Appendixes

APPENDIX A. OSTEOPOROSIS/BONE MINERAL DENSITY – SEARCH METHODOLOGIES

DATABASE SEARCHED& TIME PERIOD COVERED:
PubMed – 1966-2005 – Initial search

OTHER LIMITERS:
ENGLISH
HUMAN

SEARCH STRATEGIES:

SEARCH #1a (Specified bisphosphonates)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
alendronate* OR fosamax (860)
OR
resindronate* OR actonel (174)
OR
etidronate* OR didronel (623)
OR
ibandronate* OR boniva (93)
OR
pamidronate* OR aredia (412)
OR
zoledronic acid OR zometa (112)
OR
droloxifene* (13)

TOTAL OF ABOVE SEARCHES – DUPLICATES ELIMINATED: **1757**

SEARCH #1b (Other bisphosphonates)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
bisphosphonate*
NOT
Results of Search #1a

TOTAL NUMBER OF ITEMS: 687

SEARCH #2a (Specified SERMs)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
raloxifene* OR evista (560)
tamoxifen* OR nolvadex OR emblon OR fentamox OR soltamox OR tamofen (697)

TOTAL OF ABOVE SEARCHES – DUPLICATES ELIMINATED: 784

SEARCH #2b (Other SERMs)

osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
selective estrogen receptor modulators OR serm OR serms
NOT
Results of Search #2a

TOTAL NUMBER OF ITEMS: 186

SEARCH #3 (Calcitonin)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
calcitonin* OR miacalcin OR calcimar OR cibacalcin
NOT
pth OR parathyroid hormone

TOTAL NUMBER OF ITEMS: 1078

SEARCH #4 (PTH)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
pth OR parathyroid hormone

TOTAL NUMBER OF ITEMS: 3787

SEARCH #5 (Teriparatide)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
teriparatide OR forteo
TOTAL NUMBER OF ITEMS: 182

SEARCH #6 (Exercise)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
(exercise[mh] OR exercis*[ti] OR physical fitness OR physically fit OR physical activity)
NOT
Results of previous searches

TOTAL NUMBER OF ITEMS: 2832

SEARCH #7 (Letrozole)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
letrozole OR femora
NOT
Results of previous searches

TOTAL NUMBER OF ITEMS: 356

SEARCH #8 (AMG 162)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density

AND
amg162 OR amg 162

TOTAL NUMBER OF ITEMS: 2

SEARCH #9 (**Ospemifene)**
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
ospemifene*

TOTAL NUMBER OF ITEMS: 6

SEARCH #10 (Strontium ralenate)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
strontium ralenate*
NOT
Results of previous searches

TOTAL NUMBER OF ITEMS: 167

SEARCH #11(Testosterone)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
testosterone

TOTAL NUMBER OF ITEMS: 904

SEARCH #12 (**Tiludronate**)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
tiludronate OR skelid

TOTAL NUMBER OF ITEMS: 38

SEARCH #13 (Toremifene)
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
toremifene*
TOTAL NUMBER OF ITEMS: 27

OSTEOPOROSIS/OSTEOPENIA & THERAPIES – OTHER DATA BASES – INITIAL SEARCHES

DATABASE:
EBM Reviews On OVID (Cochrane Database of Systematic Reviews, DARE, Controlled Trials Register, and ACP Journal Club databases)

DATE LIMITERS – None

SEARCH STRATEGY:
NOTE: "mp." is a group field indicator in OVID. The fields searched are:
Title, Short Title, Abstract, Text Word, Keyword, Heading Word, Caption Text, MESH heading

osteoporosis or osteopenia or osteopaenia or fracture$ or bone mineral.mp.
AND
bisphosphonate$.mp. **258**
alendronate$ or fosamax.mp. **294**
resindronate$ or actonel.mp. **1**
etidronate$ or didronel.mp. **153**
ibandronate$ or boniva.mp. **35**
pamidronate$ or aredia.mp. **105**
zoledronic acid$ or zometa.mp. **19**
selective estrogen receptor modulator$ or serm$.mp. **108**
raloxifene or evista.mp. **141**
tamoxifen or nolvadex or emblon or fentamox or soltamox or tamofen.mp. **80**
droloxifene.mp. **1**
calcitonin$ or miacalcin or calcimar or cibacalcin.mp. **311**
parathyroid hormone$ or pth.mp. **366**
teriparatide or forteo.mp. **26**
exercis$.mp. and (calcium or vitamin d).mp. **140**

ALL RECORDS WERE IMPORTED INTO PROCITE AND DUPLICATES WERE REMOVED. TOTAL NUMBER OF UNIQUE ITEMS: 1390

OSTEOPOROSIS / LOW BONE DENSITY
(SEARCHES PERFORMED AFTER DRAFT REPORT FEEDBACK)

DATABASE SEARCHED& TIME PERIOD COVERED:
PubMed – 1966-2006

OTHER LIMITERS:
ENGLISH
HUMAN

SEARCH STRATEGIES:

SEARCH #1A (Bisphosphonates & Breast Cancer)
bisphosphonate*
AND
breast neoplasms OR breast cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 41

SEARCH #1B (Bisphosphonates & Colon Cancer)
bisphosphonate*
AND
colonic neoplasms OR colon cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 5

SEARCH #1C (Bisphosphonates & Lung Cancer)
bisphosphonate*
AND
lung neoplasms OR lung cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 5

SEARCH #1D (Bisphosphonates & Osteosarcoma)
bisphosphonate*
AND
osteosarcoma*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 2

SEARCH #1E (Bisphosphonates & Esophageal Ulcer)
bisphosphonate*
AND
(esophagus OR esophageal) AND ulcer*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #1F(Bisphosphonates & PUBS)
bisphosphonate*
AND
perforation* OR ulcer* OR bleed*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 7

SEARCH #1G(Bisphosphonates & Osteonecrosis)
bisphosphonate*
AND
osteonecrosis
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 29

SEARCH #2A(Alendronate & Breast Cancer)
alendronate*
AND
breast neoplasms OR breast cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 9

SEARCH #2B(Alendronate & Colon Cancer)
alendronate*
AND
colonic neoplasms OR colon cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #2C(Alendronate & Lung Cancer)
alendronate*
AND

lung neoplasms OR lung cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 2

SEARCH #2D(Alendronate & Osteosarcoma)
alendronate*
AND
osteosarcoma*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #2E(Alendronate & Esophageal Ulcers)
alendronate*
AND
(esophagus OR esophageal) AND ulcer*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 8

SEARCH #2F(Alendronate & PUBS)
alendronate*
AND
perforation* OR ulcer* OR bleed*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 20

SEARCH #2G(Alendronate & Osteonecrosis)
alendronate*
AND
osteonecrosis
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 4

SEARCH #3A(Etidronate & Breast Cancer)
etidronate*
AND
breast neoplasms OR breast cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 2

SEARCH #3B(Etidronate & Colon Cancer)
etidronate*
AND
colonic neoplasms OR colon cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #3C(Etidronate & Lung Cancer)
etidronate*
AND
lung neoplasms OR lung cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #3D(Etidronate & Osteosarcoma)
etidronate*
AND
osteosarcoma*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #3E(Etidronate & Esophageal Ulcers)
etidronate*
AND
(esophagus OR esophageal) AND ulcer*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 4

SEARCH #3F(Etidronate & PUBS)
etidronate*
AND
perforation* OR ulcer* OR bleed*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 9

SEARCH #3G(Etidronate & Osteonecrosis)
etidronate*
AND
osteonecrosis
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #4A(Ibandronate & Breast Cancer)
ibandronate*
AND
breast neoplasms OR breast cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 4

SEARCH #4B(Ibandronate & Colon Cancer)
ibandronate*
AND
colonic neoplasms OR colon cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #4C(Ibandronate & Lung Cancer)
ibandronate*
AND
lung neoplasms OR lung cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #4D(Ibandronate & Osteosarcoma)
ibandronate*
AND
osteosarcoma*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #4E(Ibandronate & Esophageal Ulcers)
ibandronate*

AND
(esophagus OR esophageal) AND ulcer*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #4F(Ibandronate & PUBS)
ibandronate*
AND
perforation* OR ulcer* OR bleed*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #4G(Ibandronate & Osteonecrosis)
ibandronate*
AND
osteonecrosis
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #5A(Pamidronate & Breast Cancer)
pamidronate*
AND
breast neoplasms OR breast cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 23

SEARCH #5B(Pamidronate & Colon Cancer)
pamidronate*
AND
colonic neoplasms OR colon cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #5C(Pamidronate & Lung Cancer)
pamidronate*
AND
lung neoplasms OR lung cancer[tiab]
AND

observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 13

SEARCH #5D(Pamidronate & Osteosarcoma)
pamidronate*
AND
osteosarcoma*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #5E(Pamidronate & Esophageal Ulcers)
pamidronate*
AND
(esophagus OR esophageal) AND ulcer*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #5F(Pamidronate & PUBS)
pamidronate*
AND
perforation* OR ulcer* OR bleed*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 5

SEARCH #5G(Pamidronate & Osteonecrosis)
pamidronate*
AND
osteonecrosis
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 10

SEARCH #6A(Risedronate & Breast Cancer)
risedronate*
AND
breast neoplasms OR breast cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #6B(Risedronate & Colon Cancer)
risedronate*
AND
colonic neoplasms OR colon cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #6C(Risedronate & Lung Cancer)
risedronate*
AND
lung neoplasms OR lung cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #6D(Risedronate & Osteosarcoma)
risedronate*
AND
osteosarcoma*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #6E(Risedronate & Esophageal Ulcers)
risedronate*
AND
(esophagus OR esophageal) AND ulcer*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #6F(Risedronate & PUBS)
risedronate*
AND
perforation* OR ulcer* OR bleed*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #6G(Risedronate & Osteonecrosis)

risedronate*
AND
osteonecrosis
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #7A(Zolendronate & Breast Cancer)
zolendronate* OR zoledronic
AND
breast neoplasms OR breast cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 15

SEARCH #7B(Zolendronate & Colon Cancer)
zolendronate* OR zoledronic
AND
colonic neoplasms OR colon cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #7C(Zolendronate & Lung Cancer)
zolendronate* OR zoledronic
AND
lung neoplasms OR lung cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 4

SEARCH #7D(Zolendronate & Osteosarcoma)
zolendronate* OR zoledronic
AND
osteosarcoma*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #7E(Zolendronate & Esophageal Ulcers)
zolendronate* OR zoledronic
AND
(esophagus OR esophageal) AND ulcer*

AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #7F(Zolendronate & PUBS)
zolendronate* OR zoledronic
AND
perforation* OR ulcer* OR bleed*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #7G(Zolendronate & Osteonecrosis)
zolendronate* OR zoledronic
AND
osteonecrosis
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 18

SEARCH #8A(Raloxifene & Breast Cancer)
raloxifene*
AND
breast neoplasms OR breast cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 27

SEARCH #8B(Raloxifene & Colon Cancer)
raloxifene*
AND
colonic neoplasms OR colon cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #8C(Raloxifene & Lung Cancer)
raloxifene*
AND
lung neoplasms OR lung cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #8D(Raloxifene & Osteosarcoma)
raloxifene*
AND
osteosarcoma*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #8E(Raloxifene & Esophageal Ulcers)
raloxifene*
AND
(esophagus OR esophageal) AND ulcer*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #8F(Raloxifene & PUBS)
raloxifene*
AND
perforation* OR ulcer* OR bleed*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 1

SEARCH #8G(Raloxifene & Osteonecrosis)
raloxifene*
AND
osteonecrosis
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #9A(Tamoxifen & Breast Cancer)
tamoxifen*
AND
breast neoplasms OR breast cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 210

SEARCH #9B(Tamoxifen & Colon Cancer)
tamoxifen*
AND
colonic neoplasms OR colon cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 15

SEARCH #9C(Tamoxifen & Lung Cancer)
tamoxifen*
AND
lung neoplasms OR lung cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 51

SEARCH #9D(Tamoxifen & Osteosarcoma)
tamoxifen*
AND
osteosarcoma*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 2

SEARCH #9E(Tamoxifen & Esophageal Ulcers)
tamoxifen*
AND
(esophagus OR esophageal) AND ulcer*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #9F(Tamoxifen & PUBS)
tamoxifen*
AND
perforation* OR ulcer* OR bleed*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 49

SEARCH #9G(Tamoxifen & Osteonecrosis)
tamoxifen*
AND

osteonecrosis
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 0

SEARCH #10 (PTH & All Diseases)
pth
AND
breast neoplasms OR breast cancer[tiab] OR colonic neoplasms OR colon cancer[tiab] OR lung neoplasms OR lung cancer[tiab] OR osteosarcoma* OR ((esophagus OR esophageal) AND ulcer*) OR perforation* OR ulcer* OR bleed* OR osteonecrosis
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 67

SEARCH #11(Testosterone & All Diseases)
testosterone*
AND
breast neoplasms OR breast cancer[tiab] OR colonic neoplasms OR colon cancer[tiab] OR lung neoplasms OR lung cancer[tiab] OR osteosarcoma* OR ((esophagus OR esophageal) AND ulcer*) OR perforation* OR ulcer* OR bleed* OR osteonecrosis
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 147

SEARCH #12A(Estrogen & Breast Cancer)
estrogen* OR estrogens[mh] OR oestrogen* OR estradiol
AND
breast neoplasms OR breast cancer[tiab]
AND
cohort*
NOT
testosterone AND (breast neoplasms OR breast cancer[tiab])

NUMBER OF ITEMS RETRIEVED: 602

SEARCH #12B(Estrogen & Colon Cancer)
estrogen* OR estrogens[mh] OR oestrogen* OR estradiol
AND
colonic neoplasms OR colon cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*
NOT
Results of Search #12A

NUMBER OF ITEMS RETRIEVED: 75

SEARCH #12C(Estrogen & Lung Cancer)
estrogen* OR estrogens[mh] OR oestrogen* OR estradiol
AND
lung neoplasms OR lung cancer[tiab]
AND
observational OR cohort* OR case control* OR case report*
NOT
Results of Searches #12A & 12B

NUMBER OF ITEMS RETRIEVED: 122

SEARCH #12D(Estrogen & Osteosarcoma)
estrogen* OR estrogens[mh] OR oestrogen* OR estradiol
AND
osteosarcoma*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 4

SEARCH #12E(Estrogen & Esophageal Ulcers)
estrogen* OR estrogens[mh] OR oestrogen* OR estradiol
AND
(esophagus OR esophageal) AND ulcer*
AND
observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 3

SEARCH #12F(Estrogen & PUBS)
estrogen* OR estrogens[mh] OR oestrogen* OR estradiol
AND
perforation* OR ulcer* OR bleed*
AND
observational OR cohort* OR case control* OR case report*
NOT
Results of Searches #12A-12E

NUMBER OF ITEMS RETRIEVED: 65

SEARCH #12G(Estrogen & Osteonecrosis)
estrogen* OR estrogens[mh] OR oestrogen* OR estradiol
AND
osteonecrosis
AND

observational OR cohort* OR case control* OR case report*

NUMBER OF ITEMS RETRIEVED: 3

SEARCH #13(Calcium & All Diseases)
calcium
AND
breast neoplasms OR breast cancer[tiab] OR colonic neoplasms OR colon cancer[tiab] OR lung neoplasms OR lung cancer[tiab] OR osteosarcoma* OR ((esophagus OR esophageal) AND ulcer*) OR perforation* OR ulcer* OR bleed* OR osteonecrosis
AND
cohort*

NUMBER OF ITEMS RETRIEVED :96

SEARCH #14(Vitamin D & All Diseases)
vitamin d
AND
breast neoplasms OR breast cancer[tiab] OR colonic neoplasms OR colon cancer[tiab] OR lung neoplasms OR lung cancer[tiab] OR osteosarcoma* OR ((esophagus OR esophageal) AND ulcer*) OR perforation* OR ulcer* OR bleed* OR osteonecrosis
AND
cohort*

NUMBER OF ITEMS RETRIEVED : 42

SEARCH #15A(PubMed Alert #1 – Run from Sept-Dec. 2006)
bisphosphonate* OR alendronate* OR etidronate* OR ibandronate* OR pamidronate* OR risedronate*
AND
randomized controlled trial* OR randomi*[tiab] OR randomized controlled trial[pt]

SEARCH #15B(PubMed Alert #2 – Run from Sept-Dec. 2006)
zolendronate* OR calcitonin* OR miacalcin OR calcimar OR cibacalcin OR calcium OR estrogen* OR estrogens[mh] OR oestrogen* OR estradiol* OR raloxifene* OR teriparatide*
AND
randomized controlled trial* OR randomi*[tiab] OR randomized controlled trial[pt]

SEARCH #15C(PubMed Alert #3 – Run from Sept-Dec. 2006)
testosterone* OR vitamin d* OR glucorticoid*
AND
randomized controlled trial* OR randomi*[tiab] OR randomized controlled trial[pt]

SEARCH #16(Compliance)
DATES SEARCHED: 1995-2006

bisphosphonate* OR alendronate* OR etidronate* OR ibandronate* OR pamidronate* OR risedronate* OR zolendronate* OR calcitonin* OR miacalcin OR calcimar OR cibacalcin OR calcium OR estrogen* OR estrogens[mh] OR oestrogen* OR estradiol* OR raloxifene* OR teriparatide* OR testosterone* OR vitamin d* OR glucorticoid*
AND
osteoporosis or osteopenia or osteopaenia or fracture* or bone mineral OR fractures[mh] OR bone density
AND
patient compliance OR patient adherence OR treatment refusal OR non complian* OR non-complian* OR noncomplian* OR non adher* OR non-adher* OR nonadher*

NUMBER OF ITEMS RETRIEVED : 254

Appendix B. Data Abstraction Forms

Evidence-based Practice Center
Bone Density Screening Form

FINAL 10-25-05

Article ID: _____

First Author: _____
(Last name of first author)

Reviewer: _____

1. Does this study include humans?
   - Yes 1
   - No ..... 2 **(STOP)**

2. Intervention(s) studied: **(Check all that apply)**
   - Alendronate (Fosamax) ..... ❒
   - AMG 162 ..... ❒
   - Calcitonin (Miacalcin) ..... ❒
   - Estrogen ..... ❒
   - Etidronate (Didronel) ..... ❒
   - Ibandronate (Boniva) ..... ❒
   - Pamidronate (Aredia) (APD) ..... ❒
   - PTH (Teriparatide) (Forteo) (Preos) ..... ❒
   - Raloxifine (Evista) ..... ❒
   - Risedronate (Actonel) ..... ❒
   - Tamoxifen ..... ❒
   - Testosterone ..... ❒
   - Zoledronic acid (Zometa) ..... ❒
   - None of the above ..... ❒ **(STOP)**

3. What is the focus of the article: **(Circle one)**
   - Efficacy 1
   - Safety/adverse events 2
   - Both 3
   - Neither 4

4. Condition(s) studied: **(Check all that apply)**
   - Fracture prevention ..... ❒
   - Osteopenia ..... ❒
   - Osteoporosis ..... ❒
   - Osteoporosis prevention ..... ❒
   - None of the above ..... ❒ **(STOP)**

5. Is the study part of a named trial?
   - No 1
   - Yes 2

   If yes, specify trial name:

   _____

6. Study design: **(Circle one)**
   - Descriptive (historical, editorial, etc.) ..... 1 **(STOP)**
   - Review/meta-analysis ..... 2 **(STOP)**
   - Randomized clinical trial 3
   - Trial with open-label extension 4
   - Controlled clinical trial 5
   - Cohort/case control - 1000+ subjects 6
   - Cohort/case control - under 1000 subjects ..... 7 **(STOP)**
   - Case Report ..... 8 **(STOP)**
   - Other design ..... 9 **(STOP)**

7. Study population: **(Check all that apply)**

   Gender
   - Men ..... ❒
   - Pre-menopausal women ..... ❒
   - Post-menopausal women ..... ❒
   - Women otherwise undefined ..... ❒

   Age
   - Adults (18 and over) ..... ❒
   - Children (under 18) ..... ❒

   Race
   - Non-caucasian ..... ❒

   Other
   - Steroid-induced osteoporosis ..... ❒

8. Which clinical markers are used? **(Check all that apply)**
   - Bone density ..... ❒
   - Bone formation or bone turnover ..... ❒
   - Fractures ..... ❒
   - Stature/height ..... ❒
   - None of the above ..... ❒

9. Does the article need a translator? **(Circle one)**
   - No 1
   - Yes 2

   If YES specify language:

   _____

10. Do you think this article might be a duplicate or include the same data as another study?
    - No 1
    - Yes 2

    If yes, which one(s)?_____
    (Enter article ID, author, or 9999 for "don't know.")

11. Is there a reference that needs to be checked?
    - No 1
    - Yes 2

    If yes, which one(s)?

    _____
    (Enter reference # &/or author, or 9999 for "don't know.")

NOTE:

DE_DATE: ___ / ___ / ___]
[Month / Day / Year]

RAND Bone Density Project
Detailed Abstraction Form

Article ID:_____ Reviewer:_____

First Author: _____
(Last name only)

Study Number: ___of____Description:_____
(Enter '1of 1' if only one) (if more than one study)

Design: (CIRCLE ONE)
RCT 1
Non-RCT 2 (STOP)

Was method of randomization appropriate? (CIRCLE ONE)
Yes 1
No 2 (STOP)
Method not described 8

Are all arms the same intervention? (CIRCLE ONE)
Yes 1 (STOP)
No 2

Is the study design trial with crossover? (CIRCLE ONE)
Yes 1 (STOP)
No 2

Is bone mineral density the only outcome measured? (CIRCLE ONE)
Yes 1
No 2 (SKIP TO Q7)

If Yes on Q4, is BMD measured by DEXA at the hip or spine? (CIRCLE ONE)
Yes 1
No 2 (STOP)

What were the study's inclusion criteria? (CHECK ALL THAT APPLY)

Men ❑ (01)
Pre-menopausal women ❑ (02)
Post-menopausal women NOS ❑ (03)
>6 months ❑ (04)
>1 year ❑ (05)
>2 years ❑ (06)
>5 years ❑ (07)
Women otherwise undefined ❑ (08)

Osteopenia NOS ❑ (09)
T-score ≤ -1.0 hip ❑ (10)
T-score ≤ -1.0 spine ❑ (11)
T-score ≤ -1.0 NOS ❑ (12)
T-score ≤ -2.0 hip ❑ (13)
T-score ≤ -2.0 spine ❑ (14)
T-score ≤ -2.0 NOS ❑ (15)
Radiographic ❑ (16)

Osteoporosis NOS ❑ (17)
T-score ≤ -2 hip ❑ (18)
T-score ≤ -2 spine ❑ (19)
T-score ≤ -2 NOS ❑ (20)
T-score ≤ -2.5 hip ❑ (21)
T-score ≤ -2.5 spine ❑ (22)
T-score ≤ -2.5 NOS ❑ (23)
Fracture ❑ (24)
Non-traumatic fracture ❑ (25)

Osteoporosis score based on t-score and/or fractures and/or radiographic ❑ (26)
Primary hyperparathyroidism ❑ (27)
Organ transplant ❑ (28)
On dialysis ❑ (29)
Asthma or COPD ❑ (30)
Breast cancer ❑ (31)
Rheumatoid arthritis ❑ (32)
SLE ❑ (33)

Additional inclusion criteria. Enter code: _____ ,

_____ , _____ , _____ , _____ , _____ , _____ , _____

Not Reported ❑ (999)

What were the study's exclusion criteria?

(CHECK ALL THAT APPLY)

Age > 75 ❑ (01)
Age > 85 ❑ (02)

Pregnancy ❑ (03)

Carcinoma or suspected carcinoma ❑ (04)
Cardiovascular disease ❑ (05)

Endocrine disease ❑ (06)
Endocrine disease except diabetes ❑ (07)
- Hypothyroidism ❑ (08)
- Hyperthyroidism ❑ (09)
- Hyperparathyroidism ❑ (10)
- Hypoparathroidism ❑ (11)

Endocrine disease requiring therapy except diabetes ❑ (12)

Diabetes ❑ (13)
Hepatic insufficiency ❑ (14)

Metabolic bone disorder other than osteoporosis (e.g. Paget's, renal osteodystrophy, osteomalacia, rheumatoid arthritis, SLE) ❑ (15)

Organ transplantation ❑ (16)
Renal insufficiency ❑ (17)

Gastrointestinal disease ❑ (18)
- Sprue ❑ (19)
- Inflammatory bowel disease ❑ (20)
- Malabsorption syndrome ❑ (21)
- Upper GI ❑ (22)

Nephrolithiasis ❑ (23)
Urolithiasis ❑ (24)

Venous thromboembolic disease ❑ (25)
- Active ❑ (26)
- Ever ❑ (27)

Anticonvulsants ❑ (28)
Aluminum ❑ (29)
Bisphosphonates ❑ (30)

Calcitonin ❑ (31)
Calcium (includes antacids) ❑ (32)
Coumarins ❑ (33)

Fluoride ❑ (34)
H2-blockers ❑ (35)
Hormone use ❑ (36)
- Androgen ❑ (37)
- HRT ❑ (38)
- Estrogen agonists (including estrogen)
- Progestin ❑ (40)
- SERMS ❑ (41)
- Estrogen antagonists ❑ (42)
- Anabolic steroids ❑ (43)
- Testosterone ❑ (44)
- Contraceptive ❑ (45)

Lipid lowering agents ❑ (46)
Proton pump inhibitors ❑ (47)
Vitamin D ❑ (48)
Corticoids/Glucocorticoids ❑ (49)
Gallium nitrate ❑ (50)
Mithramycin ❑ (51)

Additional exclusion criteria

Enter code: _____ , _____ , _____ , _____ ,

_____ , _____ , _____ , _____

Not Reported ❑ (999)

Were patients class-naive?

(CIRCLE ONE)

Yes	1
No	2
Not reported	9

Did the method of randomization provide for concealment of allocation?

(CIRCLE ONE)

Yes	1
No	2
Concealment not described	8

Is the study described as: (CIRCLE ONE)

Double blind	1
Single blind, patient	2
Single blind, outcome assessment	3
Single blind, not described	4
Blind, NOS	5
Open	6
Blinding not described	8
Not applicable	9

If reported, was the method of double blinding appropriate? (CIRCLE ONE)

Yes	1
No	2
Double blinding method not described	8
Not applicable	9

Were outcome assessors masked to the treatment allocation?

(CIRCLE ONE)

Yes	1
Yes, but not described	2
No	3
Not reported	9

Was the care provider masked to the treatment allocation?

(CIRCLE ONE)

Yes	1
Yes, but not described	2
No	3
Not reported	9

Was the patient masked to the treatment allocation?

(CIRCLE ONE)

Yes	1
Yes, but not described	2
No	3
Not reported	9

Sample size: (Enter N or 999 for not reported)

Screened: _____ Eligible: _____

Enrolled: _____ Withdrawn: _____

Loss to follow-up: _____

Are withdrawals (W) and dropouts (D) described? (CIRCLE ONE)

Yes, reason described for **all** W and D	1
Yes, reason described for **some** W and D	2
Not described	8
Not applicable	9

Run-in period table: (Enter 999 in first column if no run-in.)

Length (#)	Units (code)	Placebo/Medication (code)	How used for randomization? (code)

Wash-out period table: (Enter 999 in first column if no wash-out.)

Length (#)	Units (code)	Placebo/Medication (code)	How used for randomization? (code)

B-5

Units for run-in & wash-out

1. Day	4. Year	997. Variable
2. Week	8. NA	
3. Month	9. NR	

What was the study's setting? (CHECK ALL THAT APPLY)

Multi-center ❑
Single setting ❑
Community practice ❑

VA Health Care System ❑
Long term care facility ❑

Other (enter code: _____, _____, _____, _____)❑
Setting not reported ❑

Where was the study conducted? (CHECK ALL THAT APPLY)

US ❑
Canada ❑
Latin America ❑

UK ❑
Western Europe ❑
Eastern Europe ❑

Australia/New Zealand ❑
Japan ❑
Asia (not Japan) ❑

Other (enter code _____ , _____ , _____) .....❑
Not reported.....❑

What was the study's funding source? (CHECK ALL THAT APPLY)

Government ❑
Hospital ❑
Industry ❑
Private (non-industry) ❑

Other (enter code: _____, _____, _____, _____)❑
Unclear ❑
Not reported ❑ (SKIP TO Q25)

Any authors from drug companies funding the study? (CIRCLE ONE)

Yes 1
No 2
Unclear 3
Not reported 9

Did the article include a statement on the role of the funder? (CIRCLE ONE)

Yes 1
No 2

What was the percent of male participants? (ENTER NUMBER OR 999)

___ ___ ___ %

What was the racial/ethnic population studied? (Check all that apply)

Caucasian ..... ❑
African Ancestry ..... ❑
Hispanic..... ❑

Asian ..... ❑
Native American ..... ❑
Eskimo/Inuit..... ❑

Other-Not otherwise specified ..... ❑
Other (enter code): ..... ❑

_____ , _____ , _____ , _____
Not reported ..... ❑

What was the method of adverse events assessment?

(CHECK ALL THAT APPLY)

Monitored ❑
Elicited by investigator ❑
Reported spontaneously by patient ❑
Other (enter code: _____, _____, _____, _____)❑
Not reported ❑

What was reported for the following questions regarding subjects ages? (Enter number 999 for not reported)

Mean Age ..... _____

Median Age ..... _____

Age Range ..... _____ to _____

What were the comorbidities reported in the study?

(CHECK ALL THAT APPLY)

Asthma ❑ (01)
Breast cancer ❑ (02)
COPD ❑ (03)
Rheumatoid arthritis ❑ (04)
SLE ❑ (05)
PUD ❑ (06)
Pancreatitis ❑ (07)
Bleeding ❑ (08)
Renal calculi ❑ (09)

Additional comorbidities

Enter code: _____ , _____ , _____ , _____ ,

_____ , _____ , _____ , _____ ,

Not reported ❑ (999)

What was the total study duration?

_____ Days/Weeks/Months/Years (CIRCLE ONE)

Were groups similar at baseline, in terms of prognostic indicators?

(CIRCLE ONE)

Yes 1
No 2
Not reported 9

Did the placebo/control group receive standard care?

(CIRCLE ONE)

Yes 1
No 2

Is there relevance to the target population?

(CIRCLE ONE)

Yes 1
No 2
Limited 3

B-7

INTERVENTIONS

Interventions given to EVERYONE in the study:

Interventions given to everyone	Dose	Units	Frequency	Duration of treatment	Units
Check all that apply: Calcium ❑ Estrogen ❑ Testosterone ❑ Vitamin D ❑ None ❑	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____
	Enter # or range 998. Not applicable 999. Not reported	Enter a number 1. g 2. mg 3. µg 4. I.U. 8. NA 9.NR	Enter a number 1. Daily 2. Weekly 3. Monthly 4. Yearly 8 NA 9. NR	Enter a number 997. Variable 998. NA 999. NR	Enter a number 1.Day 2.Week 3.Month 4.Year 8.NA 9. NR

B-8

Interventions (continued)

Enter sample size and intervention/exposure data for each arm beginning with placebo or control, then in order of first mention.
Enter total number of arms _____ .

Arm/ Group	Sample size	Interventions	Dose	Units	Frequency	Duration of treatment	Units	Concurrent Interventions
___	_____ N ENTERING _____ N COMPLETING _____ N ANALYZED _____ # OF EXCLUSIONS	Check all that apply: Placebo ❑(01) Control ❑(02) Alendronate (Fosamax) ❑(03) AMG 162 ❑(04) Calcitonin (Miacalcin) ❑(05) Estrogen ❑(06) Etidronate (Didronel) ❑(07) Ibandronate (Boniva) ❑(08) Pamidronate (Aredia) (APD) ❑(09) PTH (Teriparatide) (Forteo) (Preos) ❑(10) Raloxifine (Evista) ❑(11) Risedronate (Actonel) ❑(12) Tamoxifen ❑(13) Testosterone ❑(14) Zoledronic acid (Zometa) ❑(15) Calcium ❑(16) Vitamin D ❑(17) Exercise ❑(18) _____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	Calcium ❑(01) Vitamin D ❑(02) Estrogen ❑(03) Steroids ❑(04) Testosterone ❑(05) Exercise ❑(06) _____ _____ _____ _____ _____ _____
Enter arm number.	Enter a number for N entering and N completing or enter 9999 if not reported.	Check all that apply. Enter additional codes.	Enter # or range 998. Not applicable 999. Not reported	Enter a number 1. g 2. mg 3. µg 4. I.U. 8. NA 9.NR	Enter a number 1. Daily 2. Weekly 3. Monthly 4. Yearly 8 NA 9. NR	Enter a number 997. Variable 998. NA 999. NR	Enter a number 1.Day 2.Week 3.Month 4.Year 8.NA 9. NR	Check all that apply. Enter additional codes. 998. Not applicable 999. Not reported

B-9

Interventions (continued)

Enter sample size and intervention/exposure data for each arm beginning with placebo or control, then in order of first mention.

Arm/ Group	Sample size	Interventions	Dose	Units	Frequency	Duration of treatment	Units	Concurrent Interventions
___	_____ N ENTERING _____ N COMPLETING _____ N ANALYZED _____ # OF EXCLUSIONS	Check all that apply: Placebo ❑(01) Control ❑(02) Alendronate (Fosamax) ❑(03) AMG 162 ❑(04) Calcitonin (Miacalcin) ❑(05) Estrogen ❑(06) Etidronate (Didronel) ❑(07) Ibandronate (Boniva) ❑(08) Pamidronate (Aredia) (APD) ❑(09) PTH (Teriparatide) (Forteo) (Preos) ❑(10) Raloxifine (Evista) ❑(11) Risedronate (Actonel) ❑(12) Tamoxifen ❑(13) Testosterone ❑(14) Zoledronic acid (Zometa) ❑(15) Calcium ❑(16) Vitamin D ❑(17) Exercise ❑(18) _____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	Calcium ❑(01) Vitamin D ❑(02) Estrogen ❑(03) Steroids ❑(04) Testosterone ❑(05) Exercise ❑(06) _____ _____ _____ _____ _____ _____
Enter arm number.	Enter a number for N entering and N completing or enter 9999 if not reported.	Check all that apply. Enter additional codes.	Enter # or range 998. Not applicable 999. Not reported	Enter a number 1. g 2. mg 3. µg 4. I.U. 8. NA 9.NR	Enter a number 1. Daily 2. Weekly 3. Monthly 4. Yearly 8 NA 9. NR	Enter a number 997. Variable 998. NA 999. NR	Enter a number 1.Day 2.Week 3.Month 4.Year 8.NA 9. NR	Check all that apply. Enter additional codes. 998. Not applicable 999. Not reported

B-10

Interventions (continued)

Enter sample size and intervention/exposure data for each arm beginning with placebo or control, then in order of first mention.

Arm/ Group	Sample size	Interventions	Dose	Units	Frequency	Duration of treatment	Units	Concurrent Interventions
___	_____ N ENTERING _____ N COMPLETING _____ N ANALYZED _____ # OF EXCLUSIONS	Check all that apply: Placebo ❑(01) Control ❑(02) Alendronate (Fosamax) ❑(03) AMG 162 ❑(04) Calcitonin (Miacalcin) ❑(05) Estrogen ❑(06) Etidronate (Didronel) ❑(07) Ibandronate (Boniva) ❑(08) Pamidronate (Aredia) (APD) ❑(09) PTH (Teriparatide) (Forteo) (Preos) ❑(10) Raloxifine (Evista) ❑(11) Risedronate (Actonel) ❑(12) Tamoxifen ❑(13) Testosterone ❑(14) Zoledronic acid (Zometa) ❑(15) Calcium ❑(16) Vitamin D ❑(17) Exercise ❑(18) _____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	Calcium ❑(01) Vitamin D ❑(02) Estrogen ❑(03) Steroids ❑(04) Testosterone ❑(05) Exercise ❑(06) _____ _____ _____ _____ _____ _____
Enter arm number.	Enter a number for N entering and N completing or enter 9999 if not reported.	Check all that apply. Enter additional codes.	Enter # or range 998. Not applicable 999. Not reported	Enter a number 1. g 2. mg 3. µg 4. I.U. 8. NA 9.NR	Enter a number 1. Daily 2. Weekly 3. Monthly 4. Yearly 8 NA 9. NR	Enter a number 997. Variable 998. NA 999. NR	Enter a number 1.Day 2.Week 3.Month 4.Year 8.NA 9. NR	Check all that apply. Enter additional codes. 998. Not applicable 999. Not reported

B-11

Interventions (continued)

Enter sample size and intervention/exposure data for each arm beginning with placebo or control, then in order of first mention.

