone production.

**Osteopenia**
A reduction in the amount of bone mass, leading to fractures after only minimal trauma.

**Osteoporosis**
A systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.

**P value**
In epidemiologic studies, the probability of concluding that a statistical association exists between, for instance, a risk factor and a health endpoint, when, in fact, there is no real association; the likelihood that an observed association in a study is due to the play of chance. Also called “Type I error” or “alpha,” and commonly called the level of significance. See significance level.
Parathyroid hormone (PTH) or human parathyroid hormone (hPTH)
A polypeptide hormone which regulates the concentration of extracellular fluid calcium.

Parenteral
Administration through routes other than the alimentary canal. Parenteral administration includes intravenous, subcutaneous, transdermal, intraocular, and intranasal administration.

Pathophysiology
The physiology of disordered function.

Percutaneous
Literally, “through the skin”; refers to a surgical procedure that requires only a very small incision, such as a biopsy, or aspiration of fluid beneath the skin using a needle, catheter, or syringe.

Perimenopause
The time around the menopause.

Peripheral conversion
Conversion of estrogen outside of the liver, in peripheral tissues.

Peripheral nervous system
The autonomic nervous system, the cranial nerves, and the spinal nerves including associated receptors.

Pharmacodynamics
The study of the actions of drugs on living systems.

Pharmacokinetics
The rate of change in a physical or chemical system, specifically in relation to drugs.

Placebo
A drug or procedure with no intrinsic therapeutic value. In a placebo-controlled randomized clinical trial, a placebo is given to patients in control groups as a means to blind investigators and patients as to whether an individual is receiving the experimental or control treatment. See randomized clinical trial (RCT).

Plaques
Yellowish fatty deposits formed within the intima and inner media (innermost and middle coats of the blood vessels) of large and medium-sized veins.

Platelets
Disk-shaped tissue, found in the blood of mammals, which responds to injury elsewhere in the body. Platelets are known for their role in blood coagulation (clotting). Also called “thrombocytes.”

Population-based case-control studies
In this type of study, all cases diagnosed in the community or in a sample of the general population are compared with controls selected from the community or a sample of the general population.

Postmenopause
The period of time after the menopause.

Power
The power of the study refers to the chance of finding a true difference in risk and labeling it as statistically significant. Thus the power of the study is equal to 0.80 when the sensitivity level is 0.20 (i.e., 1 - 0.20 = 0.80).

Predictive test
A medical test generally applied to asymptomatic individuals to provide information regarding the future occurrence of disease.

Premarin
Wyeth-Ayerst’s brand of conjugated estrogen. The most commonly used estrogen for HRT in the United States. See conjugated estrogens.

Premature ovarian failure
Condition characterized by the failure to ovulate before the normal age of menopause.

Premenopause
The stage of life before menstruation stops.

Premenstrual syndrome
The pattern of symptoms related to the menstrual cycle.

Preovulation
The first 14 days of a woman’s menstrual cycle, when estrogen levels are rising before ovulation takes place.
**Prevalence**
A measure of the number of individuals in a given population who have a specific disease or other condition at a designated time (or during a particular period).

**Primary prevention**
A category of health and/or related interventions that aim to eliminate a disease or disordered state before it can occur. Compare secondary prevention.

**Progestational**
Favoring pregnancy; conducive to gestation; having a stimulating effect upon the uterine changes essential for the implantation and growth of the fertilized ovum. Referring to progesterone, or to a drug with progesterone-like properties.

**Progesterone (also called progestational hormone)**
An antiestrogenic female sex hormone secreted by the ovaries (specifically by the corpus luteum, formed immediately after ovulation), by the placenta during pregnancy to prepare the inner lining of the uterus for implantation of an ovum, and in small amounts by the adrenal glands and testes, and prepares the inner lining of the uterus for pregnancy. Receptors for progesterone have been identified on osteoblasts, and although the data are not entirely clear, it appears that progesterone may stimulate bone formation. Progesterone and other agents capable of producing some or all of the biological effects similar to those of progesterone are called progestins (or progestogens).