Arm/ Group	Sample size	Interventions	Dose	Units	Frequency	Duration of treatment	Units	Concurrent Interventions
___	_____ N ENTERING _____ N COMPLETING _____ N ANALYZED _____ # OF EXCLUSIONS	Check all that apply: Placebo ❑(01) Control ❑(02) Alendronate (Fosamax) ❑(03) AMG 162 ❑(04) Calcitonin (Miacalcin) ❑(05) Estrogen ❑(06) Etidronate (Didronel) ❑(07) Ibandronate (Boniva) ❑(08) Pamidronate (Aredia) (APD) ❑(09) PTH (Teriparatide) (Forteo) (Preos) ❑(10) Raloxifine (Evista) ❑(11) Risedronate (Actonel) ❑(12) Tamoxifen ❑(13) Testosterone ❑(14) Zoledronic acid (Zometa) ❑(15) Calcium ❑(16) Vitamin D ❑(17) Exercise ❑(18) _____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	_____ _____ _____ _____	Calcium ❑(01) Vitamin D ❑(02) Estrogen ❑(03) Steroids ❑(04) Testosterone ❑(05) Exercise ❑(06) _____ _____ _____ _____ _____ _____
Enter arm number.	Enter a number for N entering and N completing or enter 9999 if not reported.	Check all that apply. Enter additional codes.	Enter # or range 998. Not applicable 999. Not reported	Enter a number 1. g 2. mg 3. µg 4. I.U. 8. NA 9.NR	Enter a number 1. Daily 2. Weekly 3. Monthly 4. Yearly 8 NA 9. NR	Enter a number 997. Variable 998. NA 999. NR	Enter a number 1.Day 2.Week 3.Month 4.Year 8.NA 9. NR	Check all that apply. Enter additional codes. 998. Not applicable 999. Not reported

B-12

Did the article report the following? (CHECK ALL THAT APPLY)

	Yes (1)	No (2)
Adherence	❑	❑
Contamination	❑	❑

Did the study include an intention-to-treat analysis, or provide the data needed to calculate it? (CIRCLE ONE)

Yes	1
No	2

B-13

OUTCOMES: (CHECK ALL THAT APPLY)

Bone mineral density by DEXA - Hip ❑ (01)
Bone mineral density by DEXA - Spine ❑ (02)
Hip fracture ❑ (03)

Proximal humerus fracture ❑ (04)
Radial fracture ❑ (05)
Vertebral fracture ❑ (06)

Total fractures ❑ (07)

Markers of bone turnover

Alkaline phosphatase ❑ (08)
Alkaline phosphatase, bone specific (BSAP) ❑ (09)
Amino-terminal propeptide of type 1 collagen (P1NP) ❑ (10)

Carboxy-terminal propeptide of type 1 collagen ❑ (11)
Cross-linked C-telopeptide cross-links of type 1 collagen (1CTP) ❑ (12)

C-telopeptide cross-links of type 1 collagen urine (uCTx) ❑ (13)
serum (sCTx) ❑ (14)

Deoxypyridinolines (Dpd) free ❑ (15)
total ❑ (16)
NOS ❑ (17)

N-telopeptide cross-links of type 1 collagen urine (uNTx) ❑ (18)
serum (sNTx) ❑ (19)

Osteocalcin ❑ (20)

Pyridinolines (Pyr) free ❑ (21)
total ❑ (22)
NOS ❑ (23)

Tartarate-resistant acid phosphatase (TRAP) ❑ (24)

None of the above ❑ (999)

B-14

Time of assessment: When were outcomes measured? **(CIRCLE ONE)**

(Enter the number/code in the appropriate box, or circle YES/NO.)

Baseline?	YES / NO	
Follow-up	Number	Unit
1st		
2nd		
3rd		
4th		
5th		
6th		
7th		
8th		
9th		
10th		
11th		
12th		
13th		
14th		
15th		
Additional		

Units for time of assessment

1. Day	4. Year	997. Variable
2. Week	8. NA	
3. Month	9. NR	

Appendix C. Evidence Tables

Author, Year, Drug, Country, Trial name	Adverse events reported
Abellan Perez M, 1995[1]	Calcitonin+Calcium vs. Calcium: Arterial hypertension: 2.3%(1/43) vs. 0.0%(0/45) Flushing skin: 2.3%(1/43) vs. 0.0%(0/45) Gastrointestinal problems: 7.0%(3/43) vs. 0.0%(0/45)
Adachi JD et al., 1997[2]	Etidronate vs. Placebo: Death: 1.5%(1/67) vs. 0.0%(0/74) Elevated serum creatinine level: 1.5%(1/67) vs. 0.0%(0/74) Gastrointestinal adverse effects: 19.4%(13/67) vs. 16.2%(12/74)
Adachi JD et al., 1997[3]	Calcitonin vs. Placebo: Death: 6.3%(1/16) vs. 0.0%(0/15) Dizziness: 6.3%(1/16) vs. 0.0%(0/15) Rash: 6.3%(1/16) vs. 0.0%(0/15)
Adachi JD et al., 2001[4]	Risedronate vs. Placebo: Any clinical adverse event: 42.9%(15/35) vs. 41.9%(13/31) Accidental injury: 0.0%(0/35) vs. 3.2%(1/31) Any upper GI tract AE: 20.0%(7/35) vs. 19.4%(6/31) Atrial fibrillation: 2.9%(1/35) vs. 0.0%(0/31) Cystitis: 2.9%(1/35) vs. 0.0%(0/31) Diarrhea: 0.0%(0/35) vs. 6.5%(2/31) Dry mouth: 0.0%(0/35) vs. 3.2%(1/31) Duodenitis: 2.9%(1/35) vs. 0.0%(0/31) Esophagitis: 2.9%(1/35) vs. 0.0%(0/31) Flatulence: 0.0%(0/35) vs. 3.2%(1/31) Gastrointestinal carcinoma: 0.0%(0/35) vs. 3.2%(1/31) Glossitis: 0.0%(0/35) vs. 3.2%(1/31) Headache: 0.0%(0/35) vs. 3.2%(1/31) Moderate to severe upper gastrointestinal adverse events: 11.4%(4/35) vs. 16.1%(5/31) Nausea: 0.0%(0/35) vs. 9.7%(3/31)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Adachi JD et al., 2001[5]	Alendronate 10mg vs. Alendronate 5mg vs. Alendronate 2.5/10mg vs. Placebo: AE -all: 92.7%(51/55) vs. 93.7%(59/63) vs. 89.7%(26/29) vs. 90.2%(55/61) Abdominal pain: 7.3%(4/55) vs. 9.5%(6/63) vs. 10.3%(3/29) vs. 14.8%(9/61) Acid regurgitation: 9.1%(5/55) vs. 1.6%(1/63) vs. 0.0%(0/29) vs. 4.9%(3/61) Gastritis: 5.5%(3/55) vs. 1.6%(1/63) vs. 3.4%(1/29) vs. 3.3%(2/61) Nausea: 5.5%(3/55) vs. 4.8%(3/63) vs. 0.0%(0/29) vs. 4.9%(3/61) Reflux esophagitis: 7.3%(4/55) vs. 0.0%(0/63) vs. 0.0%(0/29) vs. 0.0%(0/61) Serious AE: 16.4%(9/55) vs. 22.2%(14/63) vs. 17.2%(5/29) vs. 31.1%(19/61) Serious upper GI AE: 1.8%(1/55) vs. 0.0%(0/63) vs. 0.0%(0/29) vs. 4.9%(3/61) Upper GI AE: 30.9%(17/55) vs. 20.6%(13/63) vs. 17.2%(5/29) vs. 31.1%(19/61)
Adami S et al., 1993[6]	Alendronate 10 mg vs. Alendronate 20 mg vs. Calcitonin vs. Placebo: Cholelithiasis: 0.0%(0/68) vs. 0.0%(0/72) vs. 0.0%(0/75) vs. 1.4%(1/71) Unstable angina: 0.0%(0/68) vs. 0.0%(0/72) vs. 1.3%(1/75) vs. 0.0%(0/71) Upper GI AE: 13.2%(9/68) vs. 6.9%(5/72) vs. 5.3%(4/75) vs. 12.7%(9/71)
Adami S et al., 1995[7]	Alendronate 10mg vs. Alendronate 20mg vs. Intranasal calcitonin 100iu vs. Placebo: increase in liver enzymes: 0.0%(0/68) vs. 1.4%(1/72) vs. 1.3%(1/75) vs. 0.0%(0/71) Drug related AE: 11.8%(8/68) vs. 8.3%(6/72) vs. 13.3%(10/75) vs. 5.6%(4/71) Eosinophilia: 1.5%(1/68) vs. 0.0%(0/72) vs. 0.0%(0/75) vs. 0.0%(0/71) Serious AE (non drug related): 1.5%(1/68) vs. 2.8%(2/72) vs. 4.0%(3/75) vs. 1.4%(1/71) Upper GI AE: 14.7%(10/68) vs. 11.1%(8/72) vs. 5.3%(4/75) vs. 14.1%(10/71)
Adami S et al., 2000[8]	Etidronate+Calcium vs. Placebo+Calcium: Abdominal pain: 15.1%(8/53) vs. 13.0%(7/54) Adverse event: 43.4%(23/53) vs. 37.0%(20/54) Back pain: 5.7%(3/53) vs. 1.9%(1/54) Gastritis: 1.9%(1/53) vs. 1.9%(1/54) Hospitalization: 3.8%(2/53) vs. 3.7%(2/54) Severe depression: 1.9%(1/53) vs. 0.0%(0/54)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Adami S et al., 2004[9]	Ibandronate 1mg vs. Ibandronate 2mg vs. Placebo: AE related to study medication: 20.0%(26/131) vs. 19.0%(50/261) vs. 14.0%(18/128) At least one AE: 75.0%(98/131) vs. 70.0%(183/261) vs. 71.0%(91/128) Cardiovascular system: 13.0%(17/131) vs. 10.0%(26/261) vs. 5.0%(6/128) Digestive system: 17.0%(22/131) vs. 17.0%(44/261) vs. 22.0%(28/128) Hemic and lymphatic system: 1.0%(1/131) vs. 5.0%(13/261) vs. 2.0%(3/128) Metabolic and nutritional disorders: 4.0%(5/131) vs. 2.0%(5/261) vs. 5.0%(6/128) Musculoskeletal system: 27.0%(35/131) vs. 24.0%(63/261) vs. 25.0%(32/128) Nervous system: 19.0%(25/131) vs. 13.0%(34/261) vs. 16.0%(20/128) Respiratory system: 32.0%(42/131) vs. 29.0%(76/261) vs. 30.0%(38/128) Skin and appendages: 10.0%(13/131) vs. 9.0%(23/261) vs. 7.0%(9/128) Special senses: 5.0%(7/131) vs. 2.0%(5/261) vs. 4.0%(5/128) Urogenital system: 12.0%(16/131) vs. 8.0%(21/261) vs. 9.0%(12/128)
Agrawal S et al., 2006[10]	Risedronate vs. Placebo: AE - any clinical: 87.1%(27/31) vs. 89.7%(26/29) Any upper gastrointestinal AEs: 74.2%(23/31) vs. 72.4%(21/29) Drug-related AE: 35.5%(11/31) vs. 24.1%(7/29) Myocardial infarction - death: 3.2%(1/31) vs. 0.0%(0/29) Serious AE: 9.7%(3/31) vs. 3.4%(1/29) Upper GI AE - abdominal pain: 29.0%(9/31) vs. 6.9%(2/29) Upper GI AE - moderate to severe: 51.6%(16/31) vs. 58.6%(17/29)
Alexandersen P et al., 1999[11]	Estrogen vs. Estrogen+Fluoride vs. Fluoride vs. Placebo: Breast tenderness, edema, headache, nausea, weight gain, mood change: 92.3%(24/26) vs. 96.0%(24/25) vs. 52.0%(13/25) vs. 12.5%(3/24) Endometrial bleeding: 23.1%(6/26) vs. 20.0%(5/25) vs. 8.0%(2/25) vs. 8.3%(2/24) Exanthema: 30.8%(8/26) vs. 8.0%(2/25) vs. 12.0%(3/25) vs. 33.3%(8/24) Joint pain, pain in extremities, heartburn: 19.2%(5/26) vs. 32.0%(8/25) vs. 28.0%(7/25) vs. 29.2%(7/24) Severe AEs: 0.0%(0/25) vs. 0.0%(0/24)
Amory JK et al., 2004[12]	Testosterone vs. Testosterone+Finasteride vs. Placebo: Cerebral hemorrhage: 4.2%(1/24) vs. 0.0%(0/22) vs. 0.0%(0/24) Prostate cancer: 8.3%(2/24) vs. 0.0%(0/22) vs. 4.2%(1/24) Sleep apnea: 4.2%(1/24) vs. 0.0%(0/22) vs. 0.0%(0/24)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

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Author, Year, Drug, Country, Trial name	Adverse events reported
Anderson GL et al., 2003[13]	Estrogen with progestin vs. Placebo: Borderline ovarian cancer: 0.0%(1/8506) vs. 0.0%(3/8102) Cervical cancer: 0.1%(8/8506) vs. 0.1%(5/8102) Endometrial cancer: 0.3%(27/8506) vs. 0.4%(31/8102) Invasive ovarian cancer: 0.2%(20/8506) vs. 0.1%(12/8102) Non-endometrial uterine cancer: 0.0%(1/8506) vs. 0.0%(0/8102) Other gynecologic cancer: 0.1%(6/8506) vs. 0.0%(1/8102)
Anderson GL et al., 2004[14]	Estrogen vs. Placebo: Adjudicated deaths: 5.2%(278/5310) vs. 5.0%(272/5429) Breast cancer - death: 0.1%(4/5310) vs. 0.1%(8/5429) Cardiovascular - death: 1.8%(93/5310) vs. 1.7%(95/5429) Colorectal cancer: 1.1%(61/5310) vs. 1.1%(58/5429) Coronary Heart Disease: 3.3%(177/5310) vs. 3.7%(199/5429) Death: 5.5%(291/5310) vs. 5.3%(289/5429) Invasive breast cancer: 1.8%(94/5310) vs. 2.3%(124/5429) Other cancer - death: 2.1%(110/5310) vs. 2.2%(118/5429) Stroke: 3.0%(158/5310) vs. 2.2%(118/5429) Unknown cause - death: 0.4%(20/5310) vs. 0.2%(13/5429) Venous thromboembolic disease: 1.9%(101/5310) vs. 1.4%(78/5429)
Aris RM et al., 2000[15]	Pamidronate vs. Control: Bone pain: 0.0%(0/16) vs. 0.0%(0/18) Cellulitis: 0.0%(0/16) vs. 0.0%(0/18) Fever: 0.0%(0/16) vs. 0.0%(0/18) Hypocalcemia: 0.0%(0/16) vs. 0.0%(0/18) Mild hypervitaminosis D: 0.0%(0/16) vs. 0.0%(0/18) Thrombophlebitis: 0.0%(0/16) vs. 0.0%(0/18)
Aris RM et al., 2004[16]	Alendronate vs. Control: Death: 0.0%(0/24) vs. 4.2%(1/24) Diarrhea: 4.2%(1/24) vs. 8.3%(2/24) Dysphagia: 0.0%(0/24) vs. 0.0%(0/24) Nephrolithiasis: 4.2%(1/24) vs. 0.0%(0/24)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Ascott-Evans BH et al., 2003[17]	Alendronate vs. Placebo: Clinical AE: 63.2%(60/95) vs. 61.2%(30/49) Hot flashes: 2.1%(2/95) vs. 10.2%(5/49) Serious AE: 0.0%(0/95) vs. 0.0%(0/49) Upper GI AE: 15.8%(15/95) vs. 12.2%(6/49)
Barrett-Connor E et al., 2002[18]	Placebo total vs. Raloxifene 120mg vs. Raloxifene 60mg: Any cardiovascular (CV) event: 3.7%(96/2576) vs. 3.7%(94/2572) vs. 3.2%(82/2557) Any cerebrovascular event: 1.6%(41/2576) vs. 1.5%(39/2572) vs. 1.4%(37/2557) Any coronary event: 2.1%(55/2576) vs. 2.2%(56/2572) vs. 1.8%(45/2557) Coronary death, myocardial infarction, unstable angina: 1.7%(45/2576) vs. 1.7%(44/2572) vs. 1.5%(39/2557) Fatal CV event: 0.6%(15/2576) vs. 0.7%(19/2572) vs. 0.5%(12/2557) Fatal cerebrovascular event: 0.2%(6/2576) vs. 0.2%(6/2572) vs. 0.1%(3/2557) Fatal coronary event: 0.3%(9/2576) vs. 0.5%(13/2572) vs. 0.4%(9/2557) Incident MI by serial ECGs: 0.3%(9/2576) vs. 0.2%(5/2572) vs. 0.3%(8/2557) Incident MI or myocardial ischemia identified by serial ECGs: 4.3%(110/2576) vs. 3.5%(89/2572) vs. 3.5%(89/2557) Nonfatal CV event: 3.2%(82/2576) vs. 2.9%(75/2572) vs. 2.7%(70/2557) Nonfatal cerebrovascular event: 1.4%(36/2576) vs. 1.3%(33/2572) vs. 1.3%(34/2557) Nonfatal coronary event: 1.8%(46/2576) vs. 1.7%(43/2572) vs. 1.4%(36/2557)
Bartram SA et al., 2003[19]	Calcium vs. Pamidronate+Calcium+Vitamin D: Flu-like symptoms 24hrs after infusion: 0.0%(0/37) vs. 8.1%(3/37) Nausea: 8.1%(3/37) vs. 0.0%(0/37)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Bauer DC et al., 2000[20]	Alendronate vs. Placebo: Abdominal pain: 13.7%(443/3236) vs. 13.1%(422/3223) Acid regurgitation: 6.6%(214/3236) vs. 6.1%(197/3223) Anorexia: 0.7%(24/3236) vs. 0.9%(30/3223) Any UGI tract AE: 47.5%(1536/3236) vs. 46.2%(1490/3223) Any esophageal AE: 10.0%(322/3236) vs. 9.4%(303/3223) Any gastric or duodenal AE: 4.0%(130/3236) vs. 4.0%(129/3223) Any gastric or duodenal perforations, ulcers, bleeding: 1.6%(53/3236) vs. 1.9%(61/3223) Barrett's esophagus: 0.0%(1/3236) vs. 0.0%(0/3223) Duodenitis: 0.2%(7/3236) vs. 0.1%(4/3223) Dyspepsia: 18.2%(588/3236) vs. 19.1%(617/3223) Dysphagia: 0.7%(23/3236) vs. 0.7%(24/3223) Erosive esophagitis: 0.1%(2/3236) vs. 0.0%(0/3223) Esophagalgia: 0.2%(6/3236) vs. 0.1%(2/3223) Esophageal stricture: 0.3%(10/3236) vs. 0.2%(7/3223) Esophageal ulcer: 0.2%(7/3236) vs. 0.2%(6/3223) Esophagitis: 0.7%(24/3236) vs. 0.4%(14/3223) Gastritis: 2.5%(82/3236) vs. 2.3%(75/3223) Hemorrhage, GI: 0.1%(4/3236) vs. 0.2%(7/3223) Nausea: 10.9%(354/3236) vs. 11.8%(379/3223) Odynophagia: 0.1%(2/3236) vs. 0.0%(0/3223) Reflux esophagitis: 2.0%(65/3236) vs. 2.2%(72/3223) Serious UGI AE requiring hospitalization: 2.0%(65/3236) vs. 1.8%(59/3223) Serious esophageal AEs: 0.3%(11/3236) vs. 0.2%(5/3223) Ulcer gastric: 0.8%(26/3236) vs. 0.8%(27/3223) Ulcer, duodenal: 0.1%(4/3236) vs. 0.3%(11/3223) Ulcer, duodenal with hemorrhage: 0.1%(3/3236) vs. 0.0%(1/3223) Ulcer, gastric with hemorrhage: 0.3%(9/3236) vs. 0.2%(6/3223) Ulcer, gastrojejunal: 0.0%(1/3236) vs. 0.0%(0/3223) Ulcer, peptic: 0.3%(10/3236) vs. 0.4%(13/3223) Ulcer, peptic with hemorrhage: 0.0%(0/3236) vs. 0.0%(1/3223) Vomiting: 3.4%(110/3236) vs. 3.1%(99/3223)

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AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Baum M et al., 2002[21]	Anastrozole vs. Tamoxifen vs. Tamoxifen+Anastrozole: All deaths: 6.4%(200/3125) vs. 6.5%(203/3116) vs. 6.9%(215/3125) Any venous thrombembolic event: 2.0%(64/3125) vs. 3.5%(109/3116) vs. 4.0%(124/3125) Cataracts: 3.4%(107/3125) vs. 3.7%(116/3116) vs. 3.4%(105/3125) Colorectal cancer: 0.8%(24/3125) vs. 0.6%(19/3116) vs. 0.3%(9/3125) Contralateral breast cancer: 0.4%(14/3125) vs. 1.1%(33/3116) vs. 0.9%(28/3125) Deaths after recurrence: 3.9%(122/3125) vs. 3.9%(122/3116) vs. 4.6%(145/3125) Deaths before recurrence: 2.5%(78/3125) vs. 2.6%(81/3116) vs. 2.2%(70/3125) Deep venous thromboembolic events including PE: 1.0%(32/3125) vs. 1.7%(54/3116) vs. 2.0%(63/3125) Distant recurrence of breast cancer as a first event: 5.1%(158/3125) vs. 5.8%(182/3116) vs. 6.5%(204/3125) Ductal carcinoma in situ: 0.2%(5/3125) vs. 0.1%(3/3116) vs. 0.2%(5/3125) Endometrial cancer: 0.1%(3/3125) vs. 0.4%(13/3116) vs. 0.2%(6/3125) Fatigue/tiredness: 15.5%(483/3125) vs. 15.0%(466/3116) vs. 13.9%(435/3125) Head and neck cancer: 0.2%(5/3125) vs. 0.2%(5/3116) vs. 0.2%(5/3125) Hot flushes: 33.9%(1060/3125) vs. 39.4%(1229/3116) vs. 39.8%(1243/3125) Invasive breast cancer: 0.3%(9/3125) vs. 1.0%(30/3116) vs. 0.7%(23/3125) Ischemic cardiovascular disease: 2.4%(76/3125) vs. 1.9%(59/3116) vs. 2.2%(68/3125) Ischemic cerebrovascular event: 1.0%(31/3125) vs. 2.1%(65/3116) vs. 1.6%(51/3125) Local recurrence of breast cancer: 2.1%(67/3125) vs. 2.7%(83/3116) vs. 2.6%(81/3125) Lung cancer: 0.3%(8/3125) vs. 0.2%(7/3116) vs. 0.1%(4/3125) Melanoma: 0.0%(0/3125) vs. 0.2%(6/3116) vs. 0.0%(1/3125) Mood disturbances: 15.4%(480/3125) vs. 15.1%(469/3116) vs. 15.4%(482/3125) Musculoskeletal disorders: 27.5%(860/3125) vs. 21.2%(660/3116) vs. 21.9%(685/3125) Nausea and vomiting: 10.4%(324/3125) vs. 10.1%(315/3116) vs. 11.6%(363/3125) Other cancers: 0.7%(22/3125) vs. 0.9%(28/3116) vs. 0.9%(29/3125) Ovarian cancer: 0.2%(6/3125) vs. 0.3%(9/3116) vs. 0.2%(6/3125) Recurrence of breast cancer year 1: 2.5%(77/3125) vs. 2.3%(71/3116) vs. 2.8%(87/3125) Recurrence of breast cancer year 2: 2.5%(78/3125) vs. 4.1%(127/3116) vs. 3.9%(123/3125) Recurrence of breast cancer year 3: 2.0%(64/3125) vs. 2.5%(77/3116) vs. 2.6%(80/3125) Skin cancer: 1.2%(39/3125) vs. 1.0%(32/3116) vs. 0.9%(27/3125) Vaginal bleeding: 4.4%(138/3125) vs. 8.1%(253/3116) vs. 7.6%(238/3125) Vaginal discharge: 2.8%(86/3125) vs. 11.4%(354/3116) vs. 11.4%(357/3125)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Bekker PJ et al., 2004[22]	AMG 162 0.01mg/kg vs. AMG 162 0.03mg/kg vs. AMG 162 0.1mg/kg vs. AMG 162 0.3mg/kg vs. AMG 162 1mg/kg vs. AMG 162 3mg/kg vs. Placebo: Injection site pain: 0.0%(0/6) vs. 0.0%(0/6) vs. 0.0%(0/6) vs. 0.0%(0/6) vs. 16.7%(1/6) vs. 0.0%(0/7) vs. 0.0%(0/12) Injection site rash and burning: 0.0%(0/6) vs. 0.0%(0/6) vs. 0.0%(0/6) vs. 0.0%(0/6) vs. 0.0%(0/6) vs. 14.3%(1/7) vs. 0.0%(0/12)
Bell NH et al., 2002[23]	Alendronate vs. Placebo: Any AE: 90.9%(30/33) vs. 93.8%(30/32) Abdominal distension: 0.0%(0/33) vs. 3.1%(1/32) Abdominal pain: 21.2%(7/33) vs. 9.4%(3/32) Acid regurgitation: 3.0%(1/33) vs. 0.0%(0/32) Anorexia: 3.0%(1/33) vs. 0.0%(0/32) Any UGI AE: 42.4%(14/33) vs. 34.4%(11/32) Any serious AE: 9.1%(3/33) vs. 15.6%(5/32) Diaphragmatic hernia: 0.0%(0/33) vs. 3.1%(1/32) Dyspepsia: 3.0%(1/33) vs. 9.4%(3/32) Gastritis: 3.0%(1/33) vs. 0.0%(0/32) Gastric atony: 0.0%(0/33) vs. 3.1%(1/32) Gastric reflux: 3.0%(1/33) vs. 0.0%(0/32) Nausea: 6.1%(2/33) vs. 6.3%(2/32)
Black DM et al., 1996[24]	Alendronate vs. Placebo: Abdominal pain: 11.8%(121/1022) vs. 9.8%(98/1005) Acid regurgitation/reflux: 6.9%(71/1022) vs. 7.1%(71/1005) Any upper-gastrointestinal event: 41.3%(422/1022) vs. 40.0%(402/1005) Death: 2.3%(24/1022) vs. 2.1%(21/1005) Duodenal ulcer: 0.2%(2/1022) vs. 0.6%(6/1005) Dyspepsia: 15.2%(155/1022) vs. 15.7%(158/1005) Gastric ulcer: 0.7%(7/1022) vs. 1.6%(16/1005) Gastritis: 2.3%(24/1022) vs. 2.0%(20/1005) Nausea: 9.4%(96/1022) vs. 9.7%(97/1005) Esophageal ulcer: 0.3%(3/1022) vs. 0.2%(2/1005) Esophagitis: 0.7%(7/1022) vs. 0.4%(4/1005) Other gastric: 0.4%(4/1022) vs. 0.2%(2/1005) Other esophageal: 1.6%(16/1022) vs. 1.1%(11/1005) Peptic ulcer: 0.3%(3/1022) vs. 0.7%(7/1005) Total AE resulting in hospital admission: 24.5%(250/1022) vs. 29.9%(300/1005)

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Black DM et al., 2007[25]	Zoledronic acid vs Placebo: Any adverse event: 94.8%(3688/3889) vs 93.3%(3616/3876) Any serious adverse event: 29.0%(1126/3889) vs 29.9%(1158/3876) Arthralgia: 6.3%(245/3889) vs 2.0%(76/3876) Atrial fibrillation: Any event: 2.4%(94/3889) vs 1.9%(73/3876) Atrial fibrillation: Serious adverse event: 1.3%(50/3889) vs 0.5%(20/3876) Death: 3.3%(130/3889) vs 2.9%(112/3876) Death from cardiovascular causes: 1.0%(39/3889) vs 0.9%(33/3876) Headache: 7.0%(273/3889) vs 2.3%(90/3876) Influenza-like symptoms: 7.7%(301/3889) vs 1.6%(61/3876) Myalgia: 9.4%(365/3889) vs 1.7%(66/3876) Myocardial infarction: 1.0%(38/3889) vs 1.2%(45/3876) Pyrexia: 16.0%(621/3889) vs 2.0%(79/3876) Renal: Calculated creatinine clearance <30 ml/min: 4.1%(160/3889) vs 3.9%(152/3876) Renal: Increase in serum creatinine >0.5 mg/dl: 0.8%(31/3889) vs 0.3%(10/3876) Renal: Urinary protein >2+: 0.3%(13/3889) vs 0.1%(5/3876) Stroke: Death from stroke: 0.5%(20/3889) vs 0.3%(11/3876) Stroke: Serious adverse event: 2.2%(87/3889) vs 2.3%(88/3876)
Blumel JE et al., 2003[26]	Alendronate 10 mg/day vs. Alendronate 70 mg once a wk vs. Enteric alendronate 70 mg per wk: Headache: 4.0%(1/25) vs. 4.0%(1/25) vs. 4.0%(1/25) Heartburn: 28.0%(7/25) vs. 12.0%(3/25) vs. 8.0%(2/25) Nausea: 0.0%(0/25) vs. 4.0%(1/25) vs. 0.0%(0/25)
Body JJ et al., 2002[27]	Alendronate vs. PTH: Death from cardiac arrest: 0.0%(0/73) vs. 1.0%(1/73) Leg cramps: 0.0%(0/73) vs. 8.2%(6/73) New or worsened back pain: 19.2%(14/73) vs. 5.5%(4/73) Positive test for antiteriparatide antibodies: 0.0%(0/73) vs. 4.1%(3/73)
Bone HG et al., 1997[28]	Alendronate 1mg vs. Alendronate 2.5mg vs. Alendronate 5mg vs. Placebo: Drug related AEs: 19.8%(17/86) vs. 25.8%(23/89) vs. 17.2%(16/93) vs. 23.1%(21/91)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Bone HG et al., 2000[29]	Alendronate vs. Alendronate+Estrogen vs. Estrogen vs. Placebo: Any adverse experience: 87.0%(80/92) vs. 92.9%(130/140) vs. 90.2%(129/143) vs. 90.0%(45/50) Abdominal pain: 7.6%(7/92) vs. 7.9%(11/140) vs. 6.3%(9/143) vs. 4.0%(2/50) Any serious adverse experience: 14.1%(13/92) vs. 13.6%(19/140) vs. 11.9%(17/143) vs. 10.0%(5/50) Any upper gastrointestinal adverse experiences: 27.2%(25/92) vs. 33.6%(47/140) vs. 30.1%(43/143) vs. 22.0%(11/50) Dyspepsia: 7.6%(7/92) vs. 5.7%(8/140) vs. 6.3%(9/143) vs. 6.0%(3/50) Esophageal irritation: 5.4%(5/92) vs. 3.6%(5/140) vs. 3.5%(5/143) vs. 4.0%(2/50) Peptic ulcer: 0.0%(0/92) vs. 1.4%(2/140) vs. 0.0%(0/143) vs. 0.0%(0/50)
Bone HG et al., 2004[30]	10 mg alendronate for 10 yrs vs. 20 mg alendronate for 2 yrs+5 mg alendronate for 3 yrs+placebo for 5 yrs vs. 5-mg_alendronate group for 10 yrs: Any clinical AE: 89.5%(77/86) vs. 92.8%(77/83) vs. 94.9%(74/78) At least one upper GI event: 27.9%(24/86) vs. 24.1%(20/83) vs. 14.1%(11/78) Death: 0.0%(0/86) vs. 0.0%(0/83) vs. 5.1%(4/78) Duodenal ulcer: 0.0%(0/86) vs. 0.0%(0/83) vs. 1.3%(1/78) Dysphagia: 0.0%(0/86) vs. 2.4%(2/83) vs. 0.0%(0/78) Erosive esophagitis: 0.0%(0/86) vs. 2.4%(2/83) vs. 1.3%(1/78) Esophagalgia: 1.2%(1/86) vs. 0.0%(0/83) vs. 0.0%(0/78) Esophageal AE: 2.3%(2/86) vs. 7.2%(6/83) vs. 1.3%(1/78) Esophagitis: 1.2%(1/86) vs. 1.2%(1/83) vs. 0.0%(0/78) Odynophagia: 0.0%(0/86) vs. 1.2%(1/83) vs. 0.0%(0/78) Serious any clinical event: 20.9%(18/86) vs. 21.7%(18/83) vs. 32.1%(25/78) Serious upper gastrointestinal even: 0.0%(0/86) vs. 1.2%(1/83) vs. 1.3%(1/78)
Bonnick S et al., 2006[31]	Alendronate vs. Risedronate: Death due to upper gastrointestinal AE - hemorrhagic duodenal ulcer: 0.0%(0/520) vs. 0.2%(1/533) Duodenal ulcer: 0.2%(1/520) vs. 0.0%(0/533) Gastroesophageal reflux disease: 0.0%(0/520) vs. 0.2%(1/533) One or more AEs: 87.1%(453/520) vs. 86.5%(461/533) One or more upper gastrointestinal AE: 19.6%(102/520) vs. 17.8%(95/533) Serious AE: 12.4%(64/520) vs. 13.5%(72/533)
Boutsen Y et al., 1997[32]	Calcium vs. Pamidronate: Death - Severe pulmonary infection: 7.7%(1/13) vs. 0.0%(0/14) Mild hypercalciuria: 7.7%(1/13) vs. 7.1%(1/14)
Brown JP et al., 2001[33]	Etidronate vs. Placebo: Moderate to severe upper gastrointestinal adverse effect: 7.5%(4/53) vs. 4.9%(3/61)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Brown JP et al., 2002[34]	Risedronate 35 mg vs. Risedronate 5 mg vs. Risedronate 50 mg: Any upper GI tract event: 18.4%(89/485) vs. 17.5%(84/480) vs. 18.7%(92/491) Arthralgia: 14.2%(69/485) vs. 11.5%(55/480) vs. 13.4%(66/491) Constipation: 12.2%(59/485) vs. 12.5%(60/480) vs. 12.2%(60/491) Infection: 20.6%(100/485) vs. 19.0%(91/480) vs. 20.2%(99/491) Moderate to severe upper GI tract event: 4.5%(22/485) vs. 4.8%(23/480) vs. 4.3%(21/491) Serious (fatal, life threatening, etc.) clinical event: 8.2%(40/485) vs. 7.1%(34/480) vs. 9.2%(45/491)
Brumsen C et al., 2002[35]	Pamidronate vs. Placebo: Colon cancer: 2.0%(1/51) vs. 0.0%(0/50) Duodenal ulcer: 2.0%(1/51) vs. 0.0%(0/50) Esophagitis: 2.0%(1/51) vs. 4.0%(2/50) Histomorphometric AEs: 0.0%(0/51) vs. 0.0%(0/50) Obstructive cholestatic disease: 0.0%(0/51) vs. 2.0%(1/50) Transient increase AST/ALT/GGT: 2.0%(1/51) vs. 4.0%(2/50)
Campbell IA et al., 2004[36]	Calcium vs. Etidronate vs. Etidronate+Calcium vs. Placebo: Death: 23.5%(20/85) vs. 9.9%(8/81) vs. 15.9%(14/88) vs. 15.8%(15/95) Headaches: 1.2%(1/85) vs. 2.5%(2/81) vs. 0.0%(0/95) Hypercalcemia: 1.2%(1/85) vs. 0.0%(0/81) vs. 0.0%(0/95) Nausea/vomiting/diarrhea/abdominal pain: 4.7%(4/85) vs. 12.3%(10/81) vs. 0.0%(0/95) Non-specifically unwell: 0.0%(0/85) vs. 2.5%(2/81) vs. 0.0%(0/95)
Chailurkit LO et al., 2003[37]	Alendronate vs. Placebo: Abdominal pain: 2.5%(1/40) vs. 0.0%(0/40) Asthma: 0.0%(0/40) vs. 2.5%(1/40) Musculoskeletal pain: 2.5%(1/40) vs. 0.0%(0/40) Myocardial infarction resulting in death: 2.5%(1/40) vs. 0.0%(0/40)
Chen M et al., 2001[38]	Estrogen+Calcium vs. Estrogen+Calcium+Vitamin D: Intolerable breast tenderness: 6.7%(8/120) vs. 2.5%(3/120) Irregular uterine bleeding: 15.8%(19/120) vs. 14.2%(17/120)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Cherry N et al., 2002[39]	Estrogen vs. Placebo: Breast cancer: 0.8%(4/513) vs. 0.8%(4/504) Cardiac death: 4.1%(21/513) vs. 6.0%(30/504) Death from any cause: 6.2%(32/513) vs. 7.7%(39/504) Deep vein thrombosis: 0.4%(2/513) vs. 0.2%(1/504) Endometrial cancer: 0.0%(0/513) vs. 0.0%(0/504) Pulmonary embolism: 0.6%(3/513) vs. 0.6%(3/504) Reinfarction or cardiac death: 12.1%(62/513) vs. 12.1%(61/504) Stroke: 1.9%(10/513) vs. 1.2%(6/504) Transient ischemic attack: 2.9%(15/513) vs. 2.6%(13/504) Vaginal bleeding: 40.5%(208/513) vs. 5.2%(26/504)
Chesnut CH et al., 1995[40]	Alendronate 10mg vs. Alendronate 20mg vs. Alendronate 40 mg vs. Alendronate 40mg/2.5mg vs. Alendronate 5mg vs. Placebo: Death - chronic obstructive pulmonary disease: 0.0%(0/30) vs. 0.0%(0/32) vs. 0.0%(0/32) vs. 0.0%(0/31) vs. 3.1%(1/32) vs. 0.0%(0/31) Rash: 0.0%(0/30) vs. 3.1%(1/32) vs. 0.0%(0/32) vs. 0.0%(0/31) vs. 0.0%(0/32) vs. 0.0%(0/31)
Chesnut CH et al., 2000[41]	Nasal spray salmon calcitonin (100 iu) vs. Nasal spray salmon calcitonin (200 iu) vs. Nasal spray salmon calcitonin (400 iu) vs. Placebo: AE or illness not related to drug: 15.8%(50/316) vs. 16.1%(51/316) vs. 18.3%(57/312) vs. 18.0%(56/311) Drug-related AE: 6.6%(21/316) vs. 6.0%(19/316) vs. 9.9%(31/312) vs. 6.8%(21/311) Headache: 4.0%(38/944) vs. 7.0%(22/311) Rhinitis (nasal congestion, nasal discharge, or sneezing): 22.0%(208/944) vs. 15.0%(47/311)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Chesnut CH et al., 2004[42]	Ibandronate 2.5mg vs. Ibandronate 20mg vs. Placebo: Any AE: 90.9%(888/977) vs. 91.9%(898/977) vs. 88.9%(867/975) Any AE leading to death: 1.1%(11/977) vs. 0.8%(8/977) vs. 1.0%(10/975) Any drug related AE: 19.8%(193/977) vs. 18.5%(181/977) vs. 17.9%(175/975) Any drug related serious AE: 0.3%(3/977) vs. 0.7%(7/977) vs. 0.3%(3/975) Any serious AE: 24.0%(234/977) vs. 25.3%(247/977) vs. 21.6%(211/975) Belching: 0.4%(4/977) vs. 0.5%(5/977) vs. 0.2%(2/975) Duodenal ulcer: 0.1%(1/977) vs. 0.1%(1/977) vs. 0.9%(9/975) Dyspepsia: 11.4%(111/977) vs. 9.0%(88/977) vs. 9.1%(89/975) Esophageal ulcer: 0.2%(2/977) vs. 0.1%(1/977) vs. 0.1%(1/975) Esophageal stenosis: 0.2%(2/977) vs. 0.0%(0/977) vs. 0.1%(1/975) Esophagitis: 1.5%(15/977) vs. 1.0%(10/977) vs. 1.0%(10/975) GI pain: 1.9%(19/977) vs. 2.5%(24/977) vs. 2.6%(25/975) Gastritis: 2.3%(22/977) vs. 1.2%(12/977) vs. 2.2%(21/975) Gastroenteritis: 5.5%(54/977) vs. 6.3%(62/977) vs. 5.5%(54/975) Nausea: 4.2%(41/977) vs. 6.4%(63/977) vs. 6.3%(61/975) Stomach ulcer: 0.3%(3/977) vs. 0.5%(5/977) vs. 0.6%(6/975) Vomiting: 3.0%(29/977) vs. 2.8%(27/977) vs. 2.5%(24/975)
Chlebowski RT et al., 2003[43]	Conjugated equine estrogens 0.625 mg/d & medroxyprogesterone acetate 2.5 mg/d vs. Placebo: Invasive breast cancer: 2.3%(199/8506) vs. 1.9%(150/8102)
Chlebowski RT et al., 2004[44]	Estrogen with progestin vs. Placebo: Death - colorectal cancer: 0.1%(9/8506) vs. 0.1%(8/8102) Invasive colon cancer: 0.4%(35/8506) vs. 0.8%(61/8102) Invasive rectal cancer: 0.1%(8/8506) vs. 0.1%(11/8102) Non-invasive colorectal cancer - carcinoids: 0.0%(2/8506) vs. 0.0%(0/8102) Non-invasive colorectal cancer - squamous cell: 0.0%(0/8506) vs. 0.0%(1/8102) Non-invasive colorectal cancer - stage 0 carcinoma in situ: 0.0%(3/8506) vs. 0.0%(1/8102) Other non-invasive colorectal cancer: 0.5%(43/8506) vs. 0.9%(72/8102) Vaginal bleeding in first year: 58.0%(4933/8506) vs. 7.0%(567/8102)
Chow CC et al., 2003[45]	Alendronate vs. Placebo: 1st degree heart block due to beta-blocker treatment: 0.0%(0/20) vs. 5.0%(1/20) Beta-blocker-induced heart block: 0.0%(0/20) vs. 5.0%(1/20) Dizziness & fall (hospitalized): 5.0%(1/20) vs. 0.0%(0/20) Ibuprofen-induced gastric ulcer: 0.0%(0/20) vs. 5.0%(1/20) Methyldopa-induced hemolytic anemia: 5.0%(1/20) vs. 0.0%(0/20)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Ciuffetti G et al., 1991[46]	Calcitonin vs. Placebo: Flushing skin: 10.0%(1/10) vs. 0.0%(0/10)
Clemmesen B et al., 1997[47]	Continuous Risedronate vs. Cyclical Risedronate vs. Placebo: Esophagus GI AE: 2.3%(1/44) vs. 6.8%(3/44) vs. 0.0%(0/44) UGI AE moderate to severe: 6.8%(3/44) vs. 6.8%(3/44) vs. 6.8%(3/44)
Cohen S et al., 1999[48]	Risedronate 2.5mg vs. Risedronate 5mg vs. Placebo: Abdominal pain: 8.0%(6/75) vs. 7.9%(6/76) vs. 5.2%(4/77) Death - pulmonary embolism: 1.0%(1/75) vs. 0.0%(0/76) vs. 0.0%(0/77) Diarrhea: 4.0%(3/75) vs. 10.5%(8/76) vs. 3.9%(3/77) Duodenitis: 0.0%(0/75) vs. 1.3%(1/76) vs. 0.0%(0/77) Dyspepsia: 6.7%(5/75) vs. 3.9%(3/76) vs. 9.1%(7/77) Esophageal erosion: 0.0%(0/75) vs. 0.0%(0/76) vs. 1.3%(1/77) Gastritis: 1.3%(1/75) vs. 1.3%(1/76) vs. 0.0%(0/77) Hiatal hernia: 0.0%(0/75) vs. 1.3%(1/76) vs. 1.3%(1/77) Moderate-to-severe upper GI AE: 6.8%(5/75) vs. 5.3%(4/76) vs. 5.3%(4/77) Musculoskeletal: 45.3%(34/75) vs. 48.7%(37/76) vs. 48.1%(37/77) Nausea: 2.7%(2/75) vs. 7.9%(6/76) vs. 6.5%(5/77) Serious adverse events: 20.0%(15/75) vs. 22.4%(17/76) vs. 26.0%(20/77) Upper gastrointestinal: 20.0%(15/75) vs. 14.5%(11/76) vs. 16.9%(13/77)
Combe B et al., 1997[49]	Intranasal calcitonin 200iu vs. Subcutaneous calcitonin 50iu: Atrophic mucosa w/ local irritation: 0.0%(0/102) vs. 1.0%(1/102) Ears, nose, throat: 2.0%(2/102) vs. 2.0%(2/102) GI disorders: 1.0%(1/102) vs. 2.9%(3/102) Inflammatory olfactory mucosa: 1.0%(1/102) vs. 0.0%(0/102) Nausea, vomiting: 10.8%(11/102) vs. 17.6%(18/102) Neutropenia: 0.0%(0/102) vs. 1.0%(1/102) Rhinitis, rhinorrhea, hydrorrhea: 8.8%(9/102) vs. 9.8%(10/102) Sneezing, tingling: 15.7%(16/102) vs. 10.8%(11/102) Vasomotor flushes: 13.7%(14/102) vs. 14.7%(15/102)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Cooper C et al., 2003[50]	Ibandronate (daily 2.5 mg) vs. Ibandronate (weekly 20 mg): Any AEs: 81.8%(99/121) vs. 78.1%(89/114) AE for Digestive System: 29.8%(36/121) vs. 23.7%(27/114) Constipation: 6.0%(7/121) vs. 4.0%(5/114) Death: 0.0%(0/121) vs. 0.0%(0/114) Drug-related AEs: 31.4%(38/121) vs. 34.2%(39/114) Drug-related serious AEs: 0.0%(0/121) vs. 0.0%(0/114) Dyspepsia: 9.0%(11/121) vs. 6.0%(7/114) GI AE: 33.0%(40/121) vs. 28.0%(32/114) General Body: 23.0%(28/121) vs. 29.0%(33/114) Incidence of digestive system AE possibly related to study medication: 22.0%(27/121) vs. 16.0%(18/114) Musculoskeletal: 26.0%(31/121) vs. 28.0%(32/114) Serious AEs: 9.9%(12/121) vs. 7.9%(9/114)
Cortet B et al., 1999[51]	Etidronate vs. Placebo: Abdominal pains: 14.0%(6/44) vs. 18.0%(7/39) At least one unwanted event: 84.0%(37/44) vs. 87.0%(34/39) Gastrointestinal: 32.0%(14/44) vs. 31.0%(12/39)
Cortet B et al., 2001[52]	Alendronate vs. Etidronate: Abdominal distension: 4.3%(2/46) vs. 0.0%(0/53) Diarrhea: 2.2%(1/46) vs. 0.0%(0/53) Epigastric pain: 8.7%(4/46) vs. 0.0%(0/53) Osteomalacia: 0.0%(0/46) vs. 1.9%(1/53)
Cosman F et al., 2001[53]	Estrogen vs. Estrogen+ PTH: Back pain: 0.0%(0/25) vs. 3.7%(1/27) Breast cancer: 0.0%(0/25) vs. 3.7%(1/27) Depression: 0.0%(0/25) vs. 3.7%(1/27) Increased back pain: 0.0%(0/25) vs. 3.7%(1/27) New diagnosis of breast cancer: 0.0%(0/25) vs. 3.7%(1/27) New diagnosis of otosclerosis: 0.0%(0/25) vs. 3.7%(1/27) Nodules at injection site: 0.0%(0/25) vs. 7.4%(2/27) Otosclerosis: 0.0%(0/25) vs. 3.7%(1/27) Skin modules: 0.0%(0/25) vs. 3.7%(1/27) UTI and possible undocumented kidney stone: 0.0%(0/25) vs. 3.7%(1/27)

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AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Cosman F et al., 2005[54]	Alendronate 70mg + cyclical PTH vs. Alendronate 70mg + daily PTH vs. Alendronate 70mg weekly: Abnormal CBD: 10.0%(4/40) vs. 11.6%(5/43) vs. 4.7%(2/43) Breast cancer: 0.0%(0/40) vs. 0.0%(0/43) vs. 2.3%(1/43) Cardiac symptoms: 7.5%(3/40) vs. 11.6%(5/43) vs. 7.0%(3/43) Death from complications of aortic-valve surgery: 0.0%(0/40) vs. 0.0%(0/43) vs. 2.3%(1/43) GI effects: 17.5%(7/40) vs. 20.9%(9/43) vs. 9.3%(4/43) Generalized fatigue: 7.5%(3/40) vs. 4.7%(2/43) vs. 0.0%(0/43) Increase liver function tests: 0.0%(0/40) vs. 2.3%(1/43) vs. 4.7%(2/43) Increase serum creatinine: 0.0%(0/40) vs. 0.0%(0/43) vs. 0.0%(0/43) Increase total serum calcium: 2.5%(1/40) vs. 2.3%(1/43) vs. 0.0%(0/43) Increase urinary calcium: creatinine ratio: 15.0%(6/40) vs. 34.9%(15/43) vs. 7.0%(3/43) Musculoskeletal symptoms: 10.0%(4/40) vs. 23.3%(10/43) vs. 4.7%(2/43) Redness at injection site: 15.0%(6/40) vs. 2.3%(1/43) vs. 0.0%(0/43) Rheumatoid arthritis: 2.5%(1/40) vs. 0.0%(0/43) vs. 0.0%(0/43) Vascular symptoms: 2.5%(1/40) vs. 4.7%(2/43) vs. 0.0%(0/43)
Crawford BA et al., 2006[55]	Placebo vs. Zoledronic acid: Graft failure - death: 6.7%(2/30) vs. 0.0%(0/32) Hypocalcemia: 10.0%(3/30) vs. 40.6%(13/32) Nephrotic syndrome: 0.0%(0/30) vs. 3.1%(1/32) Sepsis: 3.3%(1/30) vs. 3.1%(1/32) Sepsis - death: 0.0%(0/30) vs. 3.1%(1/32) Suicide: 3.3%(1/30) vs. 0.0%(0/32)
Cryer B et al., 2005[56]	Alendronate vs. Placebo: Abdominal pain: 4.5%(10/224) vs. 0.9%(2/226) Dyspepsia: 1.8%(4/224) vs. 2.7%(6/226) Heartburn: 0.9%(2/224) vs. 1.8%(4/226) Nausea: 2.7%(6/224) vs. 3.5%(8/226) Upper GI AE: 13.4%(30/224) vs. 11.1%(25/226) Vomiting: 1.8%(4/224) vs. 0.0%(0/226)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Cryer B et al., 2005[57]	Alendronate vs. Placebo: Any clinical AE: 63.5%(141/224) vs. 52.6%(120/230) Abdominal distention: 2.7%(6/224) vs. 0.4%(1/230) Abdominal pain: 2.7%(6/224) vs. 1.3%(3/230) Any upper gastrointestinal AE: 23.7%(64/224) vs. 13.9%(32/230) Dyspepsia: 4.9%(11/224) vs. 3.9%(9/230) Endoscopically documented esophagitis: 0.0%(0/224) vs. 0.4%(1/230) Eructation: 3.1%(7/224) vs. 0.0%(0/230) Esophageal AE: 4.0%(9/224) vs. 3.0%(7/230) Gastroesophageal reflux disease (GERD): 1.3%(3/224) vs. 1.3%(3/230) Mild nausea: 58.0%(130/224) vs. 80.0%(184/230) Moderate nausea: 33.0%(74/224) vs. 20.0%(46/230) Nausea: 7.6%(17/224) vs. 4.3%(10/230) Serious AE: 4.1%(9/224) vs. 3.5%(8/230) Serious upper gastrointestinal AE - abdominal pain and nausea: 0.0%(0/224) vs. 0.4%(1/230) Upper abdominal pain: 4.0%(9/224) vs. 1.3%(3/230) Vomiting: 2.2%(5/224) vs. 1.3%(3/230)
Cummings SR et al., 1998[58]	Alendronate vs. Placebo: Abdominal pain: 14.5%(322/2214) vs. 14.7%(325/2218) Acid regurgitation/reflux: 9.2%(204/2214) vs. 8.7%(194/2218) Any AE resulting in hospitalization: 29.1%(644/2214) vs. 26.9%(596/2218) Any UGI event: 47.5%(1052/2214) vs. 47.2%(1047/2218) Deaths: 1.7%(37/2214) vs. 1.8%(40/2218) Esophageal ulcer: 0.2%(4/2214) vs. 0.2%(4/2218) Esophagitis: 0.9%(19/2214) vs. 0.5%(10/2218) Other esophageal: 2.0%(44/2214) vs. 1.8%(41/2218)
Cummings SR et al., 2007[59]	Alendronate vs Placebo: Any atrial-fibrillation adverse event: 2.5%(81/3236) vs 2.2%(71/3223) Serious atrial-fibrillation adverse event: 1.5%(47/3236) vs 1.0%(31/3223)

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AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Curb JD et al., 2006[60]	CEE vs. Placebo: DVT: 1.6%(85/5310) vs. 1.1%(59/5429) DVT & pulmonary embolism: 0.5%(26/5310) vs. 0.2%(12/5429) Non-procedure related DVT: 1.2%(64/5310) vs. 0.7%(37/5429) Non-procedure related PE: 0.6%(32/5310) vs. 0.5%(28/5429) Non-procedure related VT: 1.5%(78/5310) vs. 1.0%(54/5429) Procedure-related DVT: 0.3%(18/5310) vs. 0.4%(20/5429) Procedure-related PE: 0.3%(16/5310) vs. 0.2%(9/5429) Procedure-related VT: 0.5%(27/5310) vs. 0.5%(28/5429) Pulmonary embolism: 1.0%(52/5310) vs. 0.7%(39/5429) Venous thrombosis: 2.1%(111/5310) vs. 1.6%(86/5429)
Curtis JR et al., 2006[61]	Alendronate vs. Risedronate: GI event: 23.3%(176/754) vs. 22.5%(91/404)
Cushman M et al., 2004[62]	Estrogen,+Progesterone vs. Placebo: Non-procedure-related: deep vein thrombosis: 1.0%(87/8506) vs. 0.5%(40/8102) Non-procedure-related: pulmonary embolus: 0.8%(65/8506) vs. 0.3%(23/8102) Procedure-related: deep vein thrombosis: 0.3%(25/8506) vs. 0.2%(14/8102) Procedure-related: pulmonary embolus: 0.2%(16/8506) vs. 0.1%(12/8102)
D'Amelio P et al., 2003[63]	Raloxifene vs. Raloxifene+Clodronate: Injection site pain: 0.0%(0/23) vs. 81.8%(18/22)
Deal C et al., 2005[64]	Teriparatide + placebo vs. Teriparatide + raloxifene: Hot flushes: 4.4%(3/68) vs. 17.4%(12/69) Serious AE: 5.9%(4/68) vs. 5.8%(4/69) Vomiting: 7.4%(5/68) vs. 0.0%(0/69)
Decensi A et al., 2003[65]	Control ER neg. vs. Control ER pos vs. Tamoxifen 1mg vs. Tamoxifen 20mg vs. Tamoxifen 5mg: Any AE: 0.0%(0/34) vs. 0.0%(0/29) vs. 22.5%(9/40) vs. 27.5%(11/40) vs. 30.0%(12/40) Death: 0.0%(0/34) vs. 0.0%(0/29) vs. 2.5%(1/40) vs. 0.0%(0/40) vs. 0.0%(0/40) Hot flashes: 0.0%(0/34) vs. 0.0%(0/29) vs. 32.0%(13/40) vs. 50.0%(20/40) vs. 36.0%(14/40) Metastasis at distant organ: 0.0%(0/34) vs. 0.0%(0/29) vs. 0.0%(0/40) vs. 2.5%(1/40) vs. 0.0%(0/40) Vaginal discharge: 0.0%(0/34) vs. 0.0%(0/29) vs. 26.0%(10/40) vs. 47.0%(19/40) vs. 22.0%(9/40)
Delmas PD et al., 1997[66]	Raloxifene 150 mg vs. Raloxifene 60 mg vs. Placebo: Breast pain: 0.0%(0/147) vs. 3.3%(5/152) vs. 2.0%(3/150) Hot flashes: 0.0%(0/147) vs. 26.3%(40/152) vs. 22.7%(34/150) Vaginal bleeding: 0.0%(0/147) vs. 3.0%(4/152) vs. 2.2%(3/150)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Delmas PD et al., 1997[67]	Risedronate+Tamoxifen vs. Tamoxifen+Placebo: Abdominal pain: 18.5%(5/27) vs. 7.7%(2/26) Bone pain & rash: 3.7%(1/27) vs. 0.0%(0/26) Deaths due to relapse of breast cancer: 3.7%(1/27) vs. 3.8%(1/26) Leukoneutropenia: 0.0%(0/27) vs. 3.8%(1/26) Liver function abnormality: 7.4%(2/27) vs. 0.0%(0/26) Relapse of breast cancer: 3.7%(1/27) vs. 11.5%(3/26) Serious adverse event: 37.0%(10/27) vs. 46.2%(12/26)
Devogelaer JP et al., 1996[68]	Alendronate 10mg vs. Alendronate 20/5mg vs. Alendronate 5mg vs. Placebo: Serious AE: 6.9%(7/102) vs. 17.1%(18/105) vs. 13.5%(14/104) vs. 16.6%(34/205) Upper GI AE: 14.7%(15/102) vs. 18.1%(19/105) vs. 17.3%(18/104) vs. 17.1%(35/205)
Doran PM et al., 2001[69]	Raloxifene vs. Placebo: Breast tenderness: 8.0%(2/25) vs. 12.0%(3/25) Decrease in erectile function: 8.0%(2/25) vs. 4.0%(1/25) Hot flushes: 16.0%(4/25) vs. 0.0%(0/25) Prostatic symptom: 8.0%(2/25) vs. 12.0%(3/25) Worsening libido: 12.0%(3/25) vs. 8.0%(2/25)
Downs RW et al., 1999[70]	Alendronate 1 mg - alendronate 10 mg vs. Alendronate 2.5 mg - alendronate 10 mg vs. Alendronate 5 mg - alendronate 10 mg vs. Placebo - alendronate 10 mg: Death: 1.8%(1/57) vs. 1.6%(1/63) vs. 0.0%(0/63) vs. 0.0%(0/63) Drug-related AE: 1.8%(1/57) vs. 7.9%(5/63) vs. 6.3%(4/63) vs. 3.2%(2/63) Patients with one or more AEs: 80.7%(46/57) vs. 82.5%(52/63) vs. 79.4%(50/63) vs. 81.0%(51/63) Serious AE: 8.8%(5/57) vs. 12.7%(8/63) vs. 11.1%(7/63) vs. 12.7%(8/63) Serious GI affects: 0.0%(0/57) vs. 0.0%(0/63) vs. 0.0%(0/63) vs. 1.6%(1/63) Serious drug-related AE: 0.0%(0/57) vs. 0.0%(0/63) vs. 0.0%(0/63) vs. 0.0%(0/63) Upper GI AEs - drug-related: 1.8%(1/57) vs. 7.9%(5/63) vs. 4.8%(3/63) vs. 1.6%(1/63) Upper GI AEs - one or more: 7.0%(4/57) vs. 19.0%(12/63) vs. 9.5%(6/63) vs. 14.3%(9/63) Upper GI AEs - serious: 0.0%(0/57) vs. 0.0%(0/63) vs. 0.0%(0/63) vs. 1.6%(1/63) Upper GI AEs- serious drug-related: 0.0%(0/57) vs. 0.0%(0/63) vs. 0.0%(0/63) vs. 0.0%(0/63)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Downs RW et al., 2000[71]	Alendronate vs. Calcitonin vs. Placebo: Abdominal distension: 1.7%(2/118) vs. 0.0%(0/123) vs. 3.4%(2/58) Abdominal pain: 4.2%(5/118) vs. 0.8%(1/123) vs. 1.7%(1/58) Acid regurgitation: 2.5%(3/118) vs. 0.0%(0/123) vs. 6.9%(4/58) Any serious AE: 5.9%(7/118) vs. 4.1%(5/123) vs. 3.4%(2/58) Chest pain: 2.5%(3/118) vs. 0.0%(0/123) vs. 3.4%(2/58) Constipation: 0.8%(1/118) vs. 1.6%(2/123) vs. 3.4%(2/58) Dyspepsia: 4.2%(5/118) vs. 0.0%(0/123) vs. 0.0%(0/58) Epistaxis: 0.0%(0/118) vs. 4.9%(6/123) vs. 0.0%(0/58) Flatulence: 0.8%(1/118) vs. 0.0%(0/123) vs. 3.4%(2/58) Nasal irritation: 0.0%(0/118) vs. 6.5%(8/123) vs. 0.0%(0/58) Nausea: 3.4%(4/118) vs. 0.8%(1/123) vs. 1.7%(1/58) Rhinitis: 0.0%(0/118) vs. 3.3%(4/123) vs. 0.0%(0/58)
Draper MW et al., 1996[72]	Estrogen vs. Raloxifene 200 mg vs. Raloxifene 600 mg vs. Placebo: Back pain: 0.0%(0/64) vs. 1.7%(1/60) vs. 3.2%(2/63) vs. 10.9%(7/64) Breast pain: 15.6%(10/64) vs. 0.0%(0/60) vs. 1.6%(1/63) vs. 7.8%(5/64) Vaginitis: 12.5%(8/64) vs. 1.7%(1/60) vs. 4.8%(3/63) vs. 3.1%(2/64) Vasodilation: 3.1%(2/64) vs. 11.7%(7/60) vs. 22.2%(14/63) vs. 10.9%(7/64)
Eastell R et al., 2000[73]	Risedronate 15 mg cyclical vs. Risedronate 2.5 mg/d vs. Placebo: AE: 22.5%(9/40) vs. 15.0%(6/40) vs. 15.0%(6/40) Abdominal pain: 20.0%(8/40) vs. 20.0%(8/40) vs. 2.5%(1/40) Duodenal ulcers: 5.0%(2/40) vs. 0.0%(0/40) vs. 0.0%(0/40) Dyspepsia: 30.0%(12/40) vs. 20.0%(8/40) vs. 42.5%(17/40) Esophagitis: 2.5%(1/40) vs. 5.0%(2/40) vs. 0.0%(0/40) Esophagitis with gastric and duodenal ulcers: 0.0%(0/40) vs. 2.5%(1/40) vs. 0.0%(0/40) Gastric erosion: 0.0%(0/40) vs. 0.0%(0/40) vs. 2.5%(1/40) Gastric ulcer and esophagitis: 0.0%(0/40) vs. 0.0%(0/40) vs. 2.5%(1/40) Gastric ulcers: 0.0%(0/40) vs. 0.0%(0/40) vs. 2.5%(1/40) Gastritis: 5.0%(2/40) vs. 0.0%(0/40) vs. 2.5%(1/40) Nausea: 12.5%(5/40) vs. 12.5%(5/40) vs. 7.5%(3/40) Serious AE: 47.5%(19/40) vs. 62.5%(25/40) vs. 52.5%(21/40) Upper GI AE: 52.5%(21/40) vs. 37.5%(15/40) vs. 55.0%(22/40)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Eisman JA et al., 2004[74]	Alendronate vs. Placebo: Any adverse event: 40.4%(91/225) vs. 38.4%(86/224) Abdominal colic: 0.4%(1/225) vs. 0.4%(1/224) Abdominal pain: 0.9%(2/225) vs. 0.9%(2/224) Any drug-related* upper gastrointestinal adverse event: 8.0%(18/225) vs. 6.7%(15/224) Any serious upper gastrointestinal adverse event: 0.4%(1/225) vs. 0.4%(1/224) Any upper gastrointestinal adverse event: 9.3%(21/225) vs. 9.8%(22/224) Bloated feeling: 0.0%(0/225) vs. 0.9%(2/224) Dyspepsia: 0.9%(2/225) vs. 0.4%(1/224) Dysphagia: 0.0%(0/225) vs. 0.4%(1/224) Epigastric discomfort: 0.4%(1/225) vs. 0.0%(0/224) Epigastric pain: 1.8%(4/225) vs. 1.3%(3/224) Esophageal ulcer: 0.0%(0/225) vs. 0.4%(1/224) Gastritis: 0.0%(0/225) vs. 0.9%(2/224) Gastroenteritis: 0.4%(1/225) vs. 0.0%(0/224) Gastroesophageal reflux disease: 0.0%(0/225) vs. 0.4%(1/224) Heartburn: 2.7%(6/225) vs. 0.9%(2/224) Nausea: 3.6%(8/225) vs. 2.7%(6/224) Tympanism: 0.0%(0/225) vs. 0.4%(1/224) Vomiting: 1.3%(3/225) vs. 0.0%(0/224)
El-Agroudy AE et al., 2005[75]	Alendronate vs. Calcitonin vs. Vitamin D vs. Control: Hypocalcemia: 20.0%(3/15) vs. 13.3%(2/15) vs. 0.0%(0/15) vs. 0.0%(0/15) Nasal stuffiness: 0.0%(0/15) vs. 13.3%(2/15) vs. 0.0%(0/15) vs. 0.0%(0/15) Nausea and epigastric pain: 13.3%(2/15) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/15)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Ensrud K et al., 2006[76]	Raloxifene vs. Placebo: Cardiovascular event: 5.5%(149/2725) vs. 4.7%(61/1286) Cardiovascular event - fatal: 0.6%(17/2725) vs. 0.5%(6/1286) Cardiovascular event - nonfatal: 5.0%(137/2725) vs. 4.4%(57/1286) Cerebrovascular event: 2.7%(73/2725) vs. 2.3%(29/1286) Cerebrovascular event - nonfatal: 2.6%(70/2725) vs. 2.3%(29/1286) Coronary event: 3.1%(85/2725) vs. 2.6%(33/1286) Coronary event - fatal: 0.4%(11/2725) vs. 0.4%(5/1286) Coronary event - nonfatal: 2.7%(74/2725) vs. 2.3%(29/1286) Fatal stroke: 0.2%(6/2725) vs. 0.1%(1/1286) Myocardial infarction: 1.2%(33/2725) vs. 0.9%(12/1286) Stroke: 1.8%(49/2725) vs. 1.5%(19/1286) Transient ischemic attack: 1.0%(26/2725) vs. 0.9%(12/1286) Unstable angina: 1.5%(42/2725) vs. 1.4%(18/1286)
Ensrud KE et al., 2004[77]	Alendronate vs. Placebo: Abdominal pain: 5.0%(33/662) vs. 5.7%(25/437) Acid reflux: 3.3%(22/662) vs. 3.7%(16/437) Any AE resulting in hospitalization: 27.6%(183/662) vs. 28.6%(125/437) Any UGI tract event: 29.8%(197/662) vs. 35.7%(156/437) Deaths: 2.4%(16/662) vs. 1.8%(8/437) Duodenal ulcer: 0.5%(3/662) vs. 0.2%(1/437) Esophageal ulcer: 0.6%(4/662) vs. 0.5%(2/437) Esophagitis: 0.5%(3/662) vs. 0.7%(3/437) Gastric ulcer: 0.5%(3/662) vs. 0.9%(4/437)
Evans RA et al., 1993[78]	Calcium vs. Etidronate vs. Etidronate+Phosphate: Constipation: 18.2%(2/11) vs. 6.7%(1/15) vs. 0.0%(0/10) Diarrhea: 0.0%(0/11) vs. 46.7%(7/15) vs. 50.0%(5/10) Dry mouth: 9.1%(1/11) vs. 0.0%(0/15) vs. 0.0%(0/10) Hip pain: 0.0%(0/11) vs. 6.7%(1/15) vs. 0.0%(0/10) Indigestion: 27.3%(3/11) vs. 0.0%(0/15) vs. 0.0%(0/10) Leg cramps: 0.0%(0/11) vs. 6.7%(1/15) vs. 0.0%(0/10) Mild nausea: 0.0%(0/11) vs. 46.7%(7/15) vs. 30.0%(3/10) Skin rash: 0.0%(0/11) vs. 6.7%(1/15) vs. 0.0%(0/10)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Evio S et al., 2004[79]	Alendronate vs. Alendronate+Estrogen vs. Estrogen: Arrhythmia: 0.0%(0/30) vs. 3.3%(1/30) vs. 3.3%(1/30) Back and leg pains: 6.7%(2/30) vs. 0.0%(0/30) vs. 0.0%(0/30) Breast tenderness: 0.0%(0/30) vs. 0.0%(0/30) vs. 16.7%(5/30) Myocardial infarction: 3.3%(1/30) vs. 0.0%(0/30) vs. 0.0%(0/30) Repeated respiratory infections: 0.0%(0/30) vs. 3.3%(1/30) vs. 0.0%(0/30) Stomach problems: 6.7%(2/30) vs. 6.7%(2/30) vs. 6.7%(2/30) With night sweating: 0.0%(0/30) vs. 0.0%(0/30) vs. 3.3%(1/30)
Fan SL et al., 2003[80]	Pamidronate vs. Control: Acute rejection: 55.6%(5/9) vs. 75.0%(6/8)
Finkelstein JS et al., 1998[81]	GnRH vs. PTH+ GnRH: Acne: 13.6%(3/22) vs. 9.5%(2/21) Arthralgia: 31.8%(7/22) vs. 61.9%(13/21) Back pain: 13.6%(3/22) vs. 19.0%(4/21) Emotional lability: 40.9%(9/22) vs. 42.9%(9/21) Hair loss: 4.5%(1/22) vs. 9.5%(2/21) Headaches: 59.1%(13/22) vs. 66.7%(14/21) Mild discomfort at injection site: 0.0%(0/22) vs. 9.5%(2/21) Mild erythema at injection site: 0.0%(0/22) vs. 9.5%(2/21) Mild hypercalcemia at 24hrs after injection: 0.0%(0/22) vs. 1.0%(0/21) Mild hypercalcemia at 4hrs after injection: 0.0%(0/22) vs. 17.0%(4/21) Mild nausea: 4.5%(1/22) vs. 33.3%(7/21) Myalgias: 13.6%(3/22) vs. 19.0%(4/21) Nasal irritation: 31.8%(7/22) vs. 4.8%(1/21) Vaginal dryness: 22.7%(5/22) vs. 19.0%(4/21) Vasomotor flushes: 100.0%(22/22) vs. 95.2%(20/21) Weight gain > 5kg: 31.8%(7/22) vs. 33.3%(7/21) Weight loss > 5kg: 12.0%(3/22) vs. 12.0%(3/21)
Finkelstein JS et al., 2006[82]	Alendronate & teriparatide vs. Teriparatide: Hypercalcemia - dose reduced: 14.3%(4/28) vs. 7.4%(2/27) Hypercalciuria - dose reduced: 7.1%(2/28) vs. 14.8%(4/27)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Fisher B et al., 1998[83]	Tamoxifen 20mg vs. Placebo: Acute ischemic syndrome: 0.4%(27/6681) vs. 0.3%(20/6707) Amyotrophic lateral sclerosis resulting in death: 0.0%(0/6681) vs. 0.0%(2/6707) Angina requiring coronary artery bypass or angioplasty: 0.2%(13/6681) vs. 0.2%(14/6707) Automobile accident resulting in death: 0.0%(1/6681) vs. 0.0%(2/6707) Breast cancer: 1.9%(124/6681) vs. 3.6%(244/6707) Cancer death - primary site unknown: 0.0%(3/6681) vs. 0.1%(5/6707) Cataracts in people cataract-free at randomization: 8.6%(574/6681) vs. 7.6%(507/6707) Colon cancer: 0.2%(11/6681) vs. 0.1%(9/6707) Connective tissue cancer: 0.0%(1/6681) vs. 0.0%(2/6707) Death - Brain cancer: 0.0%(1/6681) vs. 0.0%(3/6707) Death - Breast cancer: 0.0%(3/6681) vs. 0.1%(6/6707) Death - Colon cancer: 0.0%(1/6681) vs. 0.0%(1/6707) Death - Extrahepatic bile duct cancer: 0.0%(0/6681) vs. 0.0%(1/6707) Death - Heart disease (ischemic and other): 0.2%(13/6681) vs. 0.2%(12/6707) Death - Kidney cancer: 0.0%(0/6681) vs. 0.0%(2/6707) Death - Lung cancer: 0.1%(8/6681) vs. 0.2%(11/6707) Death - Lymphatic system cancer: 0.0%(2/6681) vs. 0.1%(4/6707) Death - Melanoma cancer: 0.0%(1/6681) vs. 0.0%(0/6707) Death - Myocardial infarction: 0.1%(7/6681) vs. 0.1%(8/6707) Death - Occlusive stroke: 0.0%(0/6681) vs. 0.0%(2/6707) Death - Ovary cancer: 0.0%(2/6681) vs. 0.0%(1/6707) Death - Pancreas cancer: 0.0%(2/6681) vs. 0.1%(6/6707) Death - Pulmonary embolus: 0.0%(3/6681) vs. 0.0%(0/6707) Death - Stroke: 0.1%(4/6681) vs. 0.0%(3/6707) Death - Thyroid gland cancer: 0.0%(0/6681) vs. 0.0%(1/6707) Death - Unknown cause: 0.1%(4/6681) vs. 0.1%(4/6707) Death - Uterus (endometrium) cancer: 0.0%(0/6681) vs. 0.0%(1/6707) Death - arterial disease other than stroke: 0.0%(2/6681) vs. 0.0%(0/6707) Death - vascular disease: 0.3%(22/6681) vs. 0.2%(15/6707) Deep vein thrombosis: 0.5%(35/6681) vs. 0.3%(22/6707) Depression Center for Epidemiological Studies Depression Scale (ces-d) 0-15: 65.4%(4369/6681) vs. 65.4%(4386/6707) Depression ces-d 16-22: 15.6%(1042/6681) vs. 16.1%(1080/6707) Depression ces-d 23-29: 10.1%(675/6681) vs. 9.5%(637/6707) Depression ces-d 30-36: 5.1%(341/6681) vs. 5.4%(362/6707) Depression ces-d >=37: 3.7%(247/6681) vs. 3.6%(241/6707) Gallbladder cancer: 0.0%(0/6681) vs. 0.0%(1/6707)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Fisher B et al., 1998 Continued	Hemorrhagic stroke: 0.1%(10/6681) vs. 0.1%(6/6707) Hemorrhagic stroke - death: 0.0%(3/6681) vs. 0.0%(1/6707) Hot flashes - extremely bothersome: 17.6%(1176/6681) vs. 10.1%(677/6707) Hot flashes - moderately bothersome: 21.8%(1456/6681) vs. 21.7%(1455/6707) Hot flashes - not bothersome: 19.4%(1296/6681) vs. 31.4%(2106/6707) Hot flashes - quite a bit bothersome: 28.1%(1877/6681) vs. 18.6%(1248/6707) Hot flashes - slightly bothersome: 14.1%(942/6681) vs. 18.2%(1221/6707) In situ endometrial cancer: 0.0%(1/6681) vs. 0.0%(3/6707) Invasive breast cancer: 1.3%(89/6681) vs. 2.6%(175/6707) Invasive endometrial cancer: 0.5%(36/6681) vs. 0.2%(15/6707) Kidney cancer: 0.0%(2/6681) vs. 0.0%(3/6707) Liver cancer: 0.0%(0/6681) vs. 0.0%(0/6707) Lung, trachea, bronchus cancer: 0.3%(20/6681) vs. 0.3%(17/6707) Lymphatic, hematopoietic systems cancer: 0.2%(14/6681) vs. 0.2%(11/6707) Miscellaneous deaths (11 different causes): 0.1%(7/6681) vs. 0.1%(6/6707) Mouth, pharynx, larynx cancer: 0.0%(3/6681) vs. 0.0%(2/6707) Myocardial infarction: 0.5%(31/6681) vs. 0.4%(28/6707) Nervous system cancer: 0.0%(1/6681) vs. 0.0%(3/6707) Noninvasive breast cancer: 0.5%(35/6681) vs. 1.0%(69/6707) Occlusive stroke: 0.3%(21/6681) vs. 0.2%(14/6707) Other genital cancer: 0.1%(4/6681) vs. 0.1%(4/6707) Ovary/fallopian tube cancer: 0.1%(10/6681) vs. 0.2%(11/6707) Pancreas cancer: 0.1%(4/6681) vs. 0.1%(7/6707) Pulmonary embolism: 0.3%(18/6681) vs. 0.1%(6/6707) Rectum cancer: 0.1%(4/6681) vs. 0.0%(3/6707) Retroperitoneum cancer: 0.0%(0/6681) vs. 0.0%(1/6707) Skin cancer: 0.2%(11/6681) vs. 0.1%(9/6707) Stomach cancer: 0.0%(1/6681) vs. 0.0%(2/6707) Stroke of unknown etiology: 0.1%(7/6681) vs. 0.1%(4/6707) Thyroid gland cancer: 0.1%(4/6681) vs. 0.1%(5/6707) Transient ischemic attach: 0.3%(19/6681) vs. 0.4%(25/6707) Unknown cancer: 0.1%(4/6681) vs. 0.1%(6/6707) Urinary bladder cancer: 0.0%(3/6681) vs. 0.0%(1/6707) Vaginal discharge - extremely bothersome: 3.1%(207/6681) vs. 1.2%(80/6707) Vaginal discharge - moderately bothersome: 16.6%(1109/6681) vs. 8.5%(570/6707) Vaginal discharge - quite a bit bothersome: 9.3%(621/6681) vs. 3.3%(221/6707) Vaginal discharge - slightly bothersome: 26.2%(1750/6681) vs. 21.8%(1462/6707)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Flicker L et al., 1997[84]	Calcitonin vs. Calcitonin+Nandrolone vs. Nandrolone vs. Placebo: Death: 6.3%(2/32) vs. 3.2%(1/31) vs. 3.3%(1/30) vs. 3.3%(1/30) Erythematous vocal cords: 0.0%(0/32) vs. 3.2%(1/31) vs. 0.0%(0/30) vs. 0.0%(0/30) Increased facial hair: 0.0%(0/32) vs. 0.0%(0/31) vs. 20.0%(6/30) vs. 0.0%(0/30) Leg edema: 0.0%(0/32) vs. 0.0%(0/31) vs. 13.3%(4/30) vs. 0.0%(0/30) Nasal irritation: 0.0%(0/32) vs. 0.0%(0/31) vs. 0.0%(0/30) vs. 3.3%(1/30) Voice hoarseness: 0.0%(0/32) vs. 0.0%(0/31) vs. 83.3%(25/30) vs. 0.0%(0/30)
Fogelman I et al., 2000[85]	Etidronate vs. Placebo: Lung cancer: 0.0%(0/59) vs. 1.6%(1/62)
Fogelman I et al., 2000[86]	Risedronate 2.5mg vs. Risedronate 5mg vs. Placebo: Any clinical event: 93.5%(172/184) vs. 94.4%(169/179) vs. 95.6%(172/180) Abdominal pain: 10.9%(20/184) vs. 12.8%(23/179) vs. 12.2%(22/180) Dyspepsia: 13.6%(25/184) vs. 8.4%(15/179) vs. 10.0%(18/180) Esophageal ulcer: 1.1%(2/184) vs. 1.7%(3/179) vs. 0.6%(1/180) Esophagitis: 3.3%(6/184) vs. 1.7%(3/179) vs. 2.2%(4/180) Gastritis: 1.1%(2/184) vs. 1.7%(3/179) vs. 0.0%(0/180) Serious AE: 11.4%(21/184) vs. 14.5%(26/179) vs. 15.0%(27/180) Stomach ulcer: 1.1%(2/184) vs. 0.6%(1/179) vs. 2.8%(5/180) Withdrawal due to AE: 9.8%(18/184) vs. 10.6%(19/179) vs. 7.8%(14/180)
Frediani B et al., 1998[87]	Alendronate vs. Alendronate, Vitamin D vs. Vitamin D vs. Placebo: Gastric pain: 6.7%(2/30) vs. 10.0%(3/30) vs. 0.0%(0/30) vs. 26.7%(8/30)
Freedman M et al., 2001[88]	Estrogen vs. Raloxifene 150 mg vs. Raloxifene 60 mg vs. Placebo: Breast pain: 14.5%(8/55) vs. 6.7%(4/60) vs. 3.3%(2/61) vs. 6.8%(4/59)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Fujita T et al., 1999[89]	PTH 100 u vs. PTH 200 u vs. PTH 50 u: Abdominal pain: 0.0%(0/75) vs. 1.4%(1/72) vs. 1.4%(1/73) Anorexia: 0.0%(0/75) vs. 1.4%(1/72) vs. 0.0%(0/73) Belching: 1.3%(1/75) vs. 0.0%(0/72) vs. 0.0%(0/73) Chills: 0.0%(0/75) vs. 1.4%(1/72) vs. 0.0%(0/73) Dizziness: 2.7%(2/75) vs. 1.4%(1/72) vs. 1.4%(1/73) Eczema: 0.0%(0/75) vs. 0.0%(0/72) vs. 1.4%(1/73) Facial flush: 0.0%(0/75) vs. 1.4%(1/72) vs. 0.0%(0/73) Febrile episode: 1.3%(1/75) vs. 4.2%(3/72) vs. 0.0%(0/73) Febrile sensation: 2.7%(2/75) vs. 1.4%(1/72) vs. 1.4%(1/73) General malaise: 1.3%(1/75) vs. 4.2%(3/72) vs. 1.4%(1/73) Headache: 4.0%(3/75) vs. 5.6%(4/72) vs. 2.7%(2/73) Itching: 0.0%(0/75) vs. 0.0%(0/72) vs. 1.4%(1/73) Lumbago: 1.3%(1/75) vs. 1.4%(1/72) vs. 0.0%(0/73) Nausea: 9.3%(7/75) vs. 20.8%(15/72) vs. 5.5%(4/73) Sensation of weakness: 1.3%(1/75) vs. 1.4%(1/72) vs. 0.0%(0/73) Sleepiness: 1.3%(1/75) vs. 0.0%(0/72) vs. 0.0%(0/73) Subcutaneous hemorrhage: 0.0%(0/75) vs. 0.0%(0/72) vs. 1.4%(1/73) Thirst: 0.0%(0/75) vs. 0.0%(0/72) vs. 1.4%(1/73) Vomiting: 1.3%(1/75) vs. 5.6%(4/72) vs. 0.0%(0/73) Whole-body reddening: 1.3%(1/75) vs. 0.0%(0/72) vs. 0.0%(0/73) Yawning: 1.3%(1/75) vs. 0.0%(0/72) vs. 0.0%(0/73)
Fukunaga M et al., 2002[90]	Etidronate vs. Risedronate: Any AE: 81.2%(95/117) vs. 81.4%(96/118) Abdominal distension: 1.7%(2/117) vs. 5.9%(7/118) Abnormal lab data: 12.0%(14/117) vs. 9.3%(11/118) Cardiovascular events: 0.9%(1/117) vs. 2.5%(3/118) Constipation: 6.0%(7/117) vs. 3.4%(4/118) Dermatologic events: 2.6%(3/117) vs. 2.5%(3/118) Epigastric pain: 7.7%(9/117) vs. 7.6%(9/118) GI events**: 19.7%(23/117) vs. 22.9%(27/118) Nausea: 0.9%(1/117) vs. 3.4%(4/118) Neurologic events: 4.3%(5/117) vs. 4.2%(5/118)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Fuleihan G et al., 2005[91]	Pamidronate vs. Placebo: Amenorrheic: 52.4%(11/21) vs. 57.9%(11/19) Flu-like syndrome after first infusion: 4.8%(1/21) vs. 0.0%(0/19) Hypocalcemia: 0.0%(0/21) vs. 0.0%(0/19)
Geusens P et al., 1997[92]	Etidronate vs. Placebo: Anaphylactic shock: 0.0%(0/18) vs. 5.3%(1/19) Death: 5.6%(1/18) vs. 0.0%(0/19) Diarrhea: 0.0%(0/18) vs. 10.5%(2/19) Nausea: 11.1%(2/18) vs. 5.3%(1/19) Vomiting: 5.6%(1/18) vs. 5.3%(1/19)
Geusens P et al., 1998[93]	Etidronate vs. Placebo: Anaphylactic shock: 0.0%(0/18) vs. 5.3%(1/19) Death - Ruptured aortic aneurysm: 5.6%(1/18) vs. 0.0%(0/19) Diarrhea: 0.0%(0/18) vs. 10.5%(2/19) Nausea: 11.1%(2/18) vs. 5.3%(1/19) Vomiting: 5.6%(1/18) vs. 5.3%(1/19)
Giannini S et al., 2001[94]	Alendronate+ Calcium+Vitamin D vs. Calcium+Vitamin D: Abdominal pain: 5.0%(1/20) vs. 15.0%(3/20) Acid regurgitation: 5.0%(1/20) vs. 0.0%(0/20) Nausea: 10.0%(2/20) vs. 5.0%(1/20)
Gnudi S et al., 1988[95]	Calcitonin 100iu vs. Calcitonin 50iu vs. Placebo: Cutaneous rush: 0.0%(12/23) vs. 0.0%(12/22) vs. 0.0%(0/17) Gastrointestinal: 0.0%(25/23) vs. 0.0%(18/22) vs. 0.0%(6/17) Local pain: 0.0%(1/23) vs. 0.0%(0/22) vs. 0.0%(0/17) Vasomotor: 0.0%(31/23) vs. 0.0%(27/22) vs. 0.0%(0/17)
Golden NH et al., 2005[96]	Alendronate vs. Placebo: Dyspepsia: 0.0%(0/15) vs. 5.9%(1/17) Nausea and abdominal bloating: 13.3%(2/15) vs. 11.8%(2/17)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Grady D et al., 2004[97]	Raloxifene vs. Placebo: Any venous thrombosis: 1.2%(59/5129) vs. 0.5%(14/2576) Any venous thrombosis year 1: 0.5%(24/5129) vs. 0.1%(2/2576) Any venous thrombosis year 2: 0.3%(13/5129) vs. 0.0%(1/2576) Any venous thrombosis year 3: 0.3%(13/5129) vs. 0.3%(7/2576) Any venous thrombosis year 4: 0.2%(9/5129) vs. 0.2%(4/2576) Breast cancer: 0.0%(1/5129) vs. 0.0%(0/2576) Cancer: 0.2%(9/5129) vs. 0.2%(5/2576) Cataracts new: 4.6%(235/5129) vs. 4.9%(127/2576) Cataracts requiring surgery: 3.2%(163/5129) vs. 3.3%(86/2576) Cataracts total: 5.7%(291/5129) vs. 6.2%(160/2576) Cataracts worsening: 1.1%(56/5129) vs. 1.3%(33/2576) Death from gastrointestinal carcinoma: 0.0%(2/5129) vs. 0.0%(0/2576) Death from lung cancer: 0.0%(1/5129) vs. 0.0%(0/2576) Death from myocardial infarction: 0.0%(1/5129) vs. 0.0%(0/2576) Death from pulmonary embolism due to breast cancer: 0.1%(5/5129) vs. 0.0%(0/2576) Deep vein thrombosis: 0.8%(43/5129) vs. 0.3%(7/2576) Gallbladder disease new: 2.4%(121/5129) vs. 2.4%(63/2576) Gallbladder disease requiring surgery: 1.4%(71/5129) vs. 1.0%(25/2576) Gallbladder disease total: 2.5%(130/5129) vs. 2.6%(66/2576) Gallbladder disease worsening: 0.2%(9/5129) vs. 0.1%(3/2576) Idiopathic thromboembolic event: 0.3%(15/5129) vs. 0.0%(1/2576) Pulmonary embolism: 0.4%(18/5129) vs. 0.1%(2/2576) Retinal vein thrombosis: 0.1%(4/5129) vs. 0.2%(5/2576) Secondary thromboembolic event: 0.9%(44/5129) vs. 0.5%(13/2576) Uterine any hyperplasia: 0.2%(8/5129) vs. 0.1%(3/2576) Uterine cancer - homologous mixed mullerian tumor: 0.0%(0/5129) vs. 0.0%(1/2576) Uterine cancer - sarcoma: 0.0%(1/5129) vs. 0.0%(0/2576) Uterine complex hyperplasia: 0.0%(2/5129) vs. 0.0%(1/2576) Uterine not specified: 0.1%(3/5129) vs. 0.0%(0/2576) Uterine simple hyperplasia: 0.1%(3/5129) vs. 0.1%(2/2576)