**Progestin**
Originally, the crude hormone of the corpus luteum of the ovary; it has since been isolated in pure form and is now known as progesterone. The generic term for any substance, natural or synthetic, that effects some or all of the biological changes produced by the hormone progesterone. See progestogen.

**Progestin/estrogen replacement therapy (PERT)**
The use of estrogen combined with progestin for the treatment of menopausal symptoms, e.g., hot flashes, the prevention of heart disease, and/or the prevention of osteoporosis; progestin opposes the carcinogenic effects of estrogen on the endometrium.

**Progestogen**
See progestin.

**Prospective study**
An epidemiologic study in which data are gathered after a hypothesis has been generated and the study approved. In a prospective study, the investigator first identifies the subjects and then follows them over time for development of disease. Compare retrospective study.

**Provera**
Wyeth-Ayerst’s brand of the progestin medroxyprogesterone acetate (MPA). The most commonly used progestin for HRT in the United States. See progestin, progesterone.

**Quality-adjusted life-year (QALY)**
In cost-effectiveness analysis, a measure of health impact used to compare the benefit or effectiveness of alternative health interventions, such as the value of an extra year of life gained through kidney transplantation versus dialysis for patients with end stage renal disease; involves some degree of arbitrary valuation and weighting of different conditions.

**Quantitative computerized tomography (QCT)**
A bone densitometry technique similar to DEXA which measures the central, trabecular portion of the vertebral body, the spongiosa. Techniques have been developed to allow for quantitative measurement on most commercially available CT scanners.

**Radiographic densitometry**
Noninvasive measurement of bone mass in vivo was first performed by quantifying radiographs with an optical densitometer. The film density over the bone is compared to that over the soft tissue, and the resultant absorption is related to that obtained over a series of standards with known mineral content. Because of technical errors related to the polychromate nature of the radiation source and differences in x-ray film characteris-
tics, this technique has many errors and is rarely used clinically today.

**Radiogrammetry**
X-rays of the hand and radius, using fine grain industrial film, have been used to measure the cortical thickness of these tubular bones as an indicator of cortical bone mass. Although the proximal radius and ulna and the six middle metacarpal of both hands have been used, the mid-shaft of the second metacarpal is the usual measurement site.

**Radius**
The bone on the outer or thumb side of the forearm. The *distal radius* is the end of the radius bone adjacent to the wrist. The *proximal radius* is the end of the radius adjacent to the elbow.

**Random allocation**
In a randomized clinical trial, allocation of individuals to treatment groups such that each individual has an equal probability of being assigned to any group.

**Randomized clinical trial (RCT) (also called randomized controlled clinical trial or controlled clinical trial)**
In epidemiology, a clinical trial of a prophylactic, diagnostic, or therapeutic agent, device, regimen, procedure, etc. in which human (or animal) subjects are randomly allocated into groups, usually called “the experimental group” (in which subjects receive the treatment being studied) and “the control group” (in which subjects do not receive the treatment being studied), and outcomes are compared.

**Recall bias**
Bias caused by differences in abilities of two groups to remember exposure to suspected causative factors.

**Recency**
Time since last exposure to a suspected causative factor.

**Regression analysis**
A statistical procedure for determining the best approximation of the relationship between variables. Multiple regression analysis is a method for measuring the effects of several factors concurrently.

**Relative risk**
A measure of a relationship, defined as the chance of an outcome, such as breast cancer, among a group of persons having a suspected causative factor, divided by the chance of this outcome among a similar group without this suspect factor.

**Reliability**
The reproducibility of results over repeated measurements, and relates to the lack of random error over these repeated measurements. Reliability is a prerequisite to validity.