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AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Greenspan S et al., 2002[98]	Alendronate vs. Placebo: Abdominal distension: 0.4%(1/224) vs. 0.4%(1/226) Abdominal pain: 3.1%(7/224) vs. 3.5%(8/226) Anorexia: 0.0%(0/224) vs. 0.4%(1/226) Digestive gas symptoms: 0.0%(0/224) vs. 0.4%(1/226) Duodenal ulcer: 0.4%(1/224) vs. 0.0%(0/226) Dyspepsia: 1.8%(4/224) vs. 2.7%(6/226) Epigastric discomfort: 0.9%(2/224) vs. 0.4%(1/226) GI disorder: 0.4%(1/224) vs. 0.0%(0/226) Gastritis: 0.4%(1/224) vs. 0.0%(0/226) GERD: 1.3%(3/224) vs. 0.4%(1/226) Heartburn: 2.2%(5/224) vs. 1.8%(4/226) Nausea: 1.8%(4/224) vs. 5.8%(13/226) Serious AE not drug related: 2.7%(6/224) vs. 1.8%(4/226) Vomiting: 1.3%(3/224) vs. 0.9%(2/226)
Greenspan SL et al., 1998[99]	Alendronate vs. Placebo: GI complaints: 43.0%(26/60) vs. 47.0%(28/60)
Greenspan SL et al., 2003[100]	Alendronate vs. Alendronate+Estrogen vs. Estrogen vs. Placebo: Bloating: 4.3%(4/93) vs. 5.3%(5/94) vs. 9.7%(9/93) vs. 2.2%(2/93) Breast tenderness: 23.7%(22/93) vs. 53.2%(50/94) vs. 55.9%(52/93) vs. 17.2%(16/93) Chest pain: 17.2%(16/93) vs. 9.6%(9/94) vs. 10.8%(10/93) vs. 14.0%(13/93) Deep venous thrombosis: 1.1%(1/93) vs. 0.0%(0/94) vs. 2.2%(2/93) vs. 0.0%(0/93) Dysphagia: 3.2%(3/93) vs. 2.1%(2/94) vs. 1.1%(1/93) vs. 2.2%(2/93) Endometrial biopsy: 2.2%(2/93) vs. 11.7%(11/94) vs. 12.9%(12/93) vs. 1.1%(1/93) Esophagitis: 28.0%(26/93) vs. 21.3%(20/94) vs. 18.3%(17/93) vs. 22.6%(21/93) Falls: 55.9%(52/93) vs. 52.1%(49/94) vs. 47.3%(44/93) vs. 45.2%(42/93) Heartburn: 18.3%(17/93) vs. 17.0%(16/94) vs. 11.8%(11/93) vs. 16.1%(15/93) High blood pressure: 5.4%(5/93) vs. 2.1%(2/94) vs. 6.5%(6/93) vs. 3.2%(3/93) Hospitalization: 36.6%(34/93) vs. 34.0%(32/94) vs. 43.0%(40/93) vs. 28.0%(26/93) Indigestion: 6.5%(6/93) vs. 1.1%(1/94) vs. 5.4%(5/93) vs. 4.3%(4/93) Menstrual cramps: 0.0%(0/93) vs. 5.3%(5/94) vs. 6.5%(6/93) vs. 0.0%(0/93) Menstrual spotting: 7.5%(7/93) vs. 33.0%(31/94) vs. 31.2%(29/93) vs. 9.7%(9/93) Myocardial infarction: 2.2%(2/93) vs. 1.1%(1/94) vs. 0.0%(0/93) vs. 1.1%(1/93) Peripheral edema: 9.7%(9/93) vs. 11.7%(11/94) vs. 14.0%(13/93) vs. 12.9%(12/93) Weight gain: 6.5%(6/93) vs. 8.5%(8/94) vs. 8.6%(8/93) vs. 8.6%(8/93)

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AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Greenwald MW et al., 2005[101]	Estrogen 0.25 mg vs. Estrogen 0.5 mg vs. Estrogen 1 mg vs. Estrogen 1 mg & NETA 0.25 mg vs. Estrogen 1 mg & NETA 0.5 mg vs. Estrogen 2 mg & NETA 1 mg vs. Placebo: Endometrial hyperplasia: 0.0%(0/45) vs. 2.3%(1/44) vs. 19.6%(9/46) vs. 0.0%(0/49) vs. 0.0%(0/47) vs. 0.0%(0/48) vs. 2.1%(1/48) Serious AE: 0.0%(0/45) vs. 0.0%(0/44) vs. 0.0%(0/46) vs. 0.0%(0/49) vs. 0.0%(0/47) vs. 0.0%(0/48) vs. 0.0%(0/48)
Grey AB et al., 1995[102]	Tamoxifen vs. Placebo: Exacerbation of dyspepsia: 4.3%(1/23) vs. 0.0%(0/23) Hepatocellular carcinoma: 0.0%(0/23) vs. 4.3%(1/23) Severe flush: 4.3%(1/23) vs. 0.0%(0/23) Skin rash: 4.3%(1/23) vs. 0.0%(0/23) Vaginal discharge: 33.0%(33/23) vs. 0.0%(0/23) Vasomotor flushes: 52.2%(12/23) vs. 17.4%(4/23) Varicose eczema: 0.0%(0/23) vs. 4.3%(1/23) Xerostomia: 0.0%(0/23) vs. 4.3%(1/23)
Grotz W et al., 2001[103]	Ibandronate vs. Placebo: Bone pain, flatulence: 7.5%(3/40) vs. 0.0%(0/40) Death: 5.0%(2/40) vs. 7.5%(3/40)
Grotz WH et al., 1998[104]	Calcitonin vs. Clodronate vs. Control: Abdominal discomfort: 0.0%(0/16) vs. 6.7%(1/15) vs. 0.0%(0/15) Arthralgia: 6.3%(1/16) vs. 0.0%(0/15) vs. 0.0%(0/15) Coronary heart disease - death: 0.0%(0/16) vs. 0.0%(0/15) vs. 6.7%(1/15) Diarrhea: 0.0%(0/16) vs. 6.7%(1/15) vs. 0.0%(0/15) Heat sensation: 6.3%(1/16) vs. 0.0%(0/15) vs. 0.0%(0/15) Skin rash: 6.3%(1/16) vs. 0.0%(0/15) vs. 0.0%(0/15) Vomiting: 0.0%(0/16) vs. 0.0%(0/15) vs. 6.7%(1/15)
Gruber HE et al., 1984[105]	Calcitonin vs. Control: Bedridden - cause not presented: 0.0%(0/24) vs. 4.8%(1/21) Eschar of 1 month at injection site: 4.2%(1/24) vs. 0.0%(0/21) Flushing and local inflammatory reaction at injection site: 8.3%(2/24) vs. 0.0%(0/21) Hot flashes: 0.0%(0/24) vs. 4.8%(1/21) Redness, tender, itching: 45.8%(11/24) vs. 0.0%(0/21)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Guanabens N et al., 2000[106]	Etidronate vs. Fluoride: Death - unrelated to treatment: 1.6%(1/63) vs. 0.0%(0/55) Gastrointestinal symptoms: 15.9%(10/63) vs. 21.8%(12/55) Intercurrent illness: 3.2%(2/63) vs. 1.8%(1/55) Lower extremity pain syndrome: 0.0%(0/63) vs. 12.7%(7/55)
Guanabens N et al., 2003[107]	Alendronate vs. Etidronate: Death - Liver failure: 0.0%(0/16) vs. 6.3%(1/16) GI symptoms: 6.3%(1/16) vs. 12.5%(2/16) Minor gastric symptoms: 12.5%(2/16) vs. 6.3%(1/16)
Guaraldi G et al., 2004[108]	Alendronate+ Calcium, Vitamin D vs. Calcium, Vitamin D: Adverse gastrointestinal effects: 10.0%(2/18) vs. 10.0%(2/23)
Gurlek A et al., 1997[109]	Calcitonin+Vitamin D vs. Etidronate+Vitamin D vs. Vitamin D: Hypercalcemia: 50.0%(5/10) vs. 40.0%(4/10) vs. 40.0%(4/10) Hypercalciuria: 70.0%(7/10) vs. 90.0%(9/10) vs. 100.0%(10/10) Renal stone: 0.0%(0/10) vs. 0.0%(0/10) vs. 10.0%(1/10)
Gutteridge DH et al., 2002[110]	Calcium+Vitamin D vs. Calcium+Vitamin D+Fluoride vs. Estrogen+Calcium+Vitamin D vs. Estrogen+Calcium+Vitamin D+Fluoride: Aseptic necrosis of the left medial femoral condyle: 3.2%(1/31) vs. 0.0%(0/34) vs. 0.0%(0/17) vs. 0.0%(0/17)
Haderslev KV et al., 2000[111]	Alendronate vs. Placebo: Any adverse effect: 80.0%(12/15) vs. 76.5%(13/17) Abdominal pain: 13.3%(2/15) vs. 11.8%(2/17) Any serious adverse effect: 33.3%(5/15) vs. 29.4%(5/17) Any upper gastrointestinal adverse effects (including dyspepsia, dysphagia: 26.7%(4/15) vs. 5.9%(1/17) Diarrhea: 20.0%(3/15) vs. 35.3%(6/17) Gaseous distention: 13.3%(2/15) vs. 17.6%(3/17)
Harris ST et al., 1993[112]	Alendronate 20mg vs. Alendronate 40mg vs. Alendronate 5mg vs. Placebo: Abdominal pain: 12.5%(2/16) vs. 0.0%(0/16) vs. 6.3%(1/16) vs. 17.6%(3/17) Constipation: 6.3%(1/16) vs. 0.0%(0/16) vs. 0.0%(0/16) vs. 5.9%(1/17) Diarrhea: 6.3%(1/16) vs. 6.3%(1/16) vs. 6.3%(1/16) vs. 5.9%(1/17) Dyspepsia: 0.0%(0/16) vs. 12.5%(2/16) vs. 12.5%(2/16) vs. 5.9%(1/17) Nausea or vomiting: 12.5%(2/16) vs. 12.5%(2/16) vs. 18.8%(3/16) vs. 5.9%(1/17)

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AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Harris ST et al., 1999[113]	Risedronate vs. Placebo: Any clinical event: 96.6%(785/813) vs. 95.0%(774/815) Abdominal pain: 12.7%(103/813) vs. 11.9%(97/815) Any UGI tract event: 30.1%(245/813) vs. 26.9%(219/815) Drug related AE: 33.6%(273/813) vs. 29.0%(236/815) Duodenal ulcer: 0.1%(1/813) vs. 0.4%(3/815) Duodenitis: 1.1%(9/813) vs. 0.2%(2/815) Dyspepsia: 12.9%(105/813) vs. 11.3%(92/815) Esophagitis: 1.4%(11/813) vs. 1.6%(13/815) Gastritis: 3.8%(31/813) vs. 2.8%(23/815) Mod-severe UGI tract event: 13.0%(106/813) vs. 12.5%(102/815) Serious AE: 29.2%(237/813) vs. 26.9%(219/815)
Harris ST et al., 2001[114]	Estrogen+Placebo vs. Estrogen+Risedronate: Abdominal pain: 1.5%(4/261) vs. 0.8%(2/263) All upper gastrointestinal (GI) AEs: 16.5%(43/261) vs. 16.3%(43/263) Asthenia: 1.5%(4/261) vs. 0.0%(0/263) Breast fibrocyst: 13.4%(35/261) vs. 8.7%(23/263) Breast pain: 30.3%(79/261) vs. 27.4%(72/263) Constipation: 1.9%(5/261) vs. 6.5%(17/263) Diarrhea: 4.2%(11/261) vs. 7.6%(20/263) Dyspepsia: 0.4%(1/261) vs. 0.8%(2/263) Esophagitis: 0.8%(2/261) vs. 0.4%(1/263) Gastric or duodenal ulcer: 1.1%(3/261) vs. 0.0%(0/263) Gastric ulcer with hemorrhage: 0.4%(1/261) vs. 0.0%(0/263) Gastritis: 0.8%(2/261) vs. 1.5%(4/263) Headache: 0.0%(0/261) vs. 0.8%(2/263) Hypertension: 5.7%(15/261) vs. 2.7%(7/263) Metrorrhagia: 1.5%(4/261) vs. 0.0%(0/263) Moderate to severe upper GI AEs: 8.0%(21/261) vs. 6.8%(18/263) Nausea: 1.5%(4/261) vs. 0.0%(0/263) Peptic ulcer: 0.0%(0/261) vs. 0.4%(1/263) Serious AEs: 8.8%(23/261) vs. 5.3%(14/263) Vaginal hemorrhage: 13.4%(35/261) vs. 8.7%(23/263)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Harris ST et al., 2004[115]	Risedronate 35 mg once a week vs. Risedronate 50mg once a week vs. Risedronate 5mg daily: AE: 95.1%(461/485) vs. 94.7%(465/491) vs. 94.8%(455/480) Any upper GI AE: 25.6%(124/485) vs. 24.8%(122/491) vs. 22.7%(109/480) Moderate to severe upper GI AE: 7.2%(35/485) vs. 6.9%(34/491) vs. 8.8%(42/480) Serious AE: 13.2%(64/485) vs. 16.1%(79/491) vs. 14.0%(67/480)
Hasling C et al., 1994[116]	Calcium vs. Estrogen+Progesterone vs. Etidronate vs. Etidronate+Triiodothyronine: Breast swelling: 0.0%(0/17) vs. 30.0%(6/20) vs. 0.0%(0/19) vs. 0.0%(0/18) Breast tenderness: 0.0%(0/17) vs. 10.0%(2/20) vs. 0.0%(0/19) vs. 0.0%(0/18) Constipation: 5.9%(1/17) vs. 0.0%(0/20) vs. 0.0%(0/19) vs. 0.0%(0/18) Could not bear regular periods: 0.0%(0/17) vs. 10.0%(2/20) vs. 0.0%(0/19) vs. 0.0%(0/18) Diarrhea: 0.0%(0/17) vs. 0.0%(0/20) vs. 5.3%(1/19) vs. 0.0%(0/18) Fatigue and dizziness: 0.0%(0/17) vs. 0.0%(0/20) vs. 0.0%(0/19) vs. 5.6%(1/18) Headache or fatigue: 0.0%(0/17) vs. 0.0%(0/20) vs. 0.0%(0/19) vs. 16.7%(3/18) Hypercalcemia: 11.8%(2/17) vs. 0.0%(0/20) vs. 0.0%(0/19) vs. 0.0%(0/18) Monthly menstrual bleeding did not return: 0.0%(0/17) vs. 5.0%(1/20) vs. 0.0%(0/19) vs. 0.0%(0/18) Slight headache or fatigue: 5.9%(1/17) vs. 0.0%(0/20) vs. 0.0%(0/19) vs. 16.7%(3/18) Tachycardia and fatigue: 0.0%(0/17) vs. 0.0%(0/20) vs. 0.0%(0/19) vs. 5.6%(1/18)
Haworth CS et al., 2001[117]	Pamidronate vs. Control: Death - respiratory failure: 6.7%(1/15) vs. 6.3%(1/16) Moderate to severe bone pain after first dose: 73.3%(11/15) vs. 0.0%(0/16)
Hay JE et al., 2001[118]	Calcitonin vs. Placebo: Death: 3.4%(1/29) vs. 0.0%(0/34) Transient diarrhea: 3.4%(1/29) vs. 0.0%(0/34)
Heath DA et al., 2000[119]	Etidronate vs. Control: Back pain: 2.6%(1/38) vs. 7.7%(3/39) Breast abscess: 0.0%(0/38) vs. 2.6%(1/39) Colitis: 2.6%(1/38) vs. 0.0%(0/39) Dyspepsia: 18.4%(7/38) vs. 0.0%(0/39) Malignant breast tumor: 2.6%(1/38) vs. 0.0%(0/39) Malignant eye cyst: 2.6%(1/38) vs. 0.0%(0/39) Nausea: 10.5%(4/38) vs. 2.6%(1/39) Report adverse effect: 76.3%(29/38) vs. 51.3%(20/39) Serious adverse effect: 7.9%(3/38) vs. 2.6%(1/39)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Henderson S et al., 2006[120]	Risedronate vs. Placebo: Abdominal pain: 6.7%(2/30) vs. 9.7%(3/31) Arthralgia: 20.0%(6/30) vs. 25.8%(8/31) Bowel obstruction: 3.3%(1/30) vs. 0.0%(0/31) Constipation: 6.7%(2/30) vs. 0.0%(0/31) Diarrhea: 40.0%(12/30) vs. 54.8%(17/31) Dizziness: 6.7%(2/30) vs. 3.2%(1/31) Flu-like symptoms: 16.7%(5/30) vs. 12.9%(4/31) Headache: 6.7%(2/30) vs. 3.2%(1/31) Nausea / vomiting: 6.7%(2/30) vs. 12.9%(4/31) Palpitations: 0.0%(0/30) vs. 3.2%(1/31) Pruritus: 6.7%(2/30) vs. 3.2%(1/31) Rash: 3.3%(1/30) vs. 3.2%(1/31) Shingles: 0.0%(0/30) vs. 3.2%(1/31)
Hendrix SL et al., 2006[121]	Estrogen vs. Placebo: Cerebrovascular death: 0.1%(7/5310) vs. 0.1%(4/5429) Glasgow outcome scale - death: 0.3%(17/5310) vs. 0.3%(15/5429) Glasgow outcome scale - good recovery: 0.9%(47/5310) vs. 0.7%(39/5429) Glasgow outcome scale - moderately disabled: 0.8%(44/5310) vs. 0.6%(30/5429) Glasgow outcome scale - not yet categorized: 0.0%(1/5310) vs. 0.0%(0/5429) Glasgow outcome scale - severely disabled: 0.8%(44/5310) vs. 0.5%(28/5429) Glasgow outcome scale - unable to categorize: 0.3%(15/5310) vs. 0.3%(14/5429) Glasgow outcome scale - vegetative survival: 0.0%(0/5310) vs. 0.0%(1/5429) Hemorrhagic stroke - intraparenchymal: 0.2%(10/5310) vs. 0.3%(18/5429) Hemorrhagic stroke - subarachnoid: 0.1%(6/5310) vs. 0.1%(8/5429) Ischemic stroke - cardioembolism: 0.5%(26/5310) vs. 0.2%(13/5429) Ischemic stroke - large-artery atherosclerosis: 0.2%(8/5310) vs. 0.1%(7/5429) Ischemic stroke - small-vessel occlusion: 0.6%(33/5310) vs. 0.4%(23/5429) Ischemic stroke of other determined origin: 9.0%(478/5310) vs. 12.0%(651/5429) Moderate or severe vasomotor symptoms (night sweats, hot flashes or both): 0.4%(22/5310) vs. 0.3%(18/5429) Other stroke: 0.0%(1/5310) vs. 0.0%(1/5429) Stroke - not yet categorized: 0.0%(1/5310) vs. 0.0%(0/5429)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Herd RJ et al., 1997[122]	Etidronate vs. Placebo: Arthritis: 14.7%(11/75) vs. 13.0%(10/77) Back pain: 16.0%(12/75) vs. 18.2%(14/77) Diarrhea: 4.0%(3/75) vs. 6.5%(5/77) Dyspepsia and skin rash: 1.3%(1/75) vs. 0.0%(0/77) Dyspepsia: 4.0%(3/75) vs. 7.8%(6/77) Endometrial carcinoma: 1.3%(1/75) vs. 0.0%(0/77) Flu syndrome: 12.0%(9/75) vs. 11.7%(9/77) Headache and vertigo: 1.3%(1/75) vs. 0.0%(0/77) Infection: 24.0%(18/75) vs. 28.6%(22/77) Nausea: 4.0%(3/75) vs. 13.0%(10/77) Recurrent infection: 1.3%(1/75) vs. 0.0%(0/77) Serious AEs: 10.7%(8/75) vs. 9.1%(7/77) Worsening of arthritis: 1.3%(1/75) vs. 0.0%(0/77)
Herrera JA et al., 1999[123]	Alendronate vs. Pamidronate: Dyspepsia: 4.8%(1/21) vs. 0.0%(0/19) Endoscopic severe lesion after 1 month: 23.8%(5/21) vs. 10.5%(2/19) Epigastralgia: 4.8%(1/21) vs. 0.0%(0/19)
Ho AY et al., 2005[124]	Alendronate & calcium vs. Calcium: Abnormal liver function: 3.4%(1/29) vs. 0.0%(0/29) Constipation: 10.3%(3/29) vs. 10.3%(3/29) Dizziness: 3.4%(1/29) vs. 10.3%(3/29) Dry mouth: 0.0%(0/29) vs. 3.4%(1/29) Elevated liver transaminase enzymes secondary to viral hepatitis: 3.4%(1/29) vs. 0.0%(0/29) Flatulence: 10.3%(3/29) vs. 10.3%(3/29) Malaise: 3.4%(1/29) vs. 0.0%(0/29) Muscle cramps: 6.9%(2/29) vs. 3.4%(1/29) Musculoskeletal pain: 0.0%(0/29) vs. 3.4%(1/29)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Hooper MJ et al., 2005[125]	Risedronate 2.5mg/d vs. Risedronate 5mg/d vs. Placebo: Abdominal pain: 7.0%(9/128) vs. 7.0%(9/129) vs. 4.8%(6/126) Duodenal ulcer: 0.8%(1/128) vs. 0.8%(1/129) vs. 0.0%(0/126) Dyspepsia: 10.2%(13/128) vs. 6.2%(8/129) vs. 9.5%(12/126) Esophageal ulcer: 0.0%(0/128) vs. 0.8%(1/129) vs. 1.6%(2/126) Esophagitis: 0.8%(1/128) vs. 3.1%(4/129) vs. 3.2%(4/126) GI disorder: 2.3%(3/128) vs. 3.1%(4/129) vs. 1.6%(2/126) Gastritis: 2.3%(3/128) vs. 1.6%(2/129) vs. 2.4%(3/126) Stomach ulcer: 0.8%(1/128) vs. 0.0%(0/129) vs. 0.8%(1/126)
Horwitz MJ et al., 2003[126]	PTH vs. Placebo: Heart palpitations: 12.5%(1/8) vs. 0.0%(0/8) Shortness of breath and chest tightness: 0.0%(0/8) vs. 12.5%(1/8)
Hosking D et al., 1998[127]	Alendronate 2.5mg vs. Alendronate 5mg vs. Estrogen-progestin vs. Placebo: Abdominal pain: 10.0%(50/499) vs. 9.0%(45/498) vs. 10.9%(12/110) vs. 12.0%(60/502) Acid regurgitation: 4.6%(23/499) vs. 4.8%(24/498) vs. 0.0%(0/110) vs. 4.4%(22/502) Any type of GI symptom: 30.5%(152/499) vs. 29.7%(148/498) vs. 28.2%(31/110) vs. 29.5%(148/502) Cardiovascular system AE: 10.0%(50/499) vs. 9.8%(49/498) vs. 13.6%(15/110) vs. 9.4%(47/502) Digestive system AE: 51.7%(258/499) vs. 53.2%(265/498) vs. 50.9%(56/110) vs. 52.4%(263/502) Dyspepsia: 9.2%(46/499) vs. 9.2%(46/498) vs. 5.5%(6/110) vs. 9.8%(49/502) Musculoskeletal system AE: 63.9%(319/499) vs. 61.8%(308/498) vs. 56.4%(62/110) vs. 59.6%(299/502) Nausea: 7.6%(38/499) vs. 7.6%(38/498) vs. 7.3%(8/110) vs. 7.4%(37/502) Nervous system/psychiatric AE: 29.9%(149/499) vs. 32.7%(163/498) vs. 32.7%(36/110) vs. 31.1%(156/502) Respiratory system AE: 74.9%(374/499) vs. 74.3%(370/498) vs. 70.9%(78/110) vs. 77.1%(387/502) Skin AE: 31.9%(159/499) vs. 32.5%(162/498) vs. 28.2%(31/110) vs. 33.1%(166/502) Urogenital system AE: 36.3%(181/499) vs. 32.9%(164/498) vs. 90.0%(99/110) vs. 33.5%(168/502) Vomiting: 3.4%(17/499) vs. 4.8%(24/498) vs. 2.7%(3/110) vs. 3.4%(17/502)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Hosking D et al., 2003[128]	Alendronate vs. Risedronate vs. Placebo: Any adverse effects: 77.2%(169/219) vs. 76.1%(169/222) vs. 70.4%(76/108) Any upper gastrointestinal: 28.3%(62/219) vs. 27.5%(61/222) vs. 26.9%(29/108) Deglutition disorder: 0.0%(0/219) vs. 0.5%(1/222) vs. 0.0%(0/108) Dysphagia: 0.9%(2/219) vs. 0.0%(0/222) vs. 0.0%(0/108) Gastric ulcer: 0.0%(0/219) vs. 0.5%(1/222) vs. 0.0%(0/108) Esophagitis: 1.4%(3/219) vs. 0.9%(2/222) vs. 0.0%(0/108) One or more Esophageal AEs: 2.3%(5/219) vs. 1.8%(4/222) vs. 0.0%(0/108) One or more PUBs AEs: 0.0%(0/219) vs. 0.5%(1/222) vs. 0.0%(0/108) Reflux esophagitis: 0.0%(0/219) vs. 0.5%(1/222) vs. 0.0%(0/108) Serious upper gastrointestinal: 0.5%(1/219) vs. 0.0%(0/222) vs. 1.9%(2/108)
Howell SJ et al., 2001[129]	Placebo vs. Testosterone: Serious AE: 0.0%(0/19) vs. 0.0%(0/16) Skin reaction: 5.3%(1/19) vs. 43.8%(7/16)
Hsia J et al., 2004[130]	Conjugated estrogens 0.625mg/d & medroxyprogesterone acetate 2.5mg/d vs. Placebo: Peripheral artery disease (PAD)-abdominal aortic aneurysm (aaa): 0.1%(8/8506) vs. 0.1%(9/8102) PAD-carotid: 0.4%(31/8506) vs. 0.5%(39/8102) PAD-lower extremity: 0.3%(27/8506) vs. 0.3%(25/8102)
Hsia J et al., 2006[131]	CEE vs. Placebo: CABG or PTCA: 4.8%(253/5310) vs. 5.1%(276/5429) Hospitalized CHF with wall motion abnormality: 1.1%(60/5310) vs. 1.3%(69/5429) Hospitalized CHF without wall motion abnormality: 2.4%(125/5310) vs. 2.1%(114/5429) Hospitalized angina (confirmed angina): 3.1%(163/5310) vs. 3.1%(171/5429) Hospitalized angina (unconfirmed angina): 1.9%(102/5310) vs. 1.7%(91/5429) Myocardial infarction: 2.4%(130/5310) vs. 2.6%(139/5429) Primary outcome: coronary death: 1.2%(62/5310) vs. 1.2%(63/5429) Primary outcome: nonfatal MI - other: 2.7%(142/5310) vs. 3.0%(161/5429) Primary outcome: nonfatal MI - silent MI: 0.1%(7/5310) vs. 0.1%(7/5429)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Hulley S et al., 1998[132]	Estrogen+ Progesterone vs. Placebo: Breast cancer: 2.3%(32/1380) vs. 1.8%(25/1383) CHD Death: 5.1%(71/1380) vs. 4.2%(58/1383) Cancer death: 1.4%(19/1380) vs. 1.7%(24/1383) Coronary artery bypass graft surgery: 6.4%(88/1380) vs. 7.3%(101/1383) Deep vein thrombosis: 1.8%(25/1380) vs. 0.6%(8/1383) Endometrial cancer: 0.1%(2/1380) vs. 0.3%(4/1383) Gall bladder disease: 6.1%(84/1380) vs. 4.5%(62/1383) Hospitalization for congestive heart failure: 9.3%(128/1380) vs. 8.1%(112/1383) Hospitalization for unstable angina: 7.5%(103/1380) vs. 8.5%(117/1383) Non CHD death, non-cancer death: 2.7%(37/1380) vs. 2.6%(36/1383) Non fatal MI: 8.4%(116/1380) vs. 9.3%(129/1383) Other CHD event: 0.2%(3/1380) vs. 0.1%(1/1383) Other cancer: 4.6%(63/1380) vs. 4.2%(58/1383) Percutaneous coronary revascularization: 11.9%(164/1380) vs. 12.7%(175/1383) Peripheral arterial disease: 6.8%(94/1380) vs. 7.8%(108/1383) Pulmonary embolism: 0.8%(11/1380) vs. 0.3%(4/1383) Resuscitated cardiac arrest: 1.4%(19/1380) vs. 0.9%(13/1383) Stroke/transient ischemic attack (tia): 7.8%(108/1380) vs. 6.9%(96/1383) Unadjudicated death: 0.3%(4/1380) vs. 0.4%(5/1383)
Hulley S et al., 2002[133]	Estrogen vs. Placebo: Any cancer: 4.2%(58/1380) vs. 3.2%(44/1383) Any death: 9.5%(131/1380) vs. 8.4%(116/1383) Biliary tract surgery: 2.9%(40/1380) vs. 1.7%(24/1383) Breast cancer: 1.1%(15/1380) vs. 1.0%(14/1383) Cardiovascular disease (CVD) death: 5.1%(71/1380) vs. 5.4%(74/1383) Cancer death: 2.2%(30/1380) vs. 1.4%(20/1383) Colon cancer: 0.7%(10/1380) vs. 0.7%(10/1383) Deep vein thrombosis: 0.9%(12/1380) vs. 0.7%(10/1383) Endometrial cancer: 0.0%(0/1380) vs. 0.2%(3/1383) Lung cancer: 0.9%(13/1380) vs. 0.6%(8/1383) Non-CVD, non-cancer death: 2.2%(30/1380) vs. 1.6%(22/1383) Other cancers: 1.7%(23/1380) vs. 0.9%(12/1383) Pulmonary embolism: 0.4%(6/1380) vs. 0.1%(2/1383) Total thromboembolic events: 1.1%(15/1380) vs. 0.8%(11/1383)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Huusko TM et al., 2002[134]	Calcitonin vs. Placebo: Death - cause not stated: 5.0%(6/121) vs. 6.6%(8/122) Local irritation: 9.9%(12/121) vs. 5.7%(7/122)
Hwang JS et al., 2006[135]	Calcitonin vs. Teriparatide: Any clinical AE: 100.0%(29/29) vs. 91.2%(31/34) Alkaline phosphatase increase: 3.4%(1/29) vs. 11.8%(4/34) Any drug-related AE: 31.0%(9/29) vs. 26.5%(9/34) Any serious AE: 3.4%(1/29) vs. 2.9%(1/34) Blood urea nitrogen increased: 3.4%(1/29) vs. 0.0%(0/34) Constipation: 3.4%(1/29) vs. 0.0%(0/34) Dizziness: 10.3%(3/29) vs. 5.9%(2/34) Dyspnea: 3.4%(1/29) vs. 0.0%(0/34) Gastrointestinal disorder: 3.4%(1/29) vs. 0.0%(0/34) Hypercalcemia: 0.0%(0/29) vs. 5.9%(2/34) Hyperuricemia: 3.4%(1/29) vs. 0.0%(0/34) Liver function abnormal: 3.4%(1/29) vs. 0.0%(0/34) Nausea: 3.4%(1/29) vs. 2.9%(1/34) Palpitations: 3.4%(1/29) vs. 0.0%(0/34) Rashes: 3.4%(1/29) vs. 0.0%(0/34) Vasodilation: 10.3%(3/29) vs. 0.0%(0/34) Vomiting: 10.3%(3/29) vs. 2.9%(1/34)
Ilter E et al., 2006[136]	Risedronate 35mg/week vs. Risedronate 5mg/day vs. Placebo: Any AE: 53.7%(22/41) vs. 56.1%(23/41) vs. 53.7%(22/41) Gastrointestinal AE: 24.4%(10/41) vs. 29.3%(12/41) vs. 22.0%(9/41) Gastrointestinal, non serious: 17.1%(7/41) vs. 19.5%(8/41) vs. 14.6%(6/41) Non-serious AE: 43.9%(18/41) vs. 46.3%(19/41) vs. 43.9%(18/41) Upper gastrointestinal bleeding: 0.0%(0/41) vs. 2.4%(1/41) vs. 0.0%(0/41)
Ishida Y et al., 2004[137]	Calcitonin vs. Estrogen vs. Etidronate vs. Vitamin D vs. Vitamin K vs. Control: Bleeding: 0.0%(0/66) vs. 3.0%(2/66) vs. 0.0%(0/66) vs. 0.0%(0/66) vs. 0.0%(0/66) vs. 0.0%(0/66) Breast tenderness: 0.0%(0/66) vs. 1.5%(1/66) vs. 0.0%(0/66) vs. 0.0%(0/66) vs. 0.0%(0/66) vs. 0.0%(0/66) GI symptoms: 0.0%(0/66) vs. 0.0%(0/66) vs. 1.5%(1/66) vs. 0.0%(0/66) vs. 0.0%(0/66) vs. 0.0%(0/66)
Iwamoto J et al., 2001[138]	Calcium vs. Etidronate vs. Vitamin K: Gastrointestinal symptoms: 8.3%(2/24) vs. 20.0%(5/25) vs. 0.0%(0/23) Other adverse effect: 0.0%(0/24) vs. 0.0%(0/25) vs. 0.0%(0/23)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Iwamoto J et al., 2005[139]	Alendronate 5 mg/d vs. Etidronate: Serious AE: 0.0%(0/25) vs. 0.0%(0/25) Thirst, itchy eruption, gastric pain, diarrhea: 4.0%(1/25) vs. 0.0%(0/25)
Jeffery JR et al., 2003[140]	Alendronate vs. Vitamin D: Cardiac problems: 0.0%(0/60) vs. 1.8%(1/57) Death from sepsis: 1.7%(1/60) vs. 0.0%(0/57) Developed cancer: 0.0%(0/60) vs. 3.5%(2/57) Graft failure: 1.7%(1/60) vs. 0.0%(0/57) Not tolerate: 3.3%(2/60) vs. 3.5%(2/57) Relapse of colitis: 1.7%(1/60) vs. 0.0%(0/57)
Jeffrey J et al., 2003[141]	Alendronate vs. Vitamin D: Death: 1.7%(1/60) vs. 0.0%(0/57)
Jodar E et al., 1997[142]	Carbimazole vs. Carbimazole plus high-dose Calcitonin vs. Carbimazole plus low-dose Calcitonin: Aqueous rhinorrhea: 0.0%(0/15) vs. 7.1%(1/14) vs. 0.0%(0/14) Discomfort, nausea: 0.0%(0/15) vs. 21.4%(3/14) vs. 7.1%(1/14) Facial flushing: 0.0%(0/15) vs. 14.3%(2/14) vs. 0.0%(0/14) Headache: 0.0%(0/15) vs. 7.1%(1/14) vs. 0.0%(0/14)
Johnell O et al., 2002[143]	Alendronate vs. Alendronate+Raloxifene vs. Raloxifene vs. Placebo: Abdominal pain: 10.8%(9/83) vs. 6.0%(5/84) vs. 7.3%(6/82) vs. 6.1%(5/82) Chest pain substernal: 7.2%(6/83) vs. 3.6%(3/84) vs. 4.9%(4/82) vs. 2.4%(2/82) Sweating: 2.4%(2/83) vs. 0.0%(0/84) vs. 1.2%(1/82) vs. 2.4%(2/82) Vasodilatation: 4.8%(4/83) vs. 4.8%(4/84) vs. 4.9%(4/82) vs. 4.9%(4/82)
Johnell O et al., 2004[144]	No previous HT: Raloxifene vs. No previous HT: placebo vs. Previous HT: Placebo vs. Previous HT: Raloxifene: Breast cancer: 0.6%(23/3614) vs. 1.5%(27/1833) vs. 2.3%(17/738) vs. 0.7%(11/1497) Cardiovascular events: 3.7%(133/3614) vs. 4.2%(76/1833) vs. 2.7%(20/738) vs. 2.9%(43/1497) Cardiovascular events in high risk subgroup: 8.5%(309/3614) vs. 13.1%(240/1833) vs. 12.7%(93/738) vs. 5.9%(88/1497) Cerebrovascular events: 1.6%(59/3614) vs. 1.8%(32/1833) vs. 1.2%(9/738) vs. 1.1%(17/1497) Coronary events: 2.1%(75/3614) vs. 2.4%(44/1833) vs. 1.5%(11/738) vs. 1.7%(26/1497) Invasive breast cancer: 0.4%(14/3614) vs. 1.3%(23/1833) vs. 2.0%(15/738) vs. 0.5%(7/1497) Invasive estrogen-receptor positive breast cancer: 0.2%(6/3614) vs. 0.9%(16/1833) vs. 1.8%(13/738) vs. 0.3%(4/1497)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Johnston CC et al., 2000[145]	Raloxifene 150 mg vs. Raloxifene 30 mg vs. Raloxifene 60 mg vs. Placebo: Abdominal pain: 9.1%(26/285) vs. 6.9%(20/288) vs. 5.6%(16/286) vs. 7.0%(20/286) Breast carcinoma: 0.4%(1/285) vs. 0.7%(2/288) vs. 0.0%(0/286) vs. 0.7%(2/286) Breast pain: 2.5%(7/285) vs. 2.4%(7/288) vs. 3.8%(11/286) vs. 3.8%(11/286) Deep thrombophlebitis: 0.0%(0/285) vs. 0.0%(0/288) vs. 0.3%(1/286) vs. 0.0%(0/286) Hot flashes: 23.5%(67/285) vs. 17.0%(49/288) vs. 25.2%(72/286) vs. 18.2%(52/286) Leg cramps: 4.9%(14/285) vs. 3.1%(9/288) vs. 4.9%(14/286) vs. 2.8%(8/286) Leukorrhea: 2.5%(7/285) vs. 2.4%(7/288) vs. 2.8%(8/286) vs. 1.0%(3/286) Nausea: 8.1%(23/285) vs. 5.9%(17/288) vs. 6.3%(18/286) vs. 8.0%(23/286) Peripheral edema: 2.5%(7/285) vs. 2.4%(7/288) vs. 4.5%(13/286) vs. 2.1%(6/286) Vaginal hemorrhage: 1.4%(4/285) vs. 0.3%(1/288) vs. 2.8%(8/286) vs. 3.5%(10/286) Vaginitis: 5.3%(15/285) vs. 5.9%(17/288) vs. 3.8%(11/286) vs. 4.2%(12/286)
Jolly EE et al., 2003[146]	Raloxifene vs. Placebo: Endometrial thickness > 5mm: 18.9%(35/185) vs. 16.8%(24/143) Hot flashes: 25.4%(47/185) vs. 14.7%(21/143) Leg cramps: 6.5%(12/185) vs. 4.9%(7/143) Vaginal bleeding: 3.2%(6/185) vs. 2.8%(4/143) Venous thromboembolic events: 0.0%(0/185) vs. 0.0%(0/143)
Kananen K et al., 2005[147]	Estrogen+Calcium+Vitamin D vs. Pamidronate: Death: 30.6%(15/49) vs. 26.0%(13/50) Secondary cancer: 0.0%(0/49) vs. 2.0%(1/50)
Kaufman JM et al., 2005[148]	Teriparitide 20ug vs. Teriparitide 40ug vs. Placebo: Osteosarcoma: 0.0%(0/92) vs. 0.0%(0/84) vs. 0.0%(0/103)
Keegan TH et al., 2004[149]	Alendronate diabetic vs. Alendronate non diabetic vs. Placebo diabetic vs. Placebo non diabetic: AE resulting in hospitalization: 10.8%(16/148) vs. 4.9%(151/3087) vs. 8.7%(13/149) vs. 4.8%(147/3074) Abdominal pain: 27.0%(40/148) vs. 13.1%(403/3087) vs. 14.8%(22/149) vs. 13.0%(400/3074) Acid regurgitation/reflux: 8.8%(13/148) vs. 8.5%(262/3087) vs. 6.7%(10/149) vs. 8.3%(255/3074) Any UGI event: 53.4%(79/148) vs. 43.2%(1334/3087) vs. 45.6%(68/149) vs. 43.2%(1327/3074) Esophageal ulcer: 0.7%(1/148) vs. 0.2%(6/3087) vs. 0.0%(0/149) vs. 0.2%(6/3074) Esophagitis: 2.7%(4/148) vs. 0.7%(22/3087) vs. 0.7%(1/149) vs. 0.4%(13/3074) Other esophageal: 2.0%(3/148) vs. 1.8%(57/3087) vs. 2.0%(3/149) vs. 1.6%(49/3074)
Kendler D et al., 2004[150]	Alendronate once daily then once weekly vs. Alendronate once weekly then once daily: Body as a whole: 8.0%(16/205) vs. 10.0%(20/201) Digestive system: 10.0%(21/205) vs. 7.0%(14/201)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Kenny AM et al., 2001[151]	Testosterone vs. Placebo: Elevated PSA: 17.6%(6/34) vs. 9.1%(3/33) Intercurrent illness: 11.8%(4/34) vs. 15.2%(5/33) Rash: 8.8%(3/34) vs. 3.0%(1/33) Rash with induration, score of 2 or greater: 77.0%(26/34) vs. 40.0%(13/33)
Kim SH et al., 2004[152]	Pamidronate vs. Placebo: Hypocalcemia: 4.0%(1/25) vs. 0.0%(0/25)
Kishimoto H et al., 2006[153]	Risedronate17.5 mg/w vs. Risedronate2.5/d: Abnormal Laboratory Parameters: 8.8%(22/249) vs. 15.0%(37/247) Drug Related - Other GI AE: 0.4%(1/249) vs. 2.4%(6/247) Drug Related Abdominal distention: 0.4%(1/249) vs. 1.6%(4/247) Drug Related Constipation: 2.4%(6/249) vs. 3.6%(9/247) Drug Related Dyspepsia: 0.4%(1/249) vs. 1.2%(3/247) Drug Related Gastritis: 0.8%(2/249) vs. 1.2%(3/247) Drug Related Stomach discomfort: 6.0%(15/249) vs. 5.3%(13/247) Drug Related Upper Abdominal pain: 1.6%(4/249) vs. 2.0%(5/247) Other AE: 51.4%(128/249) vs. 40.1%(99/247) Other Drug Related AEs: 12.9%(32/249) vs. 14.6%(36/247)
Kotaniemi A et al., 1996[154]	Calcitonin+ Calcium vs. Control+ Calcium: Adverse event: 25.0%(8/32) vs. 16.1%(5/31) Dyspepsia: 0.0%(0/32) vs. 6.5%(2/31) Facial flush: 9.4%(3/32) vs. 0.0%(0/31) Gingival pain: 0.0%(0/32) vs. 3.2%(1/31) Hip arthroplasty: 0.0%(0/32) vs. 3.2%(1/31) Increased joint pain & morning stiffness: 0.0%(0/32) vs. 3.2%(1/31) Loose stools: 0.0%(0/32) vs. 3.2%(1/31) Metastatic cancer: 3.1%(1/32) vs. 0.0%(0/31)
Kristensen B et al., 1994[155]	Control vs. Tamoxifen: Hot flushes: 12.0%(3/25) vs. 20.0%(5/25) Recurrence of breast cancer AFTER trial stopped: 8.0%(2/25) vs. 4.0%(1/25)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Kung AW et al., 2000[156]	Alendronate vs. Placebo: Acid regurgitation: 0.0%(0/35) vs. 2.9%(1/35) Acute antral gastric ulcer: 2.9%(1/35) vs. 0.0%(0/35) Antral gastric ulcer - upper intestinal bleeding: 2.9%(1/35) vs. 0.0%(0/35) Chest pain: 0.0%(0/35) vs. 2.9%(1/35) Constipation: 8.6%(3/35) vs. 5.7%(2/35) Dizziness: 2.9%(1/35) vs. 8.6%(3/35) Dry mouth: 0.0%(0/35) vs. 2.9%(1/35) Esophageal ulcer: 0.0%(0/35) vs. 0.0%(0/35) Flatulence: 8.6%(3/35) vs. 8.6%(3/35) Gastric ulcer: 5.7%(2/35) vs. 0.0%(0/35) Gastritis: 0.0%(0/35) vs. 0.0%(0/35) Generalized muscle pain: 0.0%(0/35) vs. 2.9%(1/35) Malaise: 2.9%(1/35) vs. 0.0%(0/35) Mouth ulcer: 0.0%(0/35) vs. 2.9%(1/35) Muscle cramp: 8.6%(3/35) vs. 0.0%(0/35) Musculoskeletal pain: 0.0%(0/35) vs. 2.9%(1/35) Reflux esophagitis: 0.0%(0/35) vs. 0.0%(0/35)
Kung AW et al., 2003[157]	Raloxifene vs. Placebo: Dizziness: 1.7%(8/483) vs. 2.9%(14/485) Dyspepsia: 2.9%(14/483) vs. 0.8%(4/485) Leg cramps: 4.3%(21/483) vs. 2.7%(13/485) Peripheral edema: 0.4%(2/483) vs. 0.4%(2/485) Serious treatment-emergent AE: 2.7%(13/483) vs. 2.5%(12/485) Sweating: 0.6%(3/483) vs. 0.6%(3/485) Vasodilatation: 5.6%(27/483) vs. 3.5%(17/485) Venous thromboembolic events: 0.0%(0/483) vs. 0.0%(0/485) Venous thromboembolism: 0.0%(0/483) vs. 0.0%(0/485)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Kung AW et al., 2006[158]	Calcitonin vs. Teriparatide: Any AE: 73.7%(42/57) vs. 68.1%(32/47) Acute myocardial infarction: 0.0%(0/57) vs. 2.1%(1/47) Car accident: 1.8%(1/57) vs. 0.0%(0/47) Cerebral infarct: 0.0%(0/57) vs. 2.1%(1/47) Chest pain: 1.8%(1/57) vs. 0.0%(0/47) Contusion: 5.3%(3/57) vs. 0.0%(0/47) Cough: 7.0%(4/57) vs. 6.4%(3/47) Dizziness: 21.1%(12/57) vs. 10.6%(5/47) Fall and facial injury: 0.0%(0/57) vs. 2.1%(1/47) Flushing: 5.3%(3/57) vs. 0.0%(0/47) Headache: 8.8%(5/57) vs. 0.0%(0/47) Hot flush: 5.3%(3/57) vs. 0.0%(0/47) Injection site bruising: 0.0%(0/57) vs. 6.4%(3/47) Muscle cramp: 8.8%(5/57) vs. 2.1%(1/47) Musculoskeletal pain: 0.0%(0/57) vs. 2.1%(1/47) Nausea: 22.8%(13/57) vs. 12.8%(6/47) Pain in extremity: 5.3%(3/57) vs. 4.3%(2/47) Paresthesia: 5.3%(3/57) vs. 2.1%(1/47) Rash: 5.3%(3/57) vs. 2.1%(1/47) Signs of congestive heart failure and severe aortic stenosis with double vessel disease: 1.8%(1/57) vs. 0.0%(0/47) Transient ischemic attack: 1.8%(1/57) vs. 0.0%(0/47) UTI: 5.3%(3/57) vs. 2.1%(1/47) Upper respiratory tract infection: 1.8%(1/57) vs. 8.5%(4/47) Vomiting: 5.3%(3/57) vs. 4.3%(2/47)
Kurland ES et al., 2000[159]	Control vs. PTH: Hypercalcemia: 0.0%(0/13) vs. 20.0%(2/10) Redness at the injection site: 7.7%(1/13) vs. 50.0%(5/10)
Kushida K et al., 2002[160]	Alendronate vs. Vitamin D: Changes in lab test results that were considered clinically important: 14.5%(28/190) vs. 19.2%(34/175) Death: 0.0%(0/190) vs. 0.6%(1/175) Death (considered unrelated to the study treatment): 0.0%(0/190) vs. 0.6%(1/175) Gastric related symptoms(stomachache, heaviness, discomfort, fullness) and gastritis: 8.4%(16/190) vs. 5.7%(10/175) Gastrointestinal disorders: 18.4%(35/190) vs. 16.0%(28/175) People with =1 AE: 23.2%(44/190) vs. 21.7%(38/175)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Kushida K et al., 2004[161]	Etidronate vs. Risedronate: Any AE: 93.1%(255/274) vs. 91.2%(249/273) Abdominal distension: 2.2%(6/274) vs. 0.7%(2/273) Abnormal laboratory parameters: 7.3%(20/274) vs. 10.6%(29/273) Any drug related AE: 32.8%(90/274) vs. 31.5%(86/273) Constipation: 2.2%(6/274) vs. 0.7%(2/273) Epigastric pain: 6.9%(19/274) vs. 6.2%(17/273) Gastrointestinal disorders**: 19.7%(54/274) vs. 17.6%(48/273) General disorders: 1.5%(4/274) vs. 2.6%(7/273) Musculoskeletal and connective tissue disorders: 2.9%(8/274) vs. 1.5%(4/273) Nausea: 1.8%(5/274) vs. 2.2%(6/273) Nervous system disorders: 3.3%(9/274) vs. 2.9%(8/273) Skin and subcutaneous disorders: 2.9%(8/274) vs. 2.2%(6/273)
Kushida K et al., 2004[162]	Alendronate vs. Vitamin D: Abdominal pain: 0.0%(0/90) vs. 2.5%(2/80) Constipation: 3.3%(3/90) vs. 3.8%(3/80) Drug-related AEs - subjective symptoms/objective symptoms: 22.2%(20/90) vs. 16.3%(13/80) Drug-related AEs -laboratory abnormal findings: 12.2%(11/90) vs. 15.0%(12/80) Gastritis: 5.6%(5/90) vs. 3.8%(3/80) Incidence of gastrointestinal AEs: 14.4%(13/90) vs. 13.8%(11/80) Stomach discomfort: 2.2%(2/90) vs. 0.0%(0/80) Stomach heaviness: 2.2%(2/90) vs. 0.0%(0/80)
Lane NE et al., 1998[163]	Estrogen vs. Estrogen+ PTH: Hypercalcemia: 0.0%(0/23) vs. 10.7%(3/28) Hypercalciuria: 4.3%(1/23) vs. 3.6%(1/28)
Lau EM et al., 2000[164]	Alendronate vs. Placebo: Back pain: 1.9%(1/53) vs. 0.0%(0/47) Constipation: 1.9%(1/53) vs. 0.0%(0/47) Eye pain: 0.0%(0/53) vs. 2.1%(1/47) Leg pain: 1.9%(1/53) vs. 0.0%(0/47) Mild gastric discomfort: 3.8%(2/53) vs. 4.3%(2/47)
Lau EM et al., 2001[165]	Alendronate vs. Placebo: Mild gastric discomfort: 10.0%(5/50) vs. 0.0%(0/50) Nausea/abdominal pain: 12.0%(6/50) vs. 8.0%(4/50) Vague musculoskeletal discomfort: 4.0%(2/50) vs. 0.0%(0/50)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Layton D et al., 2005[166]	Raloxifene: Abnormal liver function tests: 0.1%(15/13987) Amaurosis fugax: 0.0%(5/13987) Amnesia: 0.2%(27/13987) Anaphylaxis: 0.0%(1/13987) Angioneurotic edema: 0.0%(2/13987) Anxiety: 0.9%(129/13987) Bradycardia: 0.0%(3/13987) Breast carcinoma: 0.2%(32/13987) Cardiovascular death: 0.2%(21/13987) Cataract: 0.0%(1/13987) Cerebrovascular attack, transient ischemic attack: 0.4%(60/13987) Cramp and limb pain: 3.4%(476/13987) Death - GI hemorrhage with a bleeding gastric ulcer: 0.0%(1/13987) Death - perforated duodenal ulcer: 0.0%(1/13987) Death - polycythemia rubra vera: 0.0%(1/13987) Death - thromboembolism (CVA, PE, myocardial infarction (MI)): 0.1%(14/13987) Death by neutropenia sepsis: 0.0%(1/13987) Death- GI hemorrhage: 0.0%(1/13987) Deaths (other): 0.7%(103/13987) Deep vein thrombosis: 0.1%(13/13987) Depression: 1.6%(222/13987) Diabetes mellitus: 0.3%(48/13987) Diarrhea: 1.1%(153/13987) Distension abdominal: 0.6%(84/13987) Dizziness: 1.0%(142/13987) Dyspepsia: 2.2%(302/13987) Edema: 1.9%(270/13987) Erythema multiforme: 0.0%(2/13987) Esophageal stricture: 0.0%(1/13987) Esophageal ulcer: 0.0%(1/13987) Flatulence: 0.2%(29/13987) Flushing: 6.5%(909/13987) Headache, migraine: 2.2%(302/13987) Hematuria: 0.1%(16/13987)

Author, Year, Drug, Country, Trial name	Adverse events reported
Layton D et al., 2005[166]	Raloxifene (continued): Hemorrhage GI: 0.1%(10/13987) Hemorrhage rectal: 0.2%(27/13987) Hemorrhage vaginal: 0.6%(79/13987) Hyperlipidemia: 0.2%(21/13987) Hypertension: 1.1%(156/13987) Insomnia: 0.6%(83/13987) Intolerance: 1.6%(228/13987) Ischemic heart disease: 0.5%(67/13987) Jaundice: 0.0%(3/13987) Leukopenia: 0.0%(0/13987) Malaise, lassitude: 2.4%(335/13987) Malignancies: 0.8%(110/13987) Mastalgia: 0.8%(105/13987) Mood change: 0.1%(16/13987) Nausea, vomiting: 1.8%(253/13987) Neutropenia: 0.1%(7/13987) Paget's ductal carcinoma: 0.0%(1/13987) Pain abdomen: 1.6%(222/13987) Pain back: 1.8%(250/13987) Pain limb: 1.7%(241/13987) Peptic ulcer: 0.1%(8/13987) Pulmonary embolus: 0.1%(13/13987) Renal failure: 0.0%(3/13987) Respiratory tract infection higher: 3.0%(417/13987) Retinal vein thrombosis: 0.0%(2/13987) Stevens Johnson syndrome: 0.0%(1/13987) Sweating: 1.6%(229/13987) Thrombocytopenia: 0.0%(3/13987) Thrombophlebitis: 0.2%(31/13987) Unspecified side effects: 0.6%(90/13987) Urogenital bleeding event: 0.9%(121/13987) Visual deterioration within 2 hours of the first dose in pt with history of left central retinal vein occlusion: 0.0%(1/13987)

Author, Year, Drug, Country, Trial name	Adverse events reported
Lees B et al., 1996[167]	Pamidronate 150mg vs. Pamidronate 300mg vs. Placebo: Esophagitis: 0.0%(0/41) vs. 2.6%(1/38) vs. 0.0%(0/42) Flatulence: 0.0%(0/41) vs. 0.0%(0/38) vs. 2.4%(1/42) Leg-cramps: 0.0%(0/41) vs. 0.0%(0/38) vs. 2.4%(1/42) Nausea: 26.8%(11/41) vs. 31.6%(12/38) vs. 7.1%(3/42) Nausea/indigestion: 7.3%(3/41) vs. 26.3%(10/38) vs. 0.0%(0/42) Pyrexia: 2.4%(1/41) vs. 2.6%(1/38) vs. 0.0%(0/42) Skin rash: 2.4%(1/41) vs. 0.0%(0/38) vs. 0.0%(0/42) Trembling: 0.0%(0/41) vs. 2.6%(1/38) vs. 0.0%(0/42)
Lindsay R et al., 1997[168]	Estrogen vs. Estrogen+ PTH: Back pain: 0.0%(0/17) vs. 5.9%(1/17) Breast cancer: 0.0%(0/17) vs. 5.9%(1/17) Otosclerosis: 0.0%(0/17) vs. 5.9%(1/17) Subcutaneous nodules at injection site: 0.0%(0/17) vs. 11.8%(2/17) Urinary tract infection & possible renal stone: 0.0%(0/17) vs. 5.9%(1/17)
Lindsay R et al., 1999[169]	Alendronate, Estrogen vs. Estrogen+ Placebo: Back pain: 10.0%(21/214) vs. 3.0%(6/214) GI adverse events: 10.7%(23/214) vs. 10.7%(23/214) Serious AE: 6.0%(13/214) vs. 8.0%(17/214)
Lindsay R et al., 2002[170]	CEE 0.3mg vs. CEE 0.3mg/MPA 1.5mg vs. CEE 0.45/MPA 1.5mg vs. CEE 0.45mg vs. CEE 0.45mg/MPA 2.5mg vs. CEE 0.625 vs. CEE 0.625/MPA 2.5mg vs. Placebo: AE: 6.3%(6/96) vs. 1.9%(2/107) vs. 7.8%(8/103) vs. 10.6%(11/104) vs. 4.6%(5/108) vs. 21.4%(22/103) vs. 6.1%(6/98) vs. 2.9%(3/103)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Liu JL et al., 2004[171]	Raloxifene vs. Placebo: Allergic dermatitis: 2.0%(2/102) vs. 0.0%(0/102) Arrhythmia: 2.0%(2/102) vs. 1.0%(1/102) Cerebrovascular disorder: 2.0%(2/102) vs. 0.0%(0/102) Diarrhea: 1.0%(1/102) vs. 5.9%(6/102) Enteritis: 1.0%(1/102) vs. 2.9%(3/102) Exostosis: 0.0%(0/102) vs. 2.0%(2/102) Herpes zoster: 0.0%(0/102) vs. 2.9%(3/102) Hot flushes: 2.9%(3/102) vs. 1.0%(1/102) Hypertension: 2.0%(2/102) vs. 3.9%(4/102) Muscle cramps: 8.8%(9/102) vs. 3.9%(4/102) Nasopharyngitis: 16.7%(17/102) vs. 19.6%(20/102) Non-specific urethritis: 2.9%(3/102) vs. 0.0%(0/102) Serious adverse events*: 2.0%(2/102) vs. 4.9%(5/102) UTI: 2.0%(2/102) vs. 2.0%(2/102) Uri: 3.9%(4/102) vs. 1.0%(1/102)
Love RR et al., 1992[172]	Tamoxifen vs. Placebo: Breast cancer recurrence resulting in dropout: 2.9%(2/70) vs. 7.1%(5/70) Depression and hot flashes: 2.9%(2/70) vs. 0.0%(0/70) Dropout because of AEs: 7.1%(5/70) vs. 5.7%(4/70)
Luckey M et al., 2004[173]	Alendronate vs. Raloxifene: Any AE: 73.5%(164/223) vs. 74.2%(173/233) Abdominal pain: 3.2%(7/223) vs. 1.7%(4/233) Any UGI AE: 17.0%(38/223) vs. 15.5%(36/233) Any drug related AE: 25.6%(57/223) vs. 26.6%(62/233) Any drug related UGI AE: 10.8%(24/223) vs. 10.3%(24/233) Any drug related vasomotor AE: 4.0%(9/223) vs. 6.9%(16/233) Any serious AE: 4.9%(11/223) vs. 6.9%(16/233) Any vasomotor AE: 4.5%(10/223) vs. 7.3%(17/233) Deep venous thrombosis: 0.0%(0/223) vs. 0.4%(1/233) Dyspepsia: 3.2%(7/223) vs. 2.6%(6/233) Heartburn: 2.7%(6/223) vs. 1.7%(4/233) Nausea: 5.9%(13/223) vs. 5.2%(12/233) Serious upper GI - abdominal pain: 0.0%(0/223) vs. 0.4%(1/233) Serious upper GI - gastroenteritis: 0.0%(0/223) vs. 0.4%(1/233) Serious upper GI - microperforation of the distal duodenum: 0.4%(1/223) vs. 0.0%(0/233)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Luckey MM et al., 2003[174]	Alendronate 35mg once weekly vs. Alendronate 5mg daily: Abdominal distention: 2.8%(10/362) vs. 3.3%(12/361) Abdominal pain: 7.2%(26/362) vs. 5.8%(21/361) Acid regurgitation: 6.9%(25/362) vs. 6.1%(22/361) Dyspepsia: 4.4%(16/362) vs. 4.4%(16/361) Esophagitis: 0.0%(0/362) vs. 0.0%(0/361) Gastric ulcer: 0.3%(1/362) vs. 0.0%(0/361) Nausea: 3.9%(14/362) vs. 6.1%(22/361) Patients with one or more upper GI adverse experiences: 25.1%(91/362) vs. 24.1%(87/361) Vomiting: 2.5%(9/362) vs. 5.0%(18/361)
Luengo M et al., 1994[175]	Calcitonin vs. Control: Facial redness: 9.1%(2/22) vs. 0.0%(0/22) Generalized pruritis: 4.5%(1/22) vs. 0.0%(0/22) Nausea alone: 9.1%(2/22) vs. 0.0%(0/22) Rhinorrhea: 9.1%(2/22) vs. 0.0%(0/22) Rhinorrhea and nausea: 4.5%(1/22) vs. 0.0%(0/22)
Lufkin EG et al., 1992[176]	Estrogen+ Progesterone vs. Placebo: Breast cancer: 2.8%(1/36) vs. 2.6%(1/39) Breast tenderness: 55.6%(20/36) vs. 5.1%(2/39) Endometrial hyperplasia: 8.3%(3/36) vs. 0.0%(0/39) Skin irritation: 11.1%(4/36) vs. 10.3%(4/39)
Lufkin EG et al., 1994[177]	Pamidronate vs. Placebo: Erosive esophagitis causing severe epigastric pain, dysphagia, vomiting: 12.1%(4/33) vs. 0.0%(0/16) Erosive esophagitis resulting in severe epigastric pain, dysphagia, vomiting: 15.2%(5/33) vs. 0.0%(0/16) Hiatal hernia: 6.1%(2/33) vs. 0.0%(0/16) Weight loss: 3.0%(1/33) vs. 0.0%(0/16)
Lyritis GP et al., 1997[178]	Calcitonin vs. Placebo: Mild symptoms, mostly headache: 12.0%(6/50) vs. 0.0%(0/50)
Lyritis GP et al., 1999[179]	Calcitonin vs. Placebo: Enteric disturbances: 5.0%(1/20) vs. 0.0%(0/20) Mild dizziness: 36.8%(7/20) vs. 6.3%(1/20) Mild enteric disturbance: 57.9%(12/20) vs. 43.8%(9/20)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Mackay FJ et al., 1998[180]	Alendronate: Asthma, wheezing: 1.2%(19/1523) Back pain: 2.8%(43/1523) Constipation: 1.1%(17/1523) Cough: 1.4%(22/1523) Diarrhea: 2.6%(39/1523) Dizziness: 1.0%(15/1523) Dyspepsia: 6.0%(91/1523) Headache, migraine: 1.3%(20/1523) Joint pain: 2.2%(33/1523) Malaise, lassitude: 2.8%(43/1523) Nausea, vomiting: 4.4%(67/1523) Pain abdomen: 4.0%(61/1523) Respiratory tract infection: 7.7%(117/1523) UTI: 2.0%(31/1523)
Manson JE et al., 2003[181]	Estrogen with progestin vs. Placebo: Acute coronary syndrome: 3.8%(322/8506) vs. 3.7%(299/8102) CABG or PTCA: 2.5%(214/8506) vs. 2.5%(205/8102) CHD - death: 0.5%(39/8506) vs. 0.4%(34/8102) CHD - nonfatal MI - other: 1.7%(147/8506) vs. 1.3%(109/8102) CHD - nonfatal MI - silent MI: 0.0%(4/8506) vs. 0.1%(5/8102) Congestive heart failure: 1.3%(113/8506) vs. 1.3%(109/8102) Hospitalization for angina (angina confirmed): 1.2%(106/8506) vs. 1.6%(126/8102) Hospitalization for angina (unconfirmed): 0.8%(66/8506) vs. 0.9%(69/8102) Hot flashes, night sweats, or both: 0.2%(21/8506) vs. 0.2%(17/8102) Other CHD AE: 0.4%(37/8506) vs. 0.4%(33/8102)
Masud T et al., 1998[182]	Etidronate vs. Etidronate+ Vitamin D: Mild asymptomatic hypercalcemia: 0.0%(0/28) vs. 3.3%(1/30) Mild rash: 0.0%(0/28) vs. 3.3%(1/30) Minor gastrointestinal side effects: 10.7%(3/28) vs. 3.3%(1/30)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
McClung M et al., 1998[183]	Alendronate 10mg/d vs. Alendronate 20/0 mg/d vs. Alendronate 5mg/d vs. Alendronate 1 mg/d vs. Placebo: >=1 clinically significant UGI AE: 29.5%(26/88) vs. 31.5%(28/89) vs. 26.1%(23/88) vs. 26.1%(24/92) vs. 28.9%(26/90) At least one AE: 97.7%(86/88) vs. 94.4%(84/89) vs. 92.0%(81/88) vs. 92.4%(85/92) vs. 91.1%(82/90) Flatulence: 5.7%(5/88) vs. 5.6%(5/89) vs. 1.1%(1/88) vs. 1.1%(1/92) vs. 1.1%(1/90) Odynophagia: 3.4%(3/88) vs. 3.4%(3/89) vs. 0.0%(0/88) vs. 0.0%(0/92) vs. 0.0%(0/90) One or more AE: 97.7%(86/88) vs. 94.4%(84/89) vs. 92.0%(81/88) vs. 92.4%(85/92) vs. 91.1%(82/90) One or more clinically sign. Upper GI AE: 29.5%(26/88) vs. 31.5%(28/89) vs. 26.1%(23/88) vs. 26.1%(24/92) vs. 28.9%(26/90) Serious AE: 14.8%(13/88) vs. 14.8%(13/88) vs. 9.0%(8/89) vs. 9.0%(8/89) vs. 11.4%(10/88) vs. 11.4%(10/88) vs. 5.4%(5/92) vs. 5.4%(5/92) vs. 10.0%(9/90) vs. 10.0%(9/90)
McClung MR et al., 2001[184]	Risedronate 2.5mg vs. Risedronate 5mg vs. Placebo: Any AE: 89.3%(2762/3093) vs. 89.8%(2786/3104) vs. 89.5%(2805/3134) Abdominal pain: 8.2%(255/3093) vs. 8.1%(250/3104) vs. 9.2%(288/3134) Any AE of upper GI tract: 22.3%(690/3093) vs. 21.2%(657/3104) vs. 21.8%(684/3134) Dyspepsia: 8.4%(259/3093) vs. 8.2%(255/3104) vs. 8.1%(254/3134) Esophageal ulcer: 0.3%(9/3093) vs. 0.3%(9/3104) vs. 0.4%(14/3134) Esophagitis: 1.5%(47/3093) vs. 1.7%(54/3104) vs. 1.9%(59/3134) Mod to severe: 8.4%(259/3093) vs. 9.0%(279/3104) vs. 8.2%(258/3134) Serious AE: 30.6%(946/3093) vs. 30.4%(943/3104) vs. 31.0%(973/3134)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
McClung MR et al., 2004[185]	Ibandronate 0.5mg vs. Ibandronate 1mg vs. Ibandronate 2.5mg vs. Placebo: Any AE: 92.0%(149/162) vs. 95.0%(158/166) vs. 98.0%(160/163) vs. 93.0%(151/162) Any drug related AE: 12.0%(19/162) vs. 13.0%(22/166) vs. 9.0%(15/163) vs. 12.0%(19/162) Any drug related serious AE: 0.0%(0/162) vs. 0.0%(0/166) vs. 0.0%(0/163) vs. 0.0%(0/162) Any serious AE: 6.0%(10/162) vs. 13.0%(22/166) vs. 5.0%(8/163) vs. 8.0%(13/162) Dyspepsia: 16.0%(26/162) vs. 14.0%(23/166) vs. 15.0%(24/163) vs. 14.0%(23/162) Dysphagia: 2.0%(3/162) vs. 1.0%(2/166) vs. 1.0%(2/163) vs. 0.0%(0/162) Eructation: 1.0%(2/162) vs. 1.0%(2/166) vs. 1.0%(2/163) vs. 1.0%(2/162) Esophagitis: 1.0%(2/162) vs. 0.0%(0/166) vs. 1.0%(2/163) vs. 1.0%(2/162) GI carcinoma: 0.0%(0/162) vs. 0.0%(0/166) vs. 1.0%(2/163) vs. 0.0%(0/162) GI disorder: 1.0%(2/162) vs. 2.0%(3/166) vs. 0.0%(0/163) vs. 3.0%(5/162) GI hemorrhage: 0.0%(0/162) vs. 0.0%(0/166) vs. 0.0%(0/163) vs. 1.0%(2/162) GI pain: 2.0%(3/162) vs. 0.0%(0/166) vs. 4.0%(7/163) vs. 4.0%(6/162) Gastritis: 0.0%(0/162) vs. 1.0%(2/166) vs. 2.0%(3/163) vs. 1.0%(2/162) Gastroenteritis: 9.0%(15/162) vs. 4.0%(7/166) vs. 5.0%(8/163) vs. 6.0%(10/162) Hemorrhagic gastritis: 1.0%(2/162) vs. 0.0%(0/166) vs. 0.0%(0/163) vs. 0.0%(0/162) Nausea: 6.0%(10/162) vs. 1.0%(2/166) vs. 4.0%(7/163) vs. 3.0%(5/162) Vomiting: 2.0%(3/162) vs. 0.0%(0/166) vs. 1.0%(2/163) vs. 0.0%(0/162)
McClung MR et al., 2004[186]	Alendronate 2.5mg vs. Alendronate 5mg vs. Placebo: Acid regurgitation: 9.7%(16/165) vs. 5.4%(9/168) vs. 6.7%(17/252) Digestive system disorders: 69.1%(114/165) vs. 71.4%(120/168) vs. 64.7%(163/252) Dyspepsia: 15.8%(26/165) vs. 18.5%(31/168) vs. 13.9%(35/252) Laboratory: one or more AE: 26.7%(44/165) vs. 20.8%(35/168) vs. 27.8%(70/252) Nausea: 7.3%(12/165) vs. 10.7%(18/168) vs. 13.1%(33/252) One or more AE: 95.8%(158/165) vs. 96.4%(162/168) vs. 94.0%(237/252) Serious AE: 18.8%(31/165) vs. 15.5%(26/168) vs. 16.3%(41/252) Vomiting: 7.3%(12/165) vs. 7.7%(13/168) vs. 7.1%(18/252)
McClung MR et al., 2005[187]	Alendronate vs. PTH: Hypercalcemia: 0.0%(0/101) vs. 2.9%(3/102) Moderate to severe back pain: 33.0%(33/101) vs. 15.0%(15/102) New or worsening back pain: 39.0%(39/101) vs. 26.0%(27/102) Severe back pain: 12.0%(12/101) vs. 4.0%(4/102)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
McClung MR et al., 2006[188]	Alendronate vs. Denosumab vs. Placebo: Any AE: 91.3%(42/46) vs. 87.3%(274/314) vs. 89.1%(41/46) Abnormal clinical laboratory investigation: 0.0%(0/46) vs. 0.3%(1/314) vs. 0.0%(0/46) Arthralgia: 6.5%(3/46) vs. 15.0%(47/314) vs. 23.9%(11/46) Back pain: 8.7%(4/46) vs. 11.5%(36/314) vs. 8.7%(4/46) Cardiac disorder: 0.0%(0/46) vs. 0.6%(2/314) vs. 4.3%(2/46) Contusion: 2.2%(1/46) vs. 5.1%(16/314) vs. 4.3%(2/46) Death: 0.0%(0/46) vs. 0.0%(0/314) vs. 0.0%(0/46) Diarrhea: 4.3%(2/46) vs. 6.7%(21/314) vs. 6.5%(3/46) Dyspepsia: 26.1%(12/46) vs. 8.6%(27/314) vs. 6.5%(3/46) Gastroesophageal reflux: 8.7%(4/46) vs. 7.0%(22/314) vs. 2.2%(1/46) General disorder: 0.0%(0/46) vs. 0.6%(2/314) vs. 0.0%(0/46) Headache: 10.9%(5/46) vs. 8.9%(28/314) vs. 13.0%(6/46) Hypertension: 8.7%(4/46) vs. 6.4%(20/314) vs. 0.0%(0/46) Infection: 0.0%(0/46) vs. 1.0%(3/314) vs. 0.0%(0/46) Influenza: 6.5%(3/46) vs. 8.0%(25/314) vs. 2.2%(1/46) Injury, poisoning or procedural complication: 0.0%(0/46) vs. 0.3%(1/314) vs. 2.2%(1/46) Metabolic and nutritional disorder: 2.2%(1/46) vs. 0.0%(0/314) vs. 0.0%(0/46) Musculoskeletal or connective-tissue disorder: 0.0%(0/46) vs. 0.6%(2/314) vs. 2.2%(1/46) Nasopharyngitis: 10.9%(5/46) vs. 14.6%(46/314) vs. 13.0%(6/46) Nausea: 17.4%(8/46) vs. 8.6%(27/314) vs. 4.3%(2/46) Neoplasm: 0.0%(0/46) vs. 1.9%(6/314) vs. 0.0%(0/46) Nervous system disorder: 0.0%(0/46) vs. 0.3%(1/314) vs. 0.0%(0/46) Pain in extremity: 10.9%(5/46) vs. 8.0%(25/314) vs. 8.7%(4/46) Rash: 4.3%(2/46) vs. 5.1%(16/314) vs. 0.0%(0/46) Serious AE: 2.2%(1/46) vs. 5.7%(18/314) vs. 4.3%(2/46) Sinusitis: 6.5%(3/46) vs. 6.1%(19/314) vs. 6.5%(3/46) Upper respiratory tract infection: 17.4%(8/46) vs. 19.4%(61/314) vs. 13.0%(6/46) Urinary tract infection: 6.5%(3/46) vs. 8.0%(25/314) vs. 0.0%(0/46) Vascular disorder: 0.0%(0/46) vs. 0.3%(1/314) vs. 0.0%(0/46)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Mellstrom DD et al., 2004[189]	Risedronate vs. Risedronate+ Placebo: AE: 10.8%(9/83) vs. 9.9%(8/81) Abdominal pain: 3.6%(3/83) vs. 1.2%(1/81) Dyspepsia: 2.4%(2/83) vs. 2.5%(2/81) Dysphagia: 0.0%(0/83) vs. 1.2%(1/81) Esophagitis: 2.4%(2/83) vs. 0.0%(0/81) Moderate to severe upper GI tract AE: 3.6%(3/83) vs. 3.7%(3/81) Peptic ulcer: 2.4%(2/83) vs. 1.2%(1/81) Upper GI AE: 9.6%(8/83) vs. 8.6%(7/81)
Merza Z et al., 2006[190]	Testosterone vs. Placebo: Hematocrit rise above reference range: 15.0%(3/20) vs. 5.3%(1/19)
Meunier PJ et al., 1997[191]	Etidronate vs. Placebo: Abdominal pain: 14.8%(4/27) vs. 3.7%(1/27) Adverse effect: 96.3%(26/27) vs. 96.3%(26/27) Asthenia: 22.2%(6/27) vs. 29.6%(8/27) Constipation: 11.1%(3/27) vs. 0.0%(0/27) Diarrhea: 3.7%(1/27) vs. 14.8%(4/27) Dyspepsia: 11.1%(3/27) vs. 7.4%(2/27) Flatulence: 3.7%(1/27) vs. 11.1%(3/27) Flu syndrome: 18.5%(5/27) vs. 14.8%(4/27) Gastroenteritis: 3.7%(1/27) vs. 11.1%(3/27) Nausea: 14.8%(4/27) vs. 11.1%(3/27) Pain: 18.5%(5/27) vs. 18.5%(5/27) Serious AEs: 7.4%(2/27) vs. 22.2%(6/27) Severe gastrointestinal: 0.0%(0/27) vs. 0.0%(0/27)
Meunier PJ et al., 1999[192]	Raloxifene 150mg vs. Raloxifene 60mg vs. Placebo: Deep venous thrombosis: 0.0%(0/42) vs. 0.0%(0/45) vs. 0.0%(0/42) Hot flushes: 14.3%(6/42) vs. 8.9%(4/45) vs. 9.5%(4/42) Retinal vein thrombosis: 0.0%(0/42) vs. 0.0%(0/45) vs. 2.4%(1/42)

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AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Michalska D et al., 2006[193]	Alendronate vs. Raloxifene vs. Placebo: Allergic skin reaction: 3.0%(1/33) vs. 0.0%(0/33) vs. 0.0%(0/33) Bone pain: 6.1%(2/33) vs. 0.0%(0/33) vs. 0.0%(0/33) Breast pain: 0.0%(0/33) vs. 3.0%(1/33) vs. 0.0%(0/33) Degenerative changes of the eye veins: 0.0%(0/33) vs. 3.0%(1/33) vs. 0.0%(0/33) Gastric pain: 3.0%(1/33) vs. 0.0%(0/33) vs. 0.0%(0/33) Headache: 0.0%(0/33) vs. 3.0%(1/33) vs. 0.0%(0/33) Hemorrhoids: 0.0%(0/33) vs. 3.0%(1/33) vs. 0.0%(0/33) Leg cramp: 0.0%(0/33) vs. 3.0%(1/33) vs. 3.0%(1/33) Lower back pain: 0.0%(0/33) vs. 6.1%(2/33) vs. 0.0%(0/33) Thrombophlebitis: 0.0%(0/33) vs. 3.0%(1/33) vs. 0.0%(0/33) Upper gastrointestinal symptoms: 6.1%(2/33) vs. 0.0%(0/33) vs. 3.0%(1/33)
Milgrom C et al., 2004[194]	Risedronate vs. Placebo: Abdominal pain: 9.7%(16/165) vs. 10.1%(16/159) Diarrhea: 7.9%(13/165) vs. 7.5%(12/159) Headache: 17.6%(29/165) vs. 13.2%(21/159) Heart burn: 9.7%(16/165) vs. 17.0%(27/159) Nausea: 8.5%(14/165) vs. 5.7%(9/159) Polyarthralgia: 0.6%(1/165) vs. 0.0%(0/159) Total recruits with symptoms: 36.4%(60/165) vs. 42.8%(68/159) Vomiting: 2.4%(4/165) vs. 3.1%(5/159) Weakness: 19.4%(32/165) vs. 16.4%(26/159)
Miller PD et al., 1997[195]	Control+ Calcium vs. Etidronate: Abdominal pain: 9.0%(9/100) vs. 15.1%(14/93) Death: 1.0%(1/100) vs. 0.0%(0/93) Diarrhea: 16.0%(16/100) vs. 12.9%(12/93) Nausea: 13.0%(13/100) vs. 12.9%(12/93)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Miller PD et al., 2000[196]	Alendronate vs. Placebo: Abdominal pain: 14.8%(13/88) vs. 16.7%(14/84) Acid regurgitation: 25.0%(22/88) vs. 23.8%(20/84) Dyspepsia: 14.8%(13/88) vs. 21.4%(18/84) Esophagitis: 0.0%(0/88) vs. 0.0%(0/84) GI ulcer: 0.0%(0/88) vs. 0.0%(0/84) Gastritis: 0.0%(0/88) vs. 1.2%(1/84) Gastroesophageal reflux: 10.2%(9/88) vs. 11.9%(10/84) Nausea: 13.6%(12/88) vs. 15.5%(13/84) Serious AE considered not drug related: 2.3%(2/88) vs. 2.4%(2/84) Upper GI AE: 27.3%(24/88) vs. 28.6%(24/84) Vomiting: 3.4%(3/88) vs. 2.4%(2/84)
Miller PD et al., 2006[197]	Teriparatide 20 mcg/d vs. Teriparatide 40 mcg/d vs. Placebo: Other AE: 80.2%(434/541) vs. 83.5%(461/552) vs. 84.7%(461/544) Renal related AE: 1.3%(7/541) vs. 1.6%(9/552) vs. 1.5%(8/544)
Miller et al., 1969[198]	Estrogen vs. Placebo: Vaginal bleeding: 42.1%(8/19) vs. 10.5%(2/19)
Morabito N et al., 2002[199]	Alendronate vs. Clodronate vs. Placebo: Abdominal pain: 11.1%(1/9) vs. 0.0%(0/8) vs. 0.0%(0/8) Pain at injection site: 0.0%(0/9) vs. 87.5%(7/8) vs. 0.0%(0/8)
Morabito N et al., 2003[200]	Pamidronate vs. Pamidronate+ Fluoride: Fever after first infusion: 10.0%(2/20) vs. 15.0%(3/20) Mild gastric intolerance: 0.0%(0/20) vs. 5.0%(1/20)
Moran de Brito CM et al., 2005[201]	Alendronate vs. Control: Constipation: 0.0%(0/10) vs. 11.1%(1/9)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Morii H et al., 2003[202]	Raloxifene 120mg vs. Raloxifene 60mg vs. Placebo: Anaplastic thyroid carcinoma - death: 1.0%(1/100) vs. 0.0%(0/102) vs. 0.0%(0/100) Any AE related to drug: 40.0%(40/100) vs. 31.4%(32/102) vs. 33.0%(33/100) Cartilage injury: 0.0%(0/100) vs. 1.1%(1/102) vs. 0.0%(0/100) Clinically relevant change in ultrasound breast: 0.0%(0/100) vs. 0.0%(0/102) vs. 1.0%(1/100) Clinically relevant change physical exam of breast: 1.0%(1/100) vs. 0.0%(0/102) vs. 0.0%(0/100) Clinically relevant endometrial thickness change: 1.0%(1/100) vs. 2.0%(2/102) vs. 0.0%(0/100) Colitis ischemic: 0.0%(0/100) vs. 1.0%(1/102) vs. 1.0%(1/100) Convulsions NOS: 0.0%(0/100) vs. 0.0%(0/102) vs. 1.0%(1/100) Cystitis aggravated: 1.1%(1/100) vs. 0.0%(0/102) vs. 0.0%(0/100) Dissecting aortic aneurysm: 0.0%(0/100) vs. 1.0%(1/102) vs. 0.0%(0/100) Esophageal carcinoma NOS: 0.0%(0/100) vs. 0.0%(0/102) vs. 1.0%(1/100) Eye operation NOS: 0.0%(0/100) vs. 0.0%(0/102) vs. 1.0%(1/100) Gastric cancer recurrent: 0.0%(0/100) vs. 1.0%(1/102) vs. 0.0%(0/100) Gastrointestinal disorder NOS: 1.0%(1/100) vs. 0.0%(0/102) vs. 0.0%(0/100) Gastrointestinal infection NOS: 1.1%(1/100) vs. 0.0%(0/102) vs. 0.0%(0/100) Hypertension: 0.0%(0/100) vs. 0.0%(0/102) vs. 1.0%(1/100) Patients with any serious AE: 3.0%(3/100) vs. 4.9%(5/102) vs. 7.0%(7/100) Uterine prolapse: 0.0%(0/100) vs. 1.0%(1/102) vs. 0.0%(0/100)
Mortensen L et al., 1998[203]	Risedronate 5 mg cyclical vs. Risedronate 5 mg daily vs. Placebo: Abdominal pain: 13.0%(5/38) vs. 8.0%(3/37) vs. 11.0%(4/36) Dyspepsia: 24.0%(9/38) vs. 16.0%(6/37) vs. 28.0%(10/36) Hip arthralgia: 2.6%(1/38) vs. 0.0%(0/37) vs. 0.0%(0/36)
Mosekilde L et al., 2000[204]	Control vs. Estrogen: Arthritis and joint diseases: 4.2%(54/1293) vs. 4.4%(32/723) Breast cancer: 1.0%(13/1293) vs. 0.7%(5/723) Cardiovascular incidents: 0.5%(7/1293) vs. 0.6%(4/723) Cerebrovascular incidents: 0.5%(7/1293) vs. 0.3%(2/723) Cholecystectomies: 0.9%(12/1293) vs. 1.5%(11/723) Death: 1.3%(17/1293) vs. 1.0%(7/723) Diabetes: 0.4%(5/1293) vs. 0.7%(5/723) Hyperthyroidism: 0.9%(11/1293) vs. 0.8%(6/723) Hysterectomies: 1.5%(19/1293) vs. 1.9%(14/723) Lung disease: 2.2%(29/1293) vs. 1.9%(14/723) Other cancers: 0.7%(9/1293) vs. 0.8%(6/723) Venous thromboembolism: 0.0%(0/1293) vs. 0.0%(0/723)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Murphy MG et al., 2001[205]	Alendronate vs. Alendronate+ HGH vs. HGH vs. Placebo: Abdominal distension: 0.0%(0/109) vs. 9.0%(10/111) vs. 0.0%(0/36) vs. 0.0%(0/36) Bloating/fluid retention: 0.9%(1/109) vs. 1.8%(2/111) vs. 0.0%(0/36) vs. 0.0%(0/36) Breast tenderness: 1.8%(2/109) vs. 0.0%(0/111) vs. 2.8%(1/36) vs. 0.0%(0/36) Carpal tunnel syndrome: 0.0%(0/109) vs. 0.9%(1/111) vs. 0.0%(0/36) vs. 2.8%(1/36) Esophageal ulcer: 0.9%(1/109) vs. 0.0%(0/111) vs. 0.0%(0/36) vs. 2.8%(1/36) Headache, night sweats, pain, hip/leg: 0.9%(1/109) vs. 0.9%(1/111) vs. 2.8%(1/36) vs. 0.0%(0/36) Heartburn: 0.9%(1/109) vs. 0.9%(1/111) vs. 0.0%(0/36) vs. 0.0%(0/36) Hyperglycemia: 0.0%(0/109) vs. 2.7%(3/111) vs. 0.0%(0/36) vs. 0.0%(0/36) Hyperprolactinemia: 0.0%(0/109) vs. 0.9%(1/111) vs. 2.8%(1/36) vs. 0.0%(0/36) Hypertension: 0.0%(0/109) vs. 1.8%(2/111) vs. 0.0%(0/36) vs. 0.0%(0/36) Indigestion / abdominal pain: 0.9%(1/109) vs. 0.0%(0/111) vs. 2.8%(1/36) vs. 2.8%(1/36) Rash: 0.0%(0/109) vs. 0.9%(1/111) vs. 0.0%(0/36) vs. 2.8%(1/36) Transaminase elevation: 0.0%(0/109) vs. 0.0%(0/111) vs. 5.6%(2/36) vs. 0.0%(0/36)
Nakayamada S et al., 2004[206]	Etidronate+ Vitamin D vs. Vitamin D: Any adverse event: 0.0%(0/10) vs. 0.0%(0/11) Death - underlying disease: 0.0%(0/10) vs. 9.1%(1/11)
Neer RM et al., 2001[207]	PTH 20 mcg vs. PTH 40mcg vs. Placebo: Cancer: 2.0%(11/541) vs. 2.0%(11/552) vs. 4.0%(22/544) Development of antibodies to PTH: 2.8%(15/541) vs. 8.0%(44/552) vs. 0.2%(1/544) Dizziness: 9.0%(49/541) vs. 0.0%(0/552) vs. 6.0%(33/544) Headache: 0.0%(0/541) vs. 13.0%(72/552) vs. 8.0%(44/544) Leg cramps: 3.0%(16/541) vs. 0.0%(0/552) vs. 1.0%(5/544) Mild hypercalcemia: 11.0%(60/541) vs. 28.0%(155/552) vs. 2.0%(11/544) Nausea: 0.0%(0/541) vs. 18.0%(99/552) vs. 8.0%(44/544) Persistent hypercalcemia: 2.8%(15/541) vs. 11.2%(62/552) vs. 0.6%(3/544)

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AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Neven P et al., 2003[208]	Estrogen vs. Raloxifene: Abdominal pain: 2.9%(15/513) vs. 2.0%(10/495) Bleeding/spotting rate of more than 3 days /28 days - core phase: 24.0%(123/513) vs. 0.2%(1/495) Bleeding/spotting rate of more than 3 days /28 days - extension phase: 10.2%(52/513) vs. 0.0%(0/495) Breast pain: 26.5%(136/513) vs. 1.8%(9/495) Breast pain - core phase: 26.5%(136/513) vs. 1.8%(9/495) Breast pain extension phase: 13.8%(71/513) vs. 0.8%(4/495) Cervix disorder: 2.7%(14/513) vs. 1.4%(7/495) Cervix neoplasm extension phase: 1.4%(7/513) vs. 0.0%(0/495) Death: 0.0%(0/513) vs. 0.2%(1/495) Emotional lability: 1.4%(7/513) vs. 0.0%(0/495) Endometrial thickness increase >2mm: 27.6%(142/513) vs. 10.2%(50/495) Enlarged uterine fibroids extension phase: 1.6%(8/513) vs. 0.2%(1/495) Flu syndrome: 4.3%(22/513) vs. 5.3%(26/495) Headache: 3.5%(18/513) vs. 2.0%(10/495) Leg cramps: 1.6%(8/513) vs. 2.6%(13/495) Edema: 0.4%(2/513) vs. 0.2%(1/495) Thrombophlebitis: 1.0%(5/513) vs. 0.0%(0/495) Vaginal hemorrhage: 3.7%(19/513) vs. 0.0%(0/495) Vaginal hemorrhage: 3.7%(19/513) vs. 0.0%(0/495) Vaginal hemorrhage extension phase: 1.4%(7/513) vs. 0.0%(0/495) Vaginitis: 2.1%(11/513) vs. 2.8%(14/495) Vasodilatation extension phase: 0.6%(3/513) vs. 2.6%(13/495) Vasodilation / menopause: 1.4%(7/513) vs. 6.7%(33/495) Weight gain: 2.5%(13/513) vs. 0.8%(4/495)
Neven P et al., 2004[209]	Estrogen+ Progesterone vs. Raloxifene: Benign endometrial proliferation: 8.8%(45/513) vs. 1.2%(6/495) Cervical/endocervical abnormal: 0.8%(4/513) vs. 0.2%(1/495) Inflammatory: 0.6%(3/513) vs. 0.4%(2/495) Number of non-normal diagnoses: 41.9%(215/513) vs. 11.9%(59/495) Patients adjudicated as "other than normal": 36.3%(186/513) vs. 10.7%(53/495) Polyp: 4.3%(22/513) vs. 2.0%(10/495) Preexisting polyp: 1.6%(8/513) vs. 0.6%(3/495)
Nickelsen T et al., 1999[210]	Raloxifene 120 mg vs. Raloxifene 60 mg vs. Placebo: Death from pneumonia: 0.0%(0/47) vs. 2.1%(1/48) vs. 0.0%(0/48) Hot flashes: 12.8%(6/47) vs. 14.6%(7/48) vs. 10.4%(5/48)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Ninkovic M et al., 2002[211]	Control vs. Pamidronate: Death: 20.4%(11/54) vs. 11.1%(5/45) Diarrhea: 0.0%(0/54) vs. 2.2%(1/45) Symptomatic fever: 0.0%(0/54) vs. 6.7%(3/45)
Notelovitz M et al., 2002[212]	Estrogen 0.025mg vs. Estrogen 0.05mg vs. Estrogen 0.075mg vs. Placebo: Application site reaction: 52.8%(47/89) vs. 56.7%(51/90) vs. 55.1%(49/89) vs. 58.6%(51/87) Arthralgia: 5.6%(5/89) vs. 11.1%(10/90) vs. 12.4%(11/89) vs. 13.8%(12/87) Back pain: 5.6%(5/89) vs. 3.3%(3/90) vs. 7.9%(7/89) vs. 5.7%(5/87) Benign breast neoplasm: 3.4%(3/89) vs. 5.6%(5/90) vs. 1.1%(1/89) vs. 6.9%(6/87) Breast cancer: 1.1%(1/89) vs. 0.0%(0/90) vs. 1.1%(1/89) vs. 0.0%(0/87) Breast enlargement: 1.1%(1/89) vs. 2.2%(2/90) vs. 6.7%(6/89) vs. 3.4%(3/87) Breast pain: 14.6%(13/89) vs. 17.8%(16/90) vs. 34.8%(31/89) vs. 8.0%(7/87) Death: 2.2%(2/89) vs. 0.0%(0/90) vs. 0.0%(0/89) vs. 0.0%(0/87) Flu syndrome: 9.0%(8/89) vs. 13.3%(12/90) vs. 10.1%(9/89) vs. 10.3%(9/87) Headache: 11.2%(10/89) vs. 8.9%(8/90) vs. 5.6%(5/89) vs. 12.6%(11/87) Hypertension: 3.4%(3/89) vs. 3.3%(3/90) vs. 6.7%(6/89) vs. 3.4%(3/87) Myalgia: 3.4%(3/89) vs. 2.2%(2/90) vs. 5.6%(5/89) vs. 4.6%(4/87) Pain: 10.1%(9/89) vs. 5.6%(5/90) vs. 6.7%(6/89) vs. 12.6%(11/87) Pruritis: 2.2%(2/89) vs. 1.1%(1/90) vs. 6.7%(6/89) vs. 4.6%(4/87) Respiratory infection: 24.7%(22/89) vs. 24.4%(22/90) vs. 21.3%(19/89) vs. 26.4%(23/87) Sinusitis: 10.1%(9/89) vs. 12.2%(11/90) vs. 6.7%(6/89) vs. 18.4%(16/87)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Orwoll E et al., 2000[213]	Alendronate vs. Placebo: Abdominal pain: 8.2%(12/146) vs. 4.2%(4/95) Acid regurgitation: 4.8%(7/146) vs. 5.3%(5/95) Any Upper GI event: 25.3%(37/146) vs. 22.1%(21/95) Cardiovascular system: 15.8%(23/146) vs. 16.8%(16/95) Digestive system: 34.9%(51/146) vs. 38.9%(37/95) Drug-related: 17.1%(25/146) vs. 13.7%(13/95) Dyspepsia: 6.2%(9/146) vs. 1.1%(1/95) Esophagitis: 0.7%(1/146) vs. 1.1%(1/95) High serum aspartate aminotransferase concentrations.: 0.7%(1/146) vs. 0.0%(0/95) Musculoskeletal system: 46.6%(68/146) vs. 52.6%(50/95) Nervous system: 25.3%(37/146) vs. 20.0%(19/95) Respiratory system: 45.2%(66/146) vs. 49.5%(47/95) Serious: 18.5%(27/146) vs. 23.2%(22/95) Skin: 22.6%(33/146) vs. 22.1%(21/95) Urogenital system: 17.1%(25/146) vs. 16.8%(16/95)
Orwoll ES et al., 2003[214]	Teriparatide 20 mg vs. Teriparatide 40 mg vs. Placebo: Cancer: 2.0%(3/151) vs. 0.0%(0/139) vs. 2.0%(3/147) Death: 1.3%(2/151) vs. 0.0%(0/139) vs. 0.0%(0/147) Headache: 0.0%(0/151) vs. 0.7%(1/139) vs. 0.0%(0/147) Nausea: 5.3%(8/151) vs. 18.7%(26/139) vs. 3.4%(5/147) Osteosarcoma: 0.0%(0/151) vs. 0.0%(0/139) vs. 0.0%(0/147)
Palomba S et al., 2002[215]	Alendronate 10mg vs. Alendronate 5mg vs. Placebo: Breast tenderness: 2.0%(1/50) vs. 0.0%(0/50) vs. 4.0%(2/50) Death due to MI: 0.0%(0/50) vs. 2.0%(1/50) vs. 0.0%(0/50) Gastralgia: 4.0%(2/50) vs. 2.0%(1/50) vs. 2.0%(1/50) Nausea: 2.0%(1/50) vs. 0.0%(0/50) vs. 2.0%(1/50) Upper GI: 4.0%(2/50) vs. 2.0%(1/50) vs. 2.0%(1/50) Vomiting: 0.0%(0/50) vs. 2.0%(1/50) vs. 2.0%(1/50)
Palomba S et al., 2005[216]	Risedronate 3.5 mg/wk vs. Placebo: Back pain and arthralgia: 4.4%(2/45) vs. 0.0%(0/45) Gastrointestinal drug related AE (gastralgia and nausea): 4.4%(2/45) vs. 0.0%(0/45)
Peichl P et al., 1999[217]	Calcitonin+ Calcium vs. Calcium+ Vitamin D: Transient local swelling of the nasal mucosa: 8.3%(2/24) vs. 0.0%(0/18)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Peichl P et al., 2005[218]	Calcitonin+ Calcium+ Vitamin D vs. Calcium+ Vitamin D: Death: 5.4%(2/37) vs. 5.3%(2/38) Local swelling nasal mucosa: 5.4%(2/37) vs. 0.0%(0/38) Myocardial infarction: 2.7%(1/37) vs. 2.6%(1/38) Stroke: 5.4%(2/37) vs. 5.3%(2/38)
Pereda CA et al., 2002[219]	Control vs. Estrogen: Osteoarthritis: 9.1%(1/11) vs. 0.0%(0/10) Severe migraine: 9.1%(1/11) vs. 0.0%(0/10)
Pitt P et al., 1997[220]	Etidronate vs. Placebo: Accidental injury: 0.0%(0/26) vs. 17.4%(4/23) Back pain: 15.4%(4/26) vs. 0.0%(0/23) Death: 7.7%(2/26) vs. 4.3%(1/23) Moderate to severe upper GI AE: 0.0%(0/26) vs. 8.7%(2/23) Respiratory infections: 19.2%(5/26) vs. 8.7%(2/23)
Pitt P et al., 1998[221]	Etidronate vs. Placebo: Accidental injury: 0.0%(0/26) vs. 17.4%(4/23) Back pain: 15.4%(4/26) vs. 0.0%(0/23) Death: 3.8%(1/26) vs. 4.3%(1/23) Moderate to severe upper GI adverse events: 0.0%(0/26) vs. 8.7%(2/23) One or more adverse event: 65.4%(17/26) vs. 82.6%(19/23) Respiratory infections: 19.2%(5/26) vs. 8.7%(2/23)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Pols HAP et al., 1999[222]	Alendronate vs. Placebo: Abdominal pain: 10.0%(95/950) vs. 8.5%(81/958) Acid regurgitation: 2.3%(22/950) vs. 2.5%(24/958) Any upper gastrointestinal AE: 21.3%(202/950) vs. 19.3%(185/958) Duodenal ulcer: 0.0%(0/950) vs. 0.3%(3/958) Dyspepsia: 2.5%(24/950) vs. 2.3%(22/958) Dysphagia: 0.1%(1/950) vs. 0.2%(2/958) Esophagalgia: 0.2%(2/950) vs. 0.0%(0/958) Esophageal stricture: 0.1%(1/950) vs. 0.0%(0/958) Esophagitis: 0.4%(4/950) vs. 0.5%(5/958) Gastric ulcer: 0.4%(4/950) vs. 0.1%(1/958) Gastritis/gastroenteritis: 2.7%(26/950) vs. 2.1%(20/958) Nausea: 4.6%(44/950) vs. 3.9%(37/958) Odynophagia: 0.0%(0/950) vs. 0.1%(1/958) Reflux esophagitis: 0.4%(4/950) vs. 0.3%(3/958) Serious AEs: 6.5%(62/950) vs. 6.3%(60/958) Vomiting: 1.8%(17/950) vs. 2.5%(24/958)
Pouilles JM et al., 1997[223]	Etidronate vs. Placebo: Abdominal pain: 13.0%(7/54) vs. 10.9%(6/55) At least one AE: 85.2%(46/54) vs. 83.6%(46/55) Digestive AE: 18.5%(10/54) vs. 34.5%(19/55) Moderate to severe UGI AE: 1.9%(1/54) vs. 3.6%(2/55) Serious AE: 13.0%(7/54) vs. 16.4%(9/55) Stomatitis: 1.9%(1/54) vs. 0.0%(0/55)
Ravn P et al., 1996[224]	Ibandronate 0.25mg vs. Ibandronate 0.5mg vs. Ibandronate 1.0mg vs. Ibandronate 2.5mg vs. Ibandronate 5.0mg vs. Placebo: Breast cancer: 0.0%(0/30) vs. 3.3%(1/30) vs. 0.0%(0/30) vs. 0.0%(0/30) vs. 0.0%(0/30) vs. 0.0%(0/30) Cerebral hemorrhage leading to death: 0.0%(0/30) vs. 0.0%(0/30) vs. 0.0%(0/30) vs. 0.0%(0/30) vs. 0.0%(0/30) vs. 3.3%(1/30) Death from suspected MI: 0.0%(0/30) vs. 0.0%(0/30) vs. 0.0%(0/30) vs. 3.3%(1/30) vs. 0.0%(0/30) vs. 0.0%(0/30) Infection: 3.3%(1/30) vs. 0.0%(0/30) vs. 0.0%(0/30) vs. 3.3%(1/30) vs. 0.0%(0/30) vs. 3.3%(1/30) Non-serious GI AEs: 40.0%(12/30) vs. 56.7%(17/30) vs. 26.7%(8/30) vs. 16.7%(5/30) vs. 56.7%(17/30) vs. 36.7%(11/30) Stenosis of iliac artery: 0.0%(0/30) vs. 0.0%(0/30) vs. 0.0%(0/30) vs. 3.3%(1/30) vs. 0.0%(0/30) vs. 0.0%(0/30) Subanalysis of non-serious GI AEs (diarrhea only): 20.0%(6/30) vs. 16.7%(5/30) vs. 6.7%(2/30) vs. 6.7%(2/30) vs. 30.0%(9/30) vs. 6.7%(2/30) Tachycardia: 0.0%(0/30) vs. 0.0%(0/30) vs. 0.0%(0/30) vs. 0.0%(0/30) vs. 3.3%(1/30) vs. 0.0%(0/30)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Ravn P et al., 2000[225]	Alendronate 20mg for 2yrs+ 3yr no therapy vs. Alendronate 5mg/d for 5yrs vs. Placebo 3yrs+ alendronate 5mg for 2yrs: Serious AE: 0.0%(0/52) vs. 0.0%(0/52) vs. 0.0%(0/56) Upper GI AE: 0.0%(0/52) vs. 0.0%(0/52) vs. 0.0%(0/56)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Recker R et al., 2004[226]	Ibandronate 0.5 mg vs. Ibandronate 1 mg vs. Placebo: Musculoskeletal system: 52.3%(497/951) vs. 50.5%(485/961) vs. 51.4%(488/950) Skin and appendages: 19.4%(184/951) vs. 19.6%(188/961) vs. 23.4%(222/950) At least one adverse event: 94.3%(897/951) vs. 95.2%(915/961) vs. 94.1%(894/950) At least one serious adverse event: 25.2%(240/951) vs. 23.2%(223/961) vs. 26.7%(254/950) Cardiovascular system: 24.7%(235/951) vs. 22.9%(220/961) vs. 25.3%(240/950) Cataract: 0.1%(1/951) vs. 0.0%(0/961) vs. 0.0%(0/950) Cerebral infarction: 0.0%(0/951) vs. 0.1%(1/961) vs. 0.0%(0/950) Death: 0.8%(8/951) vs. 1.6%(15/961) vs. 1.4%(13/950) Digestive system: 40.5%(385/951) vs. 38.6%(371/961) vs. 39.9%(379/950) Dyspepsia: 0.0%(0/951) vs. 0.0%(0/961) vs. 0.1%(1/950) Eczema: 0.0%(0/951) vs. 0.0%(0/961) vs. 0.1%(1/950) Experienced at least one AE probably related to treatment: 15.0%(143/951) vs. 17.0%(163/961) vs. 10.0%(95/950) Hemic and lymphatic system: 8.2%(78/951) vs. 6.3%(61/961) vs. 6.5%(62/950) Hypertension: 0.0%(0/951) vs. 0.0%(0/961) vs. 0.1%(1/950) Injection site reactions: 2.3%(22/951) vs. 2.5%(24/961) vs. 0.1%(1/950) Metabolic and nutritional disorders: 17.3%(165/951) vs. 16.6%(160/961) vs. 15.5%(147/950) Myalgia: 5.1%(49/951) vs. 7.1%(68/961) vs. 3.4%(32/950) Nervous system: 25.2%(240/951) vs. 26.0%(250/961) vs. 26.8%(255/950) Respiratory system: 53.7%(511/951) vs. 52.9%(508/961) vs. 53.2%(505/950) Serious AE - Cardiovascular system: 6.6%(63/951) vs. 6.9%(66/961) vs. 7.2%(68/950) Serious AE - Digestive system: 4.3%(41/951) vs. 4.0%(38/961) vs. 4.4%(42/950) Serious AE - Endocrine system: 0.1%(1/951) vs. 0.2%(2/961) vs. 0.1%(1/950) Serious AE - Hemic and lymphatic system: 0.4%(4/951) vs. 0.6%(6/961) vs. 0.5%(5/950) Serious AE - Metabolic and nutritional disorders: 0.7%(7/951) vs. 0.3%(3/961) vs. 0.2%(2/950) Serious AE - Musculoskeletal system: 6.0%(57/951) vs. 4.7%(45/961) vs. 6.8%(65/950) Serious AE - Nervous system: 1.2%(11/951) vs. 2.0%(19/961) vs. 2.3%(22/950) Serious AE - Respiratory system: 2.8%(27/951) vs. 2.0%(19/961) vs. 2.0%(19/950) Serious AE - Skin and appendages: 2.0%(19/951) vs. 2.2%(21/961) vs. 2.7%(26/950) Serious AE - Special senses: 1.1%(10/951) vs. 0.7%(7/961) vs. 0.5%(5/950) Serious AE - Urogenital system: 1.9%(18/951) vs. 1.9%(18/961) vs. 2.1%(20/950) Serious AE - Whole body: 4.0%(38/951) vs. 3.5%(34/961) vs. 4.5%(43/950) Special senses: 15.8%(150/951) vs. 15.3%(147/961) vs. 17.1%(162/950) Urogenital system: 17.8%(169/951) vs. 19.3%(185/961) vs. 17.2%(163/950) Whole body: 56.1%(534/951) vs. 58.6%(563/961) vs. 56.1%(533/950)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Recker R et al., 2006[227]	Alendronate vs. Alendronate, Vitamin D: 1 or more serious clinical AE: 4.2%(15/357) vs. 1.9%(7/360) Death: 0.0%(0/357) vs. 0.0%(0/360) Hypercalcemia: 0.0%(0/357) vs. 0.0%(0/360) Hypercalciuria: 3.9%(14/357) vs. 3.9%(14/360) Laboratory AE: 16.5%(59/357) vs. 4.4%(16/360)
Recker RR et al., 1999[228]	Estrogen, Progesterone vs. Placebo: Atrophic endometrium: 3.1%(2/64) vs. 0.0%(0/64) Breast tenderness/ sensitivity: 76.6%(49/64) vs. 42.2%(27/64) Endometrial cancer: 0.0%(0/64) vs. 1.6%(1/64) Thromboembolic episode: 0.0%(0/64) vs. 0.0%(0/64) Vaginal spotting/change in vaginal discharge: 45.3%(29/64) vs. 0.0%(0/64)
Recker RR et al., 2006[229]	Alendronate vs. Raloxifene: Cardiovascular AE (includes myocardial infarction, angina pectoris, unstable angina, carotid arte: 1.4%(10/716) vs. 0.8%(6/707) Diarrhea: 3.8%(27/716) vs. 1.6%(11/707) Hot flash, leg cramp, or venous thromboembolic AE (including embolism, flushing, hot flush, lower extremities: 7.3%(52/716) vs. 10.3%(73/707) Nausea: 5.3%(38/716) vs. 3.1%(22/707) Other type of AE: 32.3%(231/716) vs. 33.1%(234/707) Upper GI AE: 14.5%(104/716) vs. 10.9%(77/707)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

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Author, Year, Drug, Country, Trial name	Adverse events reported
Reginster J et al., 2000[230]	Risedronate 2.5mg vs. Risedronate 5mg vs. Control: Any clinical event: 91.7%(374/408) vs. 91.9%(374/407) vs. 90.9%(370/407) AE: 13.0%(53/408) vs. 16.0%(65/407) vs. 20.4%(83/407) Abdominal pain: 8.8%(36/408) vs. 12.3%(50/407) vs. 7.9%(32/407) Any UGI symptoms: 23.0%(94/408) vs. 26.8%(109/407) vs. 25.6%(104/407) Duodenal ulcer: 0.5%(2/408) vs. 0.5%(2/407) vs. 0.2%(1/407) Duodenitis: 0.2%(1/408) vs. 0.5%(2/407) vs. 0.0%(0/407) Drug related AE: 26.7%(109/408) vs. 28.5%(116/407) vs. 31.7%(129/407) Dyspepsia: 9.3%(38/408) vs. 8.8%(36/407) vs. 10.8%(44/407) Esophageal ulcer: 1.0%(4/408) vs. 0.5%(2/407) vs. 0.7%(3/407) Esophagitis: 2.0%(8/408) vs. 2.5%(10/407) vs. 2.7%(11/407) Gastritis: 3.4%(14/408) vs. 2.2%(9/407) vs. 3.4%(14/407) Serious AE: 30.4%(124/408) vs. 37.1%(151/407) vs. 33.2%(135/407) Serious AE cancer: 2.9%(12/408) vs. 4.7%(19/407) vs. 4.2%(17/407) Serious AE cardiovascular: 7.4%(30/408) vs. 9.3%(38/407) vs. 9.3%(38/407) Stomach ulcer: 1.2%(5/408) vs. 1.5%(6/407) vs. 0.5%(2/407)
Reginster JY et al., 1987[231]	Calcitonin+Calcium vs. Calcium: Gastrointestinal intolerance to calcium: 19.5%(8/41) vs. 21.1%(8/38) Nasal bleeding: 4.9%(2/41) vs. 0.0%(0/38) Nasal intolerance to spray: 2.4%(1/41) vs. 0.0%(0/38)
Reginster JY et al., 1995[232]	Intranasal calcitonin 200iu vs. Intranasal calcitonin 50iu vs. Placebo: Epistaxis: 0.0%(0/84) vs. 0.0%(0/84) vs. 1.2%(1/83) Nasal irritation: 1.2%(1/84) vs. 0.0%(0/84) vs. 3.6%(3/83) Pancreatitis: 2.4%(2/84) vs. 0.0%(0/84) vs. 0.0%(0/83) Phlebitis: 0.0%(0/84) vs. 0.0%(0/84) vs. 2.4%(2/83) Rhinitis: 3.6%(3/84) vs. 0.0%(0/84) vs. 0.0%(0/83) Sneezing: 0.0%(0/84) vs. 1.2%(1/84) vs. 0.0%(0/83)
Reginster JY et al., 2003[233]	Fluoride vs. Raloxifene+ Fluoride: Incidence of serious AE: 13.2%(39/296) vs. 17.7%(53/300) Vasodilatation (hot flashes): 3.7%(11/296) vs. 9.7%(29/300) Venous thromboembolism: 0.3%(1/296) vs. 0.0%(0/300)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Reginster JY et al., 2005[234]	Ibandronate 100mg / 3 mo vs. Ibandronate 150mg / 3 mo vs. Ibandronate 50mg / 1 mo ; 100mg / 2 mo vs. Ibandronate 50mg / 3 mo vs. Placebo: Any AE: 91.7%(33/36) vs. 88.9%(32/36) vs. 94.4%(17/18) vs. 100.0%(18/18) vs. 94.4%(34/36) Any drug-related AE: 5.6%(2/36) vs. 5.6%(2/36) vs. 0.0%(0/18) vs. 16.7%(3/18) vs. 8.3%(3/36) Any serious AE: 0.0%(0/36) vs. 0.0%(0/36) vs. 0.0%(0/18) vs. 0.0%(0/18) vs. 0.0%(0/36) Death due to AE: 0.0%(0/36) vs. 0.0%(0/36) vs. 0.0%(0/18) vs. 0.0%(0/18) vs. 0.0%(0/36) Flu-like symptoms: 47.2%(17/36) vs. 44.4%(16/36) vs. 33.3%(6/18) vs. 44.4%(8/18) vs. 55.6%(20/36) Upper GI any time: 41.7%(15/36) vs. 41.7%(15/36) vs. 61.1%(11/18) vs. 16.7%(3/18) vs. 33.3%(12/36) Upper GI w/i 3d of treatment: 22.2%(8/36) vs. 25.0%(9/36) vs. 22.2%(4/18) vs. 0.0%(0/18) vs. 16.7%(6/36)
Reginster JY et al., 2006[235]	Ibandronate 100mg vs. Ibandronate 150mg vs. Ibandronate 2.5mg vs. Ibandronate 50+50mg: Any AE: 79.1%(318/402) vs. 79.1%(317/401) vs. 75.1%(302/402) vs. 77.5%(313/404) Any drug-related AE: 35.6%(143/402) vs. 36.4%(146/401) vs. 31.8%(128/402) vs. 29.5%(119/404) Any serious AE: 13.7%(55/402) vs. 11.2%(45/401) vs. 9.5%(38/402) vs. 13.4%(54/404) Any serious drug-related AE: 0.7%(3/402) vs. 0.2%(1/401) vs. 0.5%(2/402) vs. 0.5%(2/404) Flu-like symptoms related to drug: 1.2%(5/402) vs. 3.2%(13/401) vs. 0.2%(1/402) vs. 1.0%(4/404) Upper GI AE: 25.4%(102/402) vs. 22.2%(89/401) vs. 22.4%(90/402) vs. 19.6%(79/404)
Reid DM et al., 2000[236]	Risedronate 5mg vs. Risedronate 2.5mg vs. Placebo: Any clinical event: 97.0%(97/100) vs. 93.6%(88/94) vs. 95.8%(92/96) Abdominal pain: 13.0%(13/100) vs. 5.3%(5/94) vs. 10.4%(10/96) Arthralgia: 16.0%(16/100) vs. 0.0%(0/94) vs. 24.0%(23/96) Back pain: 10.0%(10/100) vs. 0.0%(0/94) vs. 23.0%(22/96) Drug related: 32.0%(32/100) vs. 27.7%(26/94) vs. 37.5%(36/96) Dyspepsia: 13.0%(13/100) vs. 5.3%(5/94) vs. 9.4%(9/96) Esophageal ulcer: 0.0%(0/100) vs. 1.1%(1/94) vs. 0.0%(0/96) Esophagitis: 1.0%(1/100) vs. 1.1%(1/94) vs. 0.0%(0/96) GI disorder: 4.0%(4/100) vs. 0.0%(0/94) vs. 0.0%(0/96) Gastritis: 1.0%(1/100) vs. 1.1%(1/94) vs. 2.1%(2/96) Serious event**: 37.0%(37/100) vs. 34.0%(32/94) vs. 38.5%(37/96) Stomach ulcer: 0.0%(0/100) vs. 2.1%(2/94) vs. 1.0%(1/96) UGI symptoms: 25.0%(25/100) vs. 14.9%(14/94) vs. 21.9%(21/96)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Reid IR et al., 1988[237]	Pamidronate vs. Placebo: Death: 10.0%(2/20) vs. 0.0%(0/20) Duodenitis: 5.0%(1/20) vs. 0.0%(0/20) Epigastric discomfort: 0.0%(0/20) vs. 10.0%(2/20) Erosive gastritis: 0.0%(0/20) vs. 5.0%(1/20) Gastric ulceration: 5.0%(1/20) vs. 0.0%(0/20) Nausea: 30.0%(6/20) vs. 0.0%(0/20) Osteomalacia: 5.0%(1/20) vs. 0.0%(0/20)
Reid IR et al., 1994[238]	Pamidronate vs. Placebo: Abdominal pain: 0.0%(0/31) vs. 3.3%(1/30) Blurred vision: 0.0%(0/31) vs. 3.3%(1/30) Death due to heart failure: 0.0%(0/31) vs. 3.3%(1/30) Duodenal ulcer: 3.2%(1/31) vs. 0.0%(0/30) Duodenitis: 0.0%(0/31) vs. 3.3%(1/30) Evidence of GI bleeding: 6.5%(2/31) vs. 6.7%(2/30) Gastrointestinal AEs: 48.4%(15/31) vs. 40.0%(12/30) Nausea: 22.6%(7/31) vs. 13.3%(4/30) Skin pain: 0.0%(0/31) vs. 3.3%(1/30)
Reid IR et al., 2002[239]	Zoledronic acid 0.25 mg vs. Zoledronic acid 0.50 mg vs. Zoledronic acid 1 mg vs. Zoledronic acid 2 mg vs. Zoledronic acid 4 mg vs. Placebo: Any serious AE: 6.7%(4/60) vs. 6.9%(4/58) vs. 13.2%(7/53) vs. 8.2%(5/61) vs. 10.0%(6/60) vs. 5.1%(3/59) Arthralgia: 15.0%(9/60) vs. 13.8%(8/58) vs. 17.0%(9/53) vs. 24.6%(15/61) vs. 8.3%(5/60) vs. 15.3%(9/59) Influenza-like illness: 1.7%(1/60) vs. 6.9%(4/58) vs. 3.8%(2/53) vs. 16.4%(10/61) vs. 15.0%(9/60) vs. 6.8%(4/59) Iritis: 0.0%(0/60) vs. 0.0%(0/58) vs. 0.0%(0/53) vs. 0.0%(0/61) vs. 0.0%(0/60) vs. 0.0%(0/59) Myalgia: 20.0%(12/60) vs. 10.3%(6/58) vs. 13.2%(7/53) vs. 16.4%(10/61) vs. 10.0%(6/60) vs. 1.7%(1/59) Nausea: 5.0%(3/60) vs. 6.9%(4/58) vs. 9.4%(5/53) vs. 9.8%(6/61) vs. 13.3%(8/60) vs. 5.1%(3/59) Pyrexia: 10.0%(6/60) vs. 8.6%(5/58) vs. 13.2%(7/53) vs. 19.7%(12/61) vs. 15.0%(9/60) vs. 3.4%(2/59) Women with an adverse event: 86.7%(52/60) vs. 86.2%(50/58) vs. 94.3%(50/53) vs. 91.8%(56/61) vs. 90.0%(54/60) vs. 76.3%(45/59)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Reid IR et al., 2004[240]	Estrogen 0.625mg/d vs. Raloxifene 150mg/d vs. Raloxifene 60mg/d vs. Placebo: Breast enlargement: 4.4%(7/158) vs. 0.6%(1/157) vs. 0.7%(1/152) vs. 0.7%(1/152) Breast pain: 15.8%(25/158) vs. 5.7%(9/157) vs. 7.2%(11/152) vs. 6.6%(10/152) Hernia: 0.6%(1/158) vs. 0.6%(1/157) vs. 3.3%(5/152) vs. 4.6%(7/152) Hot flashes: 10.8%(17/158) vs. 44.6%(70/157) vs. 33.6%(51/152) vs. 27.0%(41/152) Leg cramps: 3.2%(5/158) vs. 8.9%(14/157) vs. 9.9%(15/152) vs. 1.3%(2/152) MI: 0.6%(1/158) vs. 0.6%(1/157) vs. 0.7%(1/152) vs. 0.0%(0/152) Urinary incontinence: 7.0%(11/158) vs. 0.6%(1/157) vs. 0.7%(1/152) vs. 1.3%(2/152)
Rhee Y et al., 2006[241]	Alfacalcidol vs. Maxmarvil: Abdominal pain: 2.1%(2/97) vs. 1.0%(1/102) Arthralgia: 0.0%(0/97) vs. 1.0%(1/102) Constipation or diarrhea: 2.1%(2/97) vs. 3.9%(4/102) Dizziness: 1.0%(1/97) vs. 2.0%(2/102) Dyspepsia: 13.4%(13/97) vs. 17.6%(18/102) Headache: 8.2%(8/97) vs. 3.9%(4/102) Nausea: 6.2%(6/97) vs. 5.9%(6/102) Other AE: 5.2%(5/97) vs. 2.0%(2/102)
Riis BJ et al., 2001[242]	Ibandronate 2.5mg vs. Ibandronate 20mg vs. Placebo: Cardiovascular: 9.9%(8/81) vs. 10.3%(8/78) vs. 9.9%(8/81) Constipation: 6.2%(5/81) vs. 1.2%(1/78) vs. 0.0%(0/81) Death: 0.0%(0/81) vs. 1.0%(1/78) vs. 1.2%(1/81) Diarrhea: 11.1%(9/81) vs. 10.2%(8/78) vs. 1.2%(1/81) Endocrine: 2.2%(2/81) vs. 0.0%(0/78) vs. 1.1%(1/81) GI disorder: 0.0%(0/81) vs. 2.8%(2/78) vs. 6.2%(5/81) GI pain: 2.3%(2/81) vs. 5.1%(4/78) vs. 1.2%(1/81) Gastroenteritis: 3.9%(3/81) vs. 1.2%(1/78) vs. 2.8%(2/81) Hemic/lymphatic: 0.0%(0/81) vs. 1.2%(1/78) vs. 1.1%(1/81) Metabolic: 1.2%(1/81) vs. 5.1%(4/78) vs. 1.2%(1/81) Musculoskeletal: 24.0%(19/81) vs. 14.7%(11/78) vs. 24.0%(19/81) Nausea: 3.8%(3/81) vs. 6.7%(5/78) vs. 11.1%(9/81) Nervous system: 23.8%(19/81) vs. 18.0%(14/78) vs. 19.0%(15/81) Respiratory: 34.0%(28/81) vs. 33.0%(26/78) vs. 42.0%(34/81) Skin and appendages: 12.7%(10/81) vs. 1.0%(1/78) vs. 11.5%(9/81) Special senses: 7.3%(6/81) vs. 5.2%(4/78) vs. 5.0%(4/81) Urogenital: 7.0%(6/81) vs. 10.8%(8/78) vs. 13.0%(11/81) Vomiting: 3.8%(3/81) vs. 3.9%(3/78) vs. 2.7%(2/81)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Ringe JD et al., 2001[243]	Alendronate vs. Vitamin D: Clinical AE: 38.2%(26/68) vs. 47.0%(31/66) Hypercalciuria: 4.4%(3/68) vs. 12.1%(8/66) Nephrolithiasis: 1.5%(1/68) vs. 4.5%(3/66)
Ringe JD et al., 2003[244]	Ibandronate vs. Vitamin D: Acute-phase reaction: 1.9%(1/52) vs. 0.0%(0/52) Arthralgia/myalgia: 11.5%(6/52) vs. 7.7%(4/52) Constipation: 0.0%(0/52) vs. 3.8%(2/52) Diarrhea: 5.8%(3/52) vs. 1.9%(1/52) Epigastric pain: 9.6%(5/52) vs. 17.3%(9/52) Hypercalciuria/hypercalcemia: 1.9%(1/52) vs. 7.7%(4/52) Nausea: 5.8%(3/52) vs. 3.8%(2/52) Other: 3.8%(2/52) vs. 1.9%(1/52)
Ringe JD et al., 2003[245]	Alendronate vs. Vitamin D: Acne: 1.5%(1/68) vs. 0.0%(0/66) Diarrhea/soft stools: 5.9%(4/68) vs. 4.5%(3/66) Epigastric pain: 14.7%(10/68) vs. 13.6%(9/66) Hypercalciuria: 4.4%(3/68) vs. 15.2%(10/66) Lower leg pain: 1.5%(1/68) vs. 3.0%(2/66) Meteorism: 2.9%(2/68) vs. 3.0%(2/66) Myalgia: 2.9%(2/68) vs. 1.5%(1/66) Nausea: 4.4%(3/68) vs. 3.0%(2/66) Obstipation: 5.9%(4/68) vs. 6.1%(4/66) Pruritus: 1.5%(1/68) vs. 3.0%(2/66) Renal calculi: 1.5%(1/68) vs. 4.5%(3/66) Retrosternal pain: 2.9%(2/68) vs. 1.5%(1/66)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Ringe JD et al., 2003[246]	Ibandronate vs. Vitamin D: Arthralgia or myalgia: 13.8%(8/58) vs. 7.0%(4/57) Constipation: 1.7%(1/58) vs. 5.3%(3/57) Death due to AE: 6.9%(4/58) vs. 7.0%(4/57) Diarrhea: 5.2%(3/58) vs. 5.3%(3/57) Epigastric pain: 20.7%(12/58) vs. 21.1%(12/57) Hypercalciuria or hypercalcemia: 1.7%(1/58) vs. 8.8%(5/57) Nausea: 6.9%(4/58) vs. 5.3%(3/57) Other AE: 5.2%(3/58) vs. 3.5%(2/57) Other death: 0.0%(0/58) vs. 1.8%(1/57)
Ringe JD et al., 2005[247]	Etidronate / 14 d & monofluorophosphate + CA + Vitamin D vs. Etidronate 400mg/d + CA + Vitamin D: Any AE: 46.2%(12/26) vs. 50.0%(13/26)
Ringe JD et al., 2006[248]	Alfacalcidol 1 ug & calcium 500 mg & or Vitamin D 1000 iu & calcium 800 mg vs. Risedronate 5 mg & calcium 1000 mg & Vitamin D 800 iu: Back pain: 93.0%(147/158) vs. 68.0%(109/158)
Rizzoli R et al., 2002[249]	Alendronate 10mg daily vs. Alendronate 35mg twice weekly vs. Alendronate 70mg weekly: Abdominal pain: 7.6%(28/370) vs. 7.9%(29/369) vs. 11.2%(58/519) Acid regurgitation: 4.9%(18/370) vs. 5.4%(20/369) vs. 4.6%(24/519) Dyspepsia: 6.5%(24/370) vs. 5.4%(20/369) vs. 6.6%(34/519) Nausea: 7.6%(28/370) vs. 6.8%(25/369) vs. 6.6%(34/519) Peptic ulcer perforations or bleeds: 1.4%(5/370) vs. 1.1%(4/369) vs. 0.6%(3/519) Upper GI symptoms: 30.0%(111/370) vs. 29.0%(107/369) vs. 29.3%(152/519)
Rosen CJ et al., 2005[250]	Alendronate vs. Risedronate: Any AE: 75.8%(394/520) vs. 74.9%(399/533) Any UGI AE: 22.3%(116/520) vs. 19.9%(106/533) Clinical AE: 6.3%(33/520) vs. 6.2%(33/533) Dyspepsia: 8.2%(43/520) vs. 7.8%(42/533) GERD: 2.7%(14/520) vs. 3.0%(16/533) Serious AE: 8.7%(45/520) vs. 7.7%(41/533)
Rossini M et al., 2000[251]	Alendronate 10mg(cyclical) vs. Alendronate 20 mg(once weekly) vs. Control: Moderate GI disturbance: 0.0%(0/42) vs. 7.3%(3/41) vs. 0.0%(0/41)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Rossouw JE et al., 2002[252]	Estrogen+ Progesterone vs. Placebo: Adjudicated deaths: 2.5%(215/8506) vs. 2.5%(201/8102) Breast cancer - death: 0.0%(3/8506) vs. 0.0%(2/8102) Cardiovascular - death: 0.8%(65/8506) vs. 0.7%(55/8102) Colorectal cancer: 0.5%(45/8506) vs. 0.8%(67/8102) Coronary Heart Disease: 1.9%(164/8506) vs. 1.5%(122/8102) Coronary artery bypass grafting/Percutaneous transluminal coronary angina: 2.2%(183/8506) vs. 2.1%(171/8102) Death: 2.7%(231/8506) vs. 2.7%(218/8102) Endometrial cancer: 0.3%(22/8506) vs. 0.3%(25/8102) Invasive breast cancer: 2.0%(166/8506) vs. 1.5%(124/8102) Other cancer - death: 1.2%(104/8506) vs. 1.1%(86/8102) Other known cause - death: 0.4%(34/8506) vs. 0.5%(41/8102) Stroke: 1.5%(127/8506) vs. 1.0%(85/8102) Total deaths: 2.7%(231/8506) vs. 2.7%(218/8102) Unknown cause - death: 0.1%(9/8506) vs. 0.2%(17/8102) Venous thromboembolic disease: 1.8%(151/8506) vs. 0.8%(67/8102)
Roux C et al., 1998[253]	Etidronate vs. Placebo: Abdominal pain: 17.0%(10/59) vs. 15.5%(9/58) Death: 5.1%(3/59) vs. 0.0%(0/58) Moderate UGI events: 11.9%(7/59) vs. 5.2%(3/58) Total patients reporting AEs: 86.0%(51/59) vs. 88.0%(51/58)
Rubin MR et al., 2003[254]	Raloxifene vs. Control: Chest discomfort: 0.0%(0/9) vs. 11.1%(1/9)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Ryan PJ et al., 2000[255]	Pamidronate 150 mg/day vs. Pamidronate 300 mg/day vs. Placebo: Abnormal liver function test: 0.0%(0/41) vs. 0.0%(0/40) vs. 2.4%(1/41) Ampicillin-type rash: 2.4%(1/41) vs. 0.0%(0/40) vs. 0.0%(0/41) Anemia: 2.4%(1/41) vs. 0.0%(0/40) vs. 2.4%(1/41) Back pain: 24.4%(10/41) vs. 25.0%(10/40) vs. 34.1%(14/41) Carcinoma of the bronchus: 0.0%(0/41) vs. 2.5%(1/40) vs. 0.0%(0/41) Diarrhea: 9.8%(4/41) vs. 10.0%(4/40) vs. 12.2%(5/41) Drug-related Back pain: 2.4%(1/41) vs. 12.5%(5/40) vs. 9.8%(4/41) Drug-related Diarrhea: 9.8%(4/41) vs. 10.0%(4/40) vs. 12.2%(5/41) Drug-related Head discomfort: 4.9%(2/41) vs. 10.0%(4/40) vs. 4.9%(2/41) Drug-related Heartburn: 2.4%(1/41) vs. 10.0%(4/40) vs. 0.0%(0/41) Drug-related Indigestion: 7.3%(3/41) vs. 15.0%(6/40) vs. 9.8%(4/41) Drug-related Nausea: 17.1%(7/41) vs. 30.0%(12/40) vs. 4.9%(2/41) Drug-related Vomiting: 9.8%(4/41) vs. 17.5%(7/40) vs. 0.0%(0/41) Head discomfort: 9.8%(4/41) vs. 20.0%(8/40) vs. 7.3%(3/41) Heartburn: 2.4%(1/41) vs. 10.0%(4/40) vs. 2.4%(1/41) Indigestion: 7.3%(3/41) vs. 15.0%(6/40) vs. 9.8%(4/41) Lymphatic leukemia: 0.0%(0/41) vs. 2.5%(1/40) vs. 0.0%(0/41) Multiple Myeloma: 2.4%(1/41) vs. 0.0%(0/40) vs. 0.0%(0/41) Nausea: 17.1%(7/41) vs. 35.0%(14/40) vs. 9.8%(4/41) Stroke: 2.4%(1/41) vs. 0.0%(0/40) vs. 0.0%(0/41) Vertebrobasilar insufficiency: 0.0%(0/41) vs. 2.5%(1/40) vs. 0.0%(0/41) Vomiting: 9.8%(4/41) vs. 17.5%(7/40) vs. 2.4%(1/41)
Saag KG et al., 1998[256]	Alendronate 10mg vs. Alendronate 5mg vs. Placebo: Any AE: 83.4%(131/157) vs. 80.1%(129/161) vs. 79.2%(126/159) Abdominal pain: 9.6%(15/157) vs. 5.6%(9/161) vs. 5.0%(8/159) Any UGI AE: 25.5%(40/157) vs. 18.6%(30/161) vs. 16.4%(26/159) Any serious AE: 19.1%(30/157) vs. 15.5%(25/161) vs. 21.4%(34/159) Any serious GI AE: 1.3%(2/157) vs. 0.0%(0/161) vs. 1.3%(2/159) Esophageal irritation: 1.9%(3/157) vs. 3.1%(5/161) vs. 2.5%(4/159) Headache: 8.0%(13/157) vs. 8.0%(13/161) vs. 6.0%(10/159) Musculoskeletal pain: 16.0%(25/157) vs. 14.0%(23/161) vs. 16.0%(25/159) Peptic ulcer: 1.3%(2/157) vs. 0.6%(1/161) vs. 1.3%(2/159) UTI: 6.0%(9/157) vs. 10.0%(16/161) vs. 8.0%(13/159) Urinary: 13.0%(20/157) vs. 12.0%(19/161) vs. 9.0%(14/159)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Sahota O et al., 2000[257]	Alendronate 10mg (continuous) vs. Alendronate 10mg (cyclical) vs. Calcitriol 250ng (twice a day) vs. Etidronate: Abdominal bloating: 0.0%(0/37) vs. 0.0%(0/33) vs. 2.9%(1/34) vs. 0.0%(0/36) Dyspeptic - confluent ulcerative esophagitis: 2.7%(1/37) vs. 0.0%(0/33) vs. 0.0%(0/34) vs. 0.0%(0/36) Dyspeptic side effects: 16.2%(6/37) vs. 0.0%(0/33) vs. 0.0%(0/34) vs. 0.0%(0/36) Mild/moderate esophagitis: 2.7%(1/37) vs. 0.0%(0/33) vs. 0.0%(0/34) vs. 0.0%(0/36) Nonspecific abdominal discomfort: 0.0%(0/37) vs. 3.0%(1/33) vs. 0.0%(0/34) vs. 0.0%(0/36)
Sambrook P et al., 1993[258]	Calcitonin+ Calcium+ Vitamin D vs. Calcium vs. Calcium+ Vitamin D: GI symptoms: 24.1%(7/29) vs. 3.4%(1/29) vs. 17.6%(6/34) Headache: 3.4%(1/29) vs. 0.0%(0/29) vs. 2.9%(1/34) Hypercalcemia: 27.6%(8/29) vs. 3.4%(1/29) vs. 23.5%(8/34) Nasal symptoms: 31.0%(9/29) vs. 24.1%(7/29) vs. 26.5%(9/34) Rash: 6.9%(2/29) vs. 3.4%(1/29) vs. 5.9%(2/34)
Sambrook PN et al., 2003[259]	Alendronate+ Calcium vs. Calcium+ Vitamin D vs. Vitamin D: Dyspepsia: 14.0%(9/64) vs. 13.0%(8/64) vs. 7.0%(5/67) Hypercalcemia: 0.0%(0/64) vs. 5.0%(3/64) vs. 7.0%(5/67)
Sambrook PN et al., 2004[260]	Alendronate vs. Placebo: Esophagitis: 0.0%(0/55) vs. 3.4%(1/29) Peptic ulcer: 0.0%(0/55) vs. 3.4%(1/29) Upper GI: 0.0%(0/55) vs. 0.0%(0/29)
Sambrook PN et al., 2004[261]	Alendronate vs. Raloxifene: Any AE: 62.6%(154/246) vs. 65.1%(157/241) Drug related AE: 22.8%(56/246) vs. 27.0%(65/241) Drug related UGI AE: 9.3%(23/246) vs. 16.2%(39/241) Drug related vasomotor AE: 2.4%(6/246) vs. 7.9%(19/241) Serious AE: 4.5%(11/246) vs. 5.8%(14/241) Sudden death of unknown etiology: 0.0%(0/246) vs. 0.4%(1/241) Upper GI AE: 15.4%(38/246) vs. 22.0%(53/241) Vasomotor AE: 3.7%(9/246) vs. 9.5%(23/241)
Sato S et al., 2003[262]	Control vs. Etidronate: Facial rash: 0.0%(0/51) vs. 2.0%(1/51) Gastrointestinal: 0.0%(0/51) vs. 0.0%(0/51) Headache: 0.0%(0/51) vs. 2.0%(1/51)
Sato Y et al., 2000[263]	Etidronate vs. Control vs. Placebo: Peptic ulcer: 2.0%(1/49) vs. 0.0%(0/40) vs. 0.0%(0/49)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Sato Y et al., 2004[264]	Etidronate vs. Placebo: Peptic ulcer: 2.5%(1/40) vs. 0.0%(0/40)
Sato Y et al., 2005[265]	Risedronate vs. Placebo: Abdominal pain: 0.7%(1/140) vs. 0.0%(0/140) Death or intercurrent illness: 0.7%(1/140) vs. 1.4%(2/140) Esophagitis: 1.4%(2/140) vs. 0.0%(0/140)
Sato Y et al., 2005[266]	Risedronate vs. Control: Abdominal pain: 1.2%(3/250) vs. 0.0%(0/250) Death or intercurrent illness: 4.0%(10/250) vs. 4.0%(10/250) Epigastric discomfort and nausea: 0.0%(0/250) vs. 1.2%(3/250) Esophagitis: 0.4%(1/250) vs. 0.0%(0/250) Leukopenia: 0.8%(2/250) vs. 0.0%(0/250)
Sato Y et al., 2005[267]	Risedronate 2.5mg vs. Placebo: Abdominal pain: 1.6%(3/187) vs. 0.0%(0/187) Esophagitis: 0.5%(1/187) vs. 0.0%(0/187) Leukopenia: 0.5%(1/187) vs. 0.0%(0/187)
Sato Y et al., 2006[268]	Alendronate vs. Placebo: Abdominal pain: 0.0%(0/144) vs. 2.1%(3/144) Diarrhea: 2.1%(3/144) vs. 0.0%(0/144) Esophagitis: 1.4%(2/144) vs. 0.0%(0/144) Leukopenia: 0.7%(1/144) vs. 0.0%(0/144)
Sato Y et al., 2006[269]	Etidronate vs. Placebo: Abdominal pain: 9.8%(4/41) vs. 0.0%(0/41) Anorexia: 0.0%(0/41) vs. 2.4%(1/41) Death or intercurrent illness: 2.4%(1/41) vs. 0.0%(0/41) Liver dysfunction: 0.0%(0/41) vs. 0.0%(0/41) Mechanical ventilation, artificial feeding, or death: 9.8%(4/41) vs. 7.3%(3/41) Renal dysfunction: 0.0%(0/41) vs. 0.0%(0/41)
Schwarz C et al., 2004[270]	Zoledronic acid vs. Placebo: Biopsy-proven acute rejections (Banff 2a): 20.0%(2/10) vs. 30.0%(3/10) Clinically suspected but not biopsy-confirmed rejection: 10.0%(1/10) vs. 0.0%(0/10)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Shane E et al., 2004[271]	Alendronate vs. Vitamin D: Abdominal pain: 13.5%(10/74) vs. 12.0%(9/75) Any GI effects: 59.5%(44/74) vs. 57.3%(43/75) Calcitriol dose reduced: 2.7%(2/74) vs. 5.3%(4/75) Creatinine clearance <= 30ml/min: 23.0%(17/74) vs. 30.7%(23/75) Death: 1.4%(1/74) vs. 6.7%(5/75) Heartburn or acid reflux: 6.8%(5/74) vs. 16.0%(12/75) Hemorrhage: 2.7%(2/74) vs. 1.3%(1/75) Hospitalization: 50.0%(37/74) vs. 46.7%(35/75) Hypercalcemia: 1.4%(1/74) vs. 8.0%(6/75) Hypercalciuria: 6.8%(5/74) vs. 26.7%(20/75) Infection: 32.4%(24/74) vs. 25.3%(19/75) Nausea: 28.4%(21/74) vs. 25.3%(19/75) Rejection>=Grade 3A: 18.9%(14/74) vs. 17.3%(13/75) Serum creatinine level >=3 mg/dl: 5.4%(4/74) vs. 9.3%(7/75) Severe Hypercalcemia (serum calcium level =12.2 mg/d): 0.0%(0/74) vs. 1.3%(1/75) Supplemental calcium dose reduced: 5.4%(4/74) vs. 16.0%(12/75)
Sharma RK et al., 2002[272]	Alendronate vs. Control: Upper GI symptoms: 50.0%(3/6) vs. 0.0%(0/6)
Shimon I et al., 2005[273]	Alendronate 10mg vs. Placebo / alendronate: Bacterial pneumonia: 0.0%(0/11) vs. 7.7%(1/13) Mild gastrointestinal complaints: 0.0%(0/11) vs. 7.7%(1/13)
Shiraki M et al., 1999[274]	Alendronate vs. Vitamin D: Gastric ulcer: 1.0%(1/105) vs. 0.0%(0/105) Gastrointestinal symptoms: 19.0%(20/105) vs. 20.0%(21/105) No of AEs: 18.1%(19/105) vs. 23.8%(25/105) Other minor symptoms: 16.2%(17/105) vs. 18.1%(19/105)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Shiraki M et al., 2003[275]	Risedronate 1mg vs. Risedronate 2.5mg vs. Risedronate 5mg vs. Placebo: Any AE: 21.2%(11/52) vs. 28.6%(14/49) vs. 30.4%(17/56) vs. 24.1%(13/54) Abnormal laboratory results: 13.5%(7/52) vs. 10.2%(5/49) vs. 12.5%(7/56) vs. 16.7%(9/54) Cardiac disturbances: 0.0%(0/52) vs. 0.0%(0/49) vs. 0.0%(0/56) vs. 3.7%(2/54) Constipation: 1.9%(1/52) vs. 0.0%(0/49) vs. 5.4%(3/56) vs. 1.9%(1/54) Diarrhea: 0.0%(0/52) vs. 0.0%(0/49) vs. 3.6%(2/56) vs. 0.0%(0/54) Disturbances of musculoskeletal, bone and connective tissues: 0.0%(0/52) vs. 2.0%(1/49) vs. 0.0%(0/56) vs. 1.9%(1/54) Disturbances of skin and subcutaneous tissues: 0.0%(0/52) vs. 0.0%(0/49) vs. 3.6%(2/56) vs. 0.0%(0/54) Drug related AE: 7.7%(4/52) vs. 22.4%(11/49) vs. 26.8%(15/56) vs. 18.5%(10/54) Epigastric pain: 1.9%(1/52) vs. 12.2%(6/49) vs. 7.1%(4/56) vs. 0.0%(0/54) GI disturbance: 0.0%(0/52) vs. 0.0%(0/49) vs. 1.8%(1/56) vs. 1.9%(1/54) Infectious and parasitic disease: 1.9%(1/52) vs. 0.0%(0/49) vs. 0.0%(0/56) vs. 0.0%(0/54) Metabolic and nutritional disturbances: 0.0%(0/52) vs. 2.0%(1/49) vs. 3.6%(2/56) vs. 1.9%(1/54) Nausea: 1.9%(1/52) vs. 8.2%(4/49) vs. 1.8%(1/56) vs. 0.0%(0/54) Neurological disturbances: 0.0%(0/52) vs. 2.0%(1/49) vs. 1.8%(1/56) vs. 0.0%(0/54) Serious adverse drug reaction: 0.0%(0/52) vs. 0.0%(0/49) vs. 0.0%(0/56) vs. 0.0%(0/54) Systemic and local disturbance: 0.0%(0/52) vs. 0.0%(0/49) vs. 0.0%(0/56) vs. 3.7%(2/54)
Siffledeen JS et al., 2005[276]	Etidronate vs. Control: AE: 45.8%(33/72) vs. 35.2%(25/71)
Silberstein EB et al., 1992[277]	Control vs. Etidronate: Transient nausea during phosphate therapy: 0.0%(0/20) vs. 7.1%(3/42)
Simon JA et al., 2002[278]	Alendronate 10mg/day; then alendronate 70mg once a week vs. Alendronate 70mg once a week; then alendronate 10mg/day: Abdominal pain: 2.8%(4/145) vs. 0.0%(0/143) Constipation: 3.4%(5/145) vs. 2.1%(3/143) Diarrhea: 1.4%(2/145) vs. 6.3%(9/143) Epigastric discomfort: 2.8%(4/145) vs. 1.4%(2/143) Flatulence: 2.8%(4/145) vs. 0.7%(1/143) Heartburn: 2.8%(4/145) vs. 3.5%(5/143) Nausea: 3.4%(5/145) vs. 5.6%(8/143) Nonserious GI: 2.8%(4/145) vs. 1.4%(2/143)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Smith MR et al., 2001[279]	GnRH vs. Pamidronate+ GnRH: Acute-phase reaction: 0.0%(0/22) vs. 14.3%(3/21) Anemia: 90.9%(20/22) vs. 90.5%(19/21) Angiosarcoma: 0.0%(0/22) vs. 4.8%(1/21) Fatigue: 36.4%(8/22) vs. 33.3%(7/21) Fevers: 0.0%(0/22) vs. 14.3%(3/21) Memory disorder: 0.0%(0/22) vs. 4.8%(1/21) Serious events*: 13.6%(3/22) vs. 23.8%(5/21) Transient arthralgias: 0.0%(0/22) vs. 14.3%(3/21) Weight gain > 5 kg: 13.6%(3/22) vs. 9.5%(2/21)
Smith MR et al., 2003[280]	Zoledronic acid vs. Placebo: Arthralgia: 21.8%(12/55) vs. 13.7%(7/51) Back pain: 10.9%(6/55) vs. 5.9%(3/51) Constipation: 16.4%(9/55) vs. 15.7%(8/51) Death: 1.8%(1/55) vs. 0.0%(0/51) Dysuria: 12.7%(7/55) vs. 9.8%(5/51) Erectile dysfunction: 10.9%(6/55) vs. 9.8%(5/51) Fatigue: 38.2%(21/55) vs. 35.3%(18/51) Hematuria: 10.9%(6/55) vs. 0.0%(0/51) Hot flushes: 58.2%(32/55) vs. 51.0%(26/51) Nocturia: 16.4%(9/55) vs. 17.6%(9/51) Pain in limb: 12.7%(7/55) vs. 7.8%(4/51) Severe (grade 3 or 4) adverse events: 24.0%(13/55) vs. 39.0%(20/51) Urinary frequency: 14.5%(8/55) vs. 21.6%(11/51) Weakness: 12.7%(7/55) vs. 0.0%(0/51)
Smith MR et al., 2004[281]	Raloxifene vs. Placebo: Advanced lung cancer: 0.0%(0/24) vs. 4.2%(1/24) Death: 4.2%(1/24) vs. 0.0%(0/24) Lung cancer diagnosis: 0.0%(0/24) vs. 4.2%(1/24) Progressive prostate cancer: 0.0%(0/24) vs. 4.2%(1/24) Pulmonary embolus: 4.2%(1/24) vs. 0.0%(0/24)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Snyder PJ et al., 1999[282]	Placebo vs. Testosterone: Acute urinary retention: 0.0%(0/54) vs. 1.9%(1/54) Death: 3.7%(2/54) vs. 0.0%(0/54) Erythrocytosis: 0.0%(0/54) vs. 5.6%(3/54) Increase in residual urine volume: 1.9%(1/54) vs. 1.9%(1/54) Increase in respiratory distress index: 1.9%(1/54) vs. 1.9%(1/54) PSA increase persistent: 1.9%(1/54) vs. 5.6%(3/54) PSA increase transient: 11.1%(6/54) vs. 18.5%(10/54) Prostate cancer: 0.0%(0/54) vs. 1.9%(1/54) Prostate nodule: 1.9%(1/54) vs. 1.9%(1/54) Prostatitis: 1.9%(1/54) vs. 1.9%(1/54) Urosepsis: 1.9%(1/54) vs. 0.0%(0/54)
Stakkestad JA et al., 2003[283]	Ibandronate 0.5 mg vs. Ibandronate 1 mg vs. Ibandronate 2 mg vs. Placebo: Musculoskeletal chest pain: 0.0%(0/157) vs. 0.6%(1/156) vs. 0.0%(0/158) vs. 0.0%(0/156) Myalgia: 14.0%(22/157) vs. 11.5%(18/156) vs. 21.5%(34/158) vs. 4.5%(7/156)
Stefanick ML et al., 2006[284]	CEE vs. Placebo: In situ breast cancer: 0.5%(25/5310) vs. 0.6%(30/5429) Invasive breast cancer: 2.0%(104/5310) vs. 2.4%(133/5429)
Steiniche T et al., 1991[285]	Etidronate vs. Etidronate+ Triiodothyronine: Diarrhea: 10.5%(2/19) vs. 0.0%(0/18)
Storm T et al., 1990[286]	Etidronate vs. Placebo: Death: 15.2%(5/33) vs. 15.2%(5/33)
Storm T et al., 1996[287]	Etidronate vs. Placebo: Death from MI: 5.9%(1/17) vs. 0.0%(0/20) General weakness, tiredness, and loss of appetite: 0.0%(0/17) vs. 5.0%(1/20)
Struys A et al., 1995[288]	Calcium vs. Etidronate: Epigastric distress: 0.0%(0/20) vs. 5.3%(1/19)
Tanko LB et al., 2003[289]	Ibandronate 30 min. before breakfast vs. Ibandronate 60 min. before breakfast: Any AE: 84.0%(80/95) vs. 69.0%(61/89) Dyspepsia: 3.7%(4/95) vs. 8.5%(8/89) Headache: 8.4%(8/95) vs. 6.6%(6/89) Serious AE: 5.6%(5/95) vs. 4.7%(4/89) Upper respiratory tract infection: 21.5%(20/95) vs. 17.9%(16/89)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Tanko LB et al., 2003[290]	Ibandronate 10 mg vs. Ibandronate 20 mg vs. Ibandronate 5 mg vs. Placebo: Drug related AE: 9.0%(14/154) vs. 5.0%(8/159) vs. 10.0%(16/159) vs. 5.0%(8/158) Gastrointestinal AE: 5.0%(8/154) vs. 3.0%(5/159) vs. 6.0%(10/159) vs. 3.0%(5/158)
Tauchmanova L et al., 2003[291]	Calcium & Vitamin D vs. Risedronate 5mg + calcium & Vitamin D: Arthralgia: 17.6%(3/17) vs. 23.5%(4/17) Mild back pain: 11.8%(2/17) vs. 17.6%(3/17)
Tauchmanova L et al., 2006[292]	Calcium & Vitamin D vs. Estradiol + dihydroprogesterone + calcium & Vitamin D vs. Risedronate + calcium & Vitamin D vs. Zoledronic acid + calcium & Vitamin D: Breast tenderness: 0.0%(0/15) vs. 40.0%(6/15) vs. 0.0%(0/15) vs. 0.0%(0/15) Flu-like symptoms (inc. myalgia, body temp increase, nausea): 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 80.0%(12/15) Mild to moderate gastric pain: 0.0%(0/15) vs. 0.0%(0/15) vs. 20.0%(3/15) vs. 0.0%(0/15) Moderate headache: 0.0%(0/15) vs. 33.3%(5/15) vs. 0.0%(0/15) vs. 0.0%(0/15)
Tekeoglu I et al., 2005[293]	SCT nasal spray 200 iu everyday vs. SCT nasal spray 200 iu on 10 days consecutively per month vs. SCT nasal spray 200 iu on alternating 15 days per month: Local and temporary AEs - nasal burning or itching, rhinorrhea: 10.0%(4/40) vs. 5.0%(2/40) vs. 10.0%(4/40) Systemic AEs: 0.0%(0/40) vs. 0.0%(0/40) vs. 0.0%(0/40) Temporary nausea: 0.0%(0/40) vs. 0.0%(0/40) vs. 2.5%(1/40)
Terranova R et al., 1999[294]	Etidronate+ Calcium vs. Placebo: Bruise: 3.1%(1/32) vs. 0.0%(0/19) Gastrointestinal: 3.1%(1/32) vs. 0.0%(0/19) Joint AE: 3.1%(1/32) vs. 0.0%(0/19) Polyuria: 3.1%(1/32) vs. 0.0%(0/19)
Thiebaud D et al., 1994[295]	Fluoride vs. Pamidronate: Mild phlebitis: 0.0%(0/16) vs. 6.3%(1/16) Recurrence of fever: 0.0%(0/16) vs. 6.3%(1/16) Transient arthralgias: 31.3%(5/16) vs. 0.0%(0/16) Transient fever and rigors: 0.0%(0/16) vs. 6.3%(1/16) Transient fever with or without flu-like symptoms: 0.0%(0/16) vs. 31.3%(5/16) Transient nausea and mild gastric intolerances: 25.0%(4/16) vs. 0.0%(0/16)
Thiebaud D et al., 1997[296]	Ibandronate 0.25mg vs. Ibandronate 0.5mg vs. Ibandronate 1.0mg vs. Ibandronate 2.0mg vs. Placebo: Any AE: 19.0%(19/24) vs. 21.0%(21/27) vs. 19.0%(19/26) vs. 19.0%(19/23) vs. 15.0%(15/26) Acute phase AEs: 1.0%(1/24) vs. 3.0%(3/27) vs. 1.0%(1/26) vs. 4.0%(4/23) vs. 0.0%(0/26) Gastrointestinal AE's: 6.0%(6/24) vs. 6.0%(6/27) vs. 7.0%(7/26) vs. 3.0%(3/23) vs. 4.0%(4/26)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Tiras MB et al., 2000[297]	Calcitonin vs. Calcitonin+ Clodronate vs. Clodronate vs. Estrogen+ Progesterone: Gastrointestinal complaint: 0.0%(0/25) vs. 8.0%(2/25) vs. 4.0%(1/25) vs. 0.0%(0/25) Mastalgia: 0.0%(0/25) vs. 0.0%(0/25) vs. 0.0%(0/25) vs. 8.0%(2/25) Menorrhagia: 0.0%(0/25) vs. 0.0%(0/25) vs. 0.0%(0/25) vs. 4.0%(1/25) Severe headache: 0.0%(0/25) vs. 0.0%(0/25) vs. 0.0%(0/25) vs. 4.0%(1/25)
Tiras MB et al., 2000[298]	Alendronate vs. Alendronate+ Estrogen vs. Estrogen: Epigastric pain: 2.5%(1/40) vs. 2.5%(1/40) vs. 0.0%(0/40) Heavy uterine bleeding: 0.0%(0/40) vs. 2.5%(1/40) vs. 2.5%(1/40)
Tonino RP et al., 2000[299]	Alendronate 10mg vs. Alendronate 5mg vs. Placebo: Any AE: 91.0%(111/122) vs. 85.0%(96/113) vs. 90.4%(104/115) Drug-related AE: 10.7%(13/122) vs. 8.0%(9/113) vs. 13.0%(15/115) Serious AE: 12.3%(15/122) vs. 11.5%(13/113) vs. 11.3%(13/115) Serious drug-related AE: 0.8%(1/122) vs. 0.0%(0/113) vs. 0.0%(0/115) UGI AE: 17.2%(21/122) vs. 15.9%(18/113) vs. 18.3%(21/115) UGI AE drug related: 7.4%(9/122) vs. 4.4%(5/113) vs. 9.6%(11/115)
Torregrosa JV et al., 2003[300]	Alendronate vs. Control: Minimal abdominal discomfort: 80.0%(11/14) vs. 0.0%(0/12)
Tucci JR et al., 1996[301]	Alendronate 10mg vs. Alendronate 20/5mg vs. Alendronate 5mg vs. Placebo: Abdominal pain: 20.2%(19/94) vs. 18.1%(17/94) vs. 15.3%(15/98) vs. 10.9%(21/192) Drug related AE: 26.6%(25/94) vs. 30.9%(29/94) vs. 25.5%(25/98) vs. 21.9%(42/192) Drug related UGI AE: 16.0%(15/94) vs. 20.2%(19/94) vs. 16.3%(16/98) vs. 12.5%(24/192) Hypocalcemia (mild- none less than 8.0 mg/dl): 3.3%(3/94) vs. 0.0%(0/94) vs. 3.1%(3/98) vs. 0.0%(0/192) One or more AE: 94.7%(89/94) vs. 93.6%(88/94) vs. 93.9%(92/98) vs. 94.3%(181/192) One or more UGI AE: 52.1%(49/94) vs. 41.5%(39/94) vs. 35.7%(35/98) vs. 41.1%(79/192) Serious AE: 21.3%(20/94) vs. 14.9%(14/94) vs. 12.2%(12/98) vs. 18.2%(35/192) Serious UGI AE: 0.0%(0/94) vs. 2.1%(2/94) vs. 2.0%(2/98) vs. 1.0%(2/192) Stomach pain / hiatal hernia: 0.0%(0/94) vs. 1.1%(1/94) vs. 0.0%(0/98) vs. 0.0%(0/192)
Uchida S et al., 2005[302]	Alendronate 35mg / weekly vs. Alendronate 5mg / day: Aggravation of allergic bowel syndrome: 0.0%(0/168) vs. 0.6%(1/160) Clinical AE: 85.1%(143/168) vs. 89.7%(140/160) Drug-related clinical AE: 13.1%(22/168) vs. 17.9%(28/160) Reflux esophagitis - drug-related: 0.0%(0/168) vs. 0.6%(1/160) Serious AE: 6.5%(11/168) vs. 4.4%(7/160) Upper gastrointestinal AEs: 10.7%(18/168) vs. 8.8%(14/160)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Ushiroyama T et al., 2001[303]	Calcitonin vs. Calcitonin+ Vitamin D vs. Vitamin D vs. Placebo: Any other abnormal signs or clinical symptoms: 0.0%(0/49) vs. 0.0%(0/51) vs. 0.0%(0/50) vs. 0.0%(0/52) Hypercalcemia: 0.0%(0/49) vs. 0.0%(0/51) vs. 0.0%(0/50) vs. 0.0%(0/52) Throat discomfort: 14.3%(7/49) vs. 17.6%(9/51) vs. 0.0%(0/50) vs. 0.0%(0/52)
Uusi-Rasi K et al., 2003[304]	Alendronate vs. Control: Abdominal pain: 0.0%(0/82) vs. 3.7%(3/82) Mild allergic-type skin reaction: 1.2%(1/82) vs. 0.0%(0/82) Severe abdominal pain w/ suspicion of GI bleeding: 0.0%(0/82) vs. 1.2%(1/82) Upper gastrointestinal symptom: 19.5%(16/82) vs. 32.9%(27/82)
Vogel VG et al., 2006[305]	Raloxifene vs. Tamoxifen: Bone/cartilage/connective tissue cancer: 0.0%(2/9875) vs. 0.0%(3/9872) Buckle cavity and pharynx cancer: 0.0%(3/9875) vs. 0.0%(4/9872) Cancer of the esophagus: 0.0%(0/9875) vs. 0.0%(1/9872) Cancer of the spleen: 0.0%(1/9875) vs. 0.0%(0/9872) Colorectal cancer: 0.3%(30/9875) vs. 0.3%(31/9872) Eye: 0.0%(1/9875) vs. 0.0%(0/9872) Gallbladder cancer: 0.0%(1/9875) vs. 0.0%(1/9872) Gynecologic: cervix: 0.0%(0/9875) vs. 0.0%(1/9872) Gynecologic: other: 0.0%(2/9875) vs. 0.0%(1/9872) Gynecologic: ovary: 0.2%(18/9875) vs. 0.1%(12/9872) Kidney: 0.1%(13/9875) vs. 0.1%(9/9872) Leukemia or other lymphatic/hematopoietic: 0.3%(28/9875) vs. 0.3%(32/9872) Liver cancer: 0.0%(1/9875) vs. 0.0%(4/9872) Lung, trachea, bronchus cancer: 0.4%(39/9875) vs. 0.3%(28/9872) Nasal/middle ear/sinus cancer: 0.0%(1/9875) vs. 0.0%(1/9872) Nervous system: 0.1%(7/9875) vs. 0.1%(6/9872) Pancreas cancer: 0.1%(5/9875) vs. 0.1%(6/9872) Retroperitoneum cancer: 0.0%(1/9875) vs. 0.0%(4/9872) Secondary/uncertain: 0.0%(2/9875) vs. 0.0%(4/9872) Skin cancer: 0.1%(12/9875) vs. 0.1%(14/9872) Stomach cancer: 0.0%(1/9875) vs. 0.0%(3/9872) Thyroid gland: 0.2%(18/9875) vs. 0.1%(8/9872)
Wang C et al., 2004[306]	Androgel 10g vs. Androgel 5.0g vs. Androgel 7.5g: Application site skin reaction: 10.3%(4/39) vs. 8.1%(5/62) vs. 13.6%(3/22) Prostate problem: 5.1%(2/39) vs. 1.6%(1/62) vs. 9.1%(2/22)

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Author, Year, Drug, Country, Trial name	Adverse events reported
Wasnich RD et al., 2004[307]	Alendronate 5mg for 2 yrs followed by 4yrs placebo vs. Alendronate 5mg for 4 yrs followed by 2 yrs placebo vs. Open label estrogen/progestin for 4yrs followed by 2yrs off therapy vs. Placebo: At least one drug-related AE: 0.0%(0/165) vs. 11.1%(18/165) vs. 88.2%(97/110) vs. 13.0%(33/252) Breast pain: 0.0%(0/165) vs. 0.0%(0/165) vs. 25.5%(28/110) vs. 0.0%(0/252) Menopause disorder: 0.0%(0/165) vs. 0.0%(0/165) vs. 48.2%(53/110) vs. 0.0%(0/252) Menstruation disorder: 0.0%(0/165) vs. 0.0%(0/165) vs. 53.6%(59/110) vs. 0.0%(0/252) Urogenital system disorders: 0.0%(0/165) vs. 0.0%(0/165) vs. 87.3%(96/110) vs. 0.0%(0/252)
Wassertheil-Smoller S et al., 2003[308]	Estrogen with progestin vs. Placebo: Hemorrhagic stroke - intraparenchymal: 0.2%(13/8506) vs. 0.2%(14/8102) Hemorrhagic stroke - other or unspecified intracranial: 0.0%(0/8506) vs. 1.0%(81/8102) Hemorrhagic stroke - subarachnoid: 5.0%(425/8506) vs. 5.0%(405/8102) Ischemic stroke: 1.5%(125/8506) vs. 1.0%(81/8102) Other stroke: 0.0%(2/8506) vs. 0.0%(1/8102) Report of cerebrovascular death only: 0.1%(6/8506) vs. 0.1%(5/8102)
Weinstein RS et al., 2003[309]	Estrogen vs. Raloxifene vs. Placebo: Adverse event: 39.0%(9/23) vs. 20.0%(4/20) vs. 13.0%(3/23)
Wimalawansa SJ, 1995[310]	Control+ Calcium vs. Estrogen vs. Estrogen+ Etidronate vs. Etidronate: Breast tenderness: 0.0%(0/14) vs. 66.7%(10/15) vs. 0.0%(0/15) vs. 0.0%(0/14) Carcinoma of the ovary: 7.1%(1/14) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/14) Cerebrovascular accident: 7.1%(1/14) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/14) Hepatitis B: 0.0%(0/14) vs. 0.0%(0/15) vs. 6.7%(1/15) vs. 0.0%(0/14) Inability to tolerate medicine: 7.1%(1/14) vs. 13.3%(2/15) vs. 6.7%(1/15) vs. 14.3%(2/14) Menstrual bleeding: 0.0%(0/14) vs. 100.0%(15/15) vs. 0.0%(0/15) vs. 0.0%(0/14) Nausea initially: 0.0%(0/14) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 21.4%(3/14) Osteomalacia: 0.0%(0/14) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 21.4%(3/14)
Wimalawansa SJ, 1998[311]	Control vs. Estrogen vs. Estrogen+ Etidronate vs. Etidronate: Death due to myocardial infarction: 0.0%(0/18) vs. 0.0%(0/18) vs. 0.0%(0/19) vs. 5.9%(1/17) Estrogen-related adverse effects: 0.0%(0/18) vs. 16.7%(3/18) vs. 10.5%(2/19) vs. 0.0%(0/17) Nausea: 0.0%(0/18) vs. 0.0%(0/18) vs. 0.0%(0/19) vs. 35.3%(6/17)
Worth H et al., 1994[312]	Etidronate+ Vitamin D vs. Control: Exacerbation of underlying disease: 0.0%(0/20) vs. 5.0%(1/20) Nausea: 15.0%(3/20) vs. 0.0%(0/20)

Author, Year, Drug, Country, Trial name	Adverse events reported
Yang TS et al., 1998[313]	Alendronate vs. Placebo: Climacteric syndrome: 3.3%(1/30) vs. 3.3%(1/30) Common cold: 3.3%(1/30) vs. 0.0%(0/30) Constipation: 0.0%(0/30) vs. 0.0%(0/30) Diarrhea: 0.0%(0/30) vs. 0.0%(0/30) Dyspepsia: 0.0%(0/30) vs. 0.0%(0/30) Dysphasia: 0.0%(0/30) vs. 0.0%(0/30) Esophageal ulcer: 0.0%(0/30) vs. 0.0%(0/30) Flatulence: 0.0%(0/30) vs. 0.0%(0/30) Hot flush, dry mouth (climacteric syndrome): 0.0%(0/30) vs. 3.3%(1/30) Menstrual bleeding: 3.3%(1/30) vs. 3.3%(1/30) Palpitation, fatigue (climacteric syndrome): 3.3%(1/30) vs. 0.0%(0/30) Unspecified GI: 6.7%(2/30) vs. 3.3%(1/30) Unspecified GI discomfort: 6.6%(2/30) vs. 3.3%(1/30)
Zegels B et al., 2001[314]	Placebo vs. Risedronate followed by Calcium vs. Risedronate followed by Calcium followed by Risedronate followed by Calcium vs. Risedronate followed by placebo: Fatigue: 0.0%(0/8) vs. 0.0%(0/8) vs. 0.0%(0/8) vs. 12.5%(1/8) Flu and bronchitis: 0.0%(0/8) vs. 0.0%(0/8) vs. 0.0%(0/8) vs. 12.5%(1/8) Moderate-to-severe upper gastrointestinal adverse events: 0.0%(0/8) vs. 0.0%(0/8) vs. 0.0%(0/8) vs. 0.0%(0/8) Myocardial infarction: 12.5%(1/8) vs. 0.0%(0/8) vs. 0.0%(0/8) vs. 0.0%(0/8)
Zehnder Y et al., 2004[315]	Alendronate+ Calcium vs. Control+Calcium: Chronic headache: 3.0%(1/33) vs. 0.0%(0/32) Diarrhea: 3.0%(1/33) vs. 3.1%(1/32) Dizziness: 3.0%(1/33) vs. 0.0%(0/32) Gastrointestinal adverse events: 12.1%(4/33) vs. 12.5%(4/32) Neurological adverse events: 6.1%(2/33) vs. 0.0%(0/32) Obstipation: 3.0%(1/33) vs. 3.1%(1/32) Pyrosis: 3.0%(1/33) vs. 6.3%(2/32) Syringomyelia: 0.0%(0/33) vs. 3.1%(1/32) Transitory retrosternal pain: 3.0%(1/33) vs. 0.0%(0/32)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
Zein CO et al., 2005[316]	Alendronate vs. Placebo: Abdominal distention: 5.9%(1/17) vs. 0.0%(0/17) Abdominal pain: 5.9%(1/17) vs. 11.8%(2/17) Any GI AE: 17.6%(3/17) vs. 17.6%(3/17) Flatulence: 0.0%(0/17) vs. 5.9%(1/17) Heartburn: 5.9%(1/17) vs. 0.0%(0/17) Musculoskeletal bone or joint pain: 6.0%(1/17) vs. 0.0%(0/17) Nausea: 0.0%(0/17) vs. 11.8%(2/17)
Zheng S et al., 2003[317]	Raloxifene vs. Placebo: Angina pectoris: 0.0%(0/102) vs. 1.0%(1/102) Cardiac neurosis: 1.0%(1/102) vs. 0.0%(0/102) Deep venous thrombosis: 0.0%(0/102) vs. 0.0%(0/102) Endometrial carcinoma: 1.0%(1/102) vs. 0.0%(0/102) Enlarged uterine fibroids: 1.0%(1/102) vs. 0.0%(0/102) Flushes: 12.7%(13/102) vs. 7.8%(8/102) Leg cramps: 12.7%(13/102) vs. 7.8%(8/102) One or more serious adverse effect: 3.9%(4/102) vs. 1.0%(1/102) Vertebrobasilar blood supply insufficiency: 1.0%(1/102) vs. 0.0%(0/102)
Zheng SR et al., 2003[318]	Raloxifene vs. Placebo: Adverse event: 2.9%(3/102) vs. 2.0%(2/102)
van Staa T et al., 1997[319]	Etidronate vs. Nonosteoporosis control vs. Osteoporosis control: Abdominal pain: 7.6%(609/7977) vs. 4.6%(370/7977) vs. 7.3%(586/7977) Abdominal pain during NSAID use: 1.1%(88/7977) vs. 0.4%(32/7977) vs. 0.8%(67/7977) Abdominal pain during aspirin use: 0.3%(22/7977) vs. 0.3%(25/7977) vs. 0.5%(43/7977) Abdominal pain during corticosteroid use: 0.9%(68/7977) vs. 0.1%(5/7977) vs. 0.7%(54/7977) Esophagitis/esophageal ulcers: 1.6%(126/7977) vs. 1.0%(78/7977) vs. 1.4%(112/7977) Gastritis/duodenitis: 1.6%(125/7977) vs. 0.8%(64/7977) vs. 1.2%(99/7977) Gastrointestinal hemorrhage: 0.6%(49/7977) vs. 0.4%(31/7977) vs. 0.7%(56/7977) Peptic ulcers: 0.9%(72/7977) vs. 0.5%(38/7977) vs. 0.8%(61/7977) UGI AE: 3.8%(303/7977) vs. 2.2%(173/7977) vs. 3.2%(256/7977) UGI AE during aspirin use: 0.1%(11/7977) vs. 0.1%(8/7977) vs. 0.1%(10/7977) UGI AE during corticosteroid use: 0.4%(33/7977) vs. 0.1%(7/7977) vs. 0.2%(19/7977) Upper GI event during NSAID use: 0.5%(41/7977) vs. 0.1%(9/7977) vs. 0.5%(39/7977)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

Author, Year, Drug, Country, Trial name	Adverse events reported
van der Poest Clement E et al., 200[320]	Alendronate vs. Placebo: Serious adverse event: 4.8%(1/21) vs. 0.0%(0/20)
von Tirpitz C et al., 2003[321]	Calcium+ Vitamin D vs. Calcium+ Vitamin D+ Fluoride vs. Ibandronate+ Calcium+ Vitamin D: AE: 23.1%(3/13) vs. 30.6%(11/36) vs. 25.7%(9/35) Bone pain: 0.0%(0/13) vs. 0.0%(0/36) vs. 5.7%(2/35) Testicular cancer: 0.0%(0/13) vs. 2.8%(1/36) vs. 0.0%(0/35) Undigested pills in feces: 0.0%(0/13) vs. 5.6%(2/36) vs. 0.0%(0/35)

Drugs: CEE=Conjugated Equine Estrogen, PTH=Parathyroid Hormone

AEs: MI=Myocardial Infarction, UTI=Urinary Tract Infection, GI=Gastrointestinal

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Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Agrawal S et al., 2006[1] Risedronate US	Setting: Single center Jadad: 4	Inclusion criteria: Men, Post-menopausal women NOS, ambulatory, cognitively intact Exclusion criteria: Carcinoma or suspected carcinoma, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Med known to affect skeleton, age <65, any significant lab abnormalities, Osteoporotic fracture within 2yrs
Aris RM et al., 2000[2] Pamidronate US	Setting: Single center Jadad: 3	Inclusion criteria: Men, Women otherwise undefined, Organ transplant, Cystic Fibrosis Exclusion criteria: Pregnancy, Renal insufficiency, Life expectancy <5 years, Graft Failure
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal women NOS, Osteoporosis score based on t-score and/or fractures and/or radiographic, Age > 65, age <=89 Exclusion criteria: Bisphosphonates, Fluoride, Anabolic steroids, Corticoids/Glucocorticoids, Hypercalcemia, Hypocalcemia, previous PTH use, >2+ protein on urine dipstick, bisphosphonate use for >=48 weeks within 2 years prior to study, Growth Hormone use, strontium use, calculated creatinine clearance , 30.0 ml/min
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal >5 years, Osteoporosis T-score <= -2.5 hip, Osteoporosis T-score <= -2.5 spine Exclusion criteria: Age > 85, Carcinoma or suspected carcinoma, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Malabsorption syndrome, Urolithiasis, Bisphosphonates, Calcitonin, Fluoride, Androgen, Estrogen agonists (including estrogen), Anabolic steroids, Corticoids/Glucocorticoids, Alcohol Abuse, Allergy to PTH, age<30, LS spine abnormalities prohibiting DEXA, previous PTH use
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal women NOS, Osteoporosis T-score <= -2.5 spine, Prior Hysterectomy Exclusion criteria: Cardiovascular disease, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Venous thromboembolic disease - Active, Venous thromboembolic disease - Ever, Bisphosphonates, Calcitonin, Fluoride, Vitamin D deficient, recent major upper GI mucosal erosive disease, Increased risk of breast cancer, Unexplained genital bleeding x 1 year, Fasting triglycerides >400mg/dL, Contraindication to HRT, HRT within last 6 months

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal >6 months, Osteoporosis T-score <= -2 NOS, Spine/Hip anatomy suitable for Dexa, ambulatory, Age >40 Exclusion criteria: Metabolic bone disorder other than osteoporosis, Upper GI, Bisphosphonates, Fluoride, HRT, Estrogen agonists (including estrogen), Anabolic steroids, Corticoids/Glucocorticoids, Vitamin D deficient, previous PTH use, Hypocalcemia, Immunosuppressants
Boutsen Y et al., 1997[7] Pamidronate Western Europe	Setting: Multi-center Jadad: 3	Inclusion criteria: Men, Pre-menopausal women, Post-menopausal women NOS, Glucocorticoids >10mg Exclusion criteria: Carcinoma or suspected carcinoma, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Renal insufficiency, Urolithiasis, Bisphosphonates, Fluoride, Previous Glucocorticoids
Brown JP et al., 2002[8] Risedronate US, Canada	Setting: Multi-center Jadad: 3	Inclusion criteria: Post-menopausal >5 years, either spine T score <=-2.0 or hip T score <=-2.5, at least 3 evaluable lumbar vertebra without fx, age >50, ambulatory Exclusion criteria: Med known to affect skeleton, LS spine abnormalities prohibiting DEXA
Campbell IA et al., 2004[9] Etidronate UK	Setting: Multi-center Jadad: 2	Inclusion criteria: Men, Post-menopausal women NOS, Asthma or COPD, inhaled or oral glucocorticoids/steroids >=1yr Exclusion criteria: Hysterectomy, age <=50, age >=70
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal >2 years, T score<= -1.6 at the femoral neck Exclusion criteria: Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Renal insufficiency, Malabsorption syndrome, Upper GI, Bisphosphonates, Calcitonin, Fluoride, Estrogen agonists (including estrogen), age >= 80, age <=55, life expectancy =<3yrs
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal >2 years, T score<= -1.6 at the femoral neck Exclusion criteria: Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Renal insufficiency, Malabsorption syndrome, Upper GI, Bisphosphonates, Calcitonin, Fluoride, Estrogen agonists (including estrogen), age >= 80, age <=55, life expectancy =<3yrs

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal >5 years, Osteoporosis T-score <= -2 spine, Osteoporosis/Fracture Exclusion criteria: Metabolic bone disorder other than osteoporosis, Renal insufficiency, Bisphosphonates, Fluoride, Med known to affect skeleton, Diseases known to affect skeleton, > 2 fractures lumbar spine, Contraindication to Ca or Vitamin D, Hypercalcemia, Hypocalcemia, age <=55, age >= 80, T score<-5.0
Coco M et al., 2003[12] Pamidronate US	Setting: Setting not reported Jadad: 2	Inclusion criteria: Men, Women otherwise undefined, Organ transplant Exclusion criteria: Pregnancy
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1	Setting: Multi-center Jadad: 3	Inclusion criteria: Women otherwise undefined, age >60 or age 35 to 59 with a 5 year risk of breast cancer of 1.66, life expectancy great than 10 years Exclusion criteria: Pregnancy, Hepatic insufficiency, Renal insufficiency, Venous thromboembolic disease, Estrogen agonists (including estrogen), Progestin, Contraceptive, Breast Cancer, Abnormal CBC
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	Setting: Multi-center Jadad: 3	Inclusion criteria: Men, Women otherwise undefined, Osteoporosis score based on t-score and/or fractures and/or radiographic Exclusion criteria: Age > 75, Carcinoma or suspected carcinoma, Cardiovascular disease, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Upper GI, LS spine abnormalities prohibiting DEXA, Med known to affect skeleton, Drug Hypersensitivity, History of Radiotherapy
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	Setting: Multi-center Jadad: 2	Inclusion criteria: Post-menopausal >5 years, Osteoporosis score based on t-score and/or fractures and/or radiographic Exclusion criteria: Hepatic insufficiency, Renal insufficiency, Urolithiasis, nonambulatory, Alcohol Abuse, drug abuse, any medication that may alter bone and mineral metabolism, illnesses that affect bone and calcium metabolism

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe	Setting: Setting not reported Jadad: 1	Inclusion criteria: Organ transplant, ambulatory, normal diet Exclusion criteria: Med known to affect skeleton, Hypogonadism
Grant AM et al., 2005[17] Vitamin D UK	Setting: Multi-center Jadad: 4	Inclusion criteria: Men, Post-menopausal women NOS, Osteoporosis/Fracture Exclusion criteria: Carcinoma or suspected carcinoma, Nephrolithiasis, Bisphosphonates, Calcitonin, Calcium (includes antacids), Fluoride, HRT, SERMS, Vitamin D, age < 70, nonambulatory, mental condition that would preclude participation, Hypercalcemia, life expectancy <1/2 years, fracture associated with bone abnormality
Greenspan SL et al., 2003[18] Alendronate, Estrogen US	Setting: Single center Jadad: 5	Inclusion criteria: Women otherwise undefined, Age > 65 Exclusion criteria: Carcinoma or suspected carcinoma, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Renal insufficiency, Anticonvulsants, Bisphosphonates, Calcitonin, Hormone use, Corticoids/Glucocorticoids, Med known to affect skeleton, Contraindication to HRT, Contraindication to alendronate, BMD hip T score >0.0
Greenspan SL et al., 2006[19] Risedronate US	Setting: Single center Jadad: 5	Inclusion criteria: Post-menopausal women NOS, Breast cancer, Post chemotherapy with or without tamoxifen Exclusion criteria: Carcinoma or suspected carcinoma, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Malabsorption syndrome, age <18, Stage IV breast cancer, any medication that may alter bone and mineral metabolism
Grotz W et al., 2001[20] Ibandronate Germany	Setting: Single center Jadad: 2	Inclusion criteria: Men, Pre-menopausal women, Post-menopausal