**Retrospective study**
An epidemiologic study in which data that are already available are analyzed to test a hypothesis (e.g., inferences about exposure to a possible causal factor are derived from data on subjects who already have the disease in question, compared to other subjects who do not have the disease).

**Risk factor**
An aspect of personal behavior or lifestyle, an environmental exposure, or an inborn or inheritance characteristic, which on the basis of epidemiologic evidence is known to be associated with health related conditions considered important to prevent.

**Route of administration**
In pharmacology, refers to the means by which a drug is administered: namely intravenous (injected into the bloodstream), inhalation (through the lungs), oral (through ingestion), and dermal (through the skin).

**Secondary preventions**
An intervention that strives to shorten the course of an illness by early identification and rapid intervention.

**Selection bias**
A distortion in the estimate of effect resulting from the manner in which subjects are selected for a study population.
**Sensitivity**
The percentage of all those who actually have the condition being tested who are currently identified as positive by the test.

**Sensitivity analysis**
In cost-effectiveness and cost-benefit analysis, an analysis of the effect of changes in key assumptions or uncertainties on the findings and outcome of the overall study.

**Serum lipid profiles**
A quantitative representation of the level of serum lipids.

**Serum triglycerides**
Esters formed from glycerol and one to three fatty acids; fats and oils are triglycerides.

**Significance level**
The significance level, or “p” value, is the probability of concluding that a relative risk is different from 1.0 when it is not. By convention, a difference in risk is said to be statistically significant if there is less than a five percent chance of making this type of error (i.e., $p < 0.05$). The significance can also be expressed as a confidence interval.

**Single photon absorptiometry (SPA)**
A bone densitometry technique that employs a sealed source of radioactive material that emits a single energy radiation (photon), and a detector that measures the amount of photons transmitted through bone and soft tissue. The radius and calcareous can be measured with this device.

**Single photon x-ray absorptiometry (SXA)**
A bone densitometry technique similar to SPA but using an x-ray source rather than a radioactive source. Both the radius and calcareous can be measured with this device.

**Specificity**
One measure of the validity (or accuracy) of a diagnostic or screening test: the percentage of all those who do not have the condition being tested or who are correctly identified as negative by the test. Operationally, it is the number of negative test results divided by the number of patients that actually have the disease (true-negatives divided by the sum of true-negatives plus false-positives). Compare sensitivity.

**Statistically significant**
The likelihood that an observed association is not due to chance. See $P$ value.

**Steroid hormone**
Any of numerous hormones characterized by steroid structure (i.e., four carbon rings interlocked to form a hydrogenated cyclopentophenanthrene ring system). Steroid hormones include the sex hormones estrogen, progesterin, and androgen; they also include cortisone and adrenocortical hormones.

**Steroids**
Any of a class of compounds characterized by a polycyclic structure like that of the sterols and that usually include the sterols (e.g., cholesterol) and vitamin D, as well as many other naturally occurring compounds (e.g., bile acids).

**Stratification**
In randomized clinical trials, the categorization of individuals for the purpose of adjusting the groups to take into account unequal distribution of characteristics of prognostic importance. Stratification may be used during patient allocation, creating subgroups within which individuals are randomized to treatments; or stratification might be applied during data analysis to statistically adjust for differences between the groups.

**Stress incontinence**
See urinary stress incontinence.

**Stroke**
Loss of sensation, movement, or function caused by a sudden interruption of the blood supply or a leakage of blood in the brain. This can be caused by heart failure, blockage of arteries (cerebral thrombosis or cerebral embolism), or hemorrhage in the brain.

**Subcutaneous**
Beneath the skin.

**Subgroup analysis**
A separate analysis performed on a subgroup of the population being studied to identify important differences in risk. Such differences in risk maybe...
due to interactions of the purported causative factor with other risk factors for the disease.

**Surgical menopause**
Menopause following the surgical removal of the ovaries.

**Symptomatology**
The combined symptoms of a disease.

**Synthetic calcitonin**
A synthetically produced/manufactured form of the hormone calcitonin, a 32 amino acid polypeptide, one of the three calcium regulating hormones found in humans. The FDA has granted qualified approval for both natural and synthetic calcitonin for the treatment but not the prevention of osteoporosis.

**Synthetic estrogen**
A synthetically produced/manufactured estrogen product.

**Systemic circulation**
Channels through which nutrient fluids of the body flow: often restricted to the vessels conveying blood.

**Testosterone**
An androgen or steroid hormone secreted by the interstitial cells of the testes, which functions in the induction and maintenance of male secondary sex characteristics and affects sperm production; testosterone and its cypionate, enanthate, and propionate esters are used in palliative therapy in inoperable carcinoma of the female breast and certain gynecologic conditions.

**Thromboembolic disease**
Disease related to blood vessel obstruction.

**Thrombosis**
The abnormal development of a blood clot (thrombus) inside an intact blood vessel, which can be life-threatening if it obstructs the blood supply to the brain (leading to stroke), heart (leading to myocardial infarction), the lungs (leading to pulmonary embolism), or other organs (leading to tissue damage or loss of function); the presence of such clots also raises the risk that part of the clot (an embolus) may break off and travel to a distant artery or vein, causing thrombophlebitis or deep vein thrombosis. Factors contributing to thrombosis include atherosclerosis, an increase in coagulation factors, or a deficiency of anticoagulating factors in the blood.

**Total cumulative exposure**
The total dose, which is related both to the level and to the duration of exposure. For example, for estrogen replacement therapy, total dose is related to how much and for how long the estrogen is given.

**Trabecular bone**
See cancellous bone.

**Transdermal**
Through the skin.

**Transmenopausal**
Occurring across the time period of the menopause.

**Treatment group**
In a randomized clinical trial, the group receiving the treatment being evaluated for safety and efficacy. Also known as the experimental group. See randomized clinical trial (RCT).

**Tumor**
A new growth of tissue in which the multiplication of cells is uncontrolled and progressive. Also called neoplasm.

**Ultrasound**
Predictor of fracture risk using sound velocity and sound attenuation to measure both bone mass and altered bone architecture.

**Unopposed estrogen**
Estrogen used alone, without a progestin. Also known as estrogen replacement therapy (ERT).

**Unopposed progestin**
Progestin used alone. Progestins alone have been used to relieve menopausal symptoms.

**Urinary bladder**
The hollow, muscular organ that collects urine from the ureters and stores it until the urine is discharged through the urethra during urination.
Urinary incontinence
An involuntary loss of urine sufficient in quantity and/or frequency to be a social or health problem.

Urinary stress incontinence
Involuntary escape of urine due to strain on the orifice of the bladder, as in coughing or sneezing.

Urodynamics
A process that evaluates characteristics of the urine stream and the pelvic musculature, and the activity of the bladder.

Uterine prolapse
Descension of the uterus down into the vagina, caused by weakening of the support ligaments and muscles that hold the uterus in place.

Uterus
The hollow muscular organ in the female in which the fertilized ovum normally becomes embedded and in which the developing embryo and fetus are nourished. Its cavity opens into the vagina below and into a fallopian tube on either side.

Vagina
The canal in the female, from the vulva to the cervix uteri, that receives the penis in copulation and is the birth canal.

Vaginal atrophy
The wasting or diminution in size of the vagina.

Vaginismus
Painful, involuntary contraction or spasm of the muscles around the outer third of the vagina, interfering with sexual intercourse.

Validity
A measure of the extent to which an observed situation reflects the “true” situation.

Vertebra
In the human body, any of the 33 bones of the spinal column, comprising the 7 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 4 coccygeal vertebrae.

Withdrawal bleeding
Bleeding, associated with hormone replacement therapy, caused by the sloughing of the endometrium due to withdrawal of estrogen stimulation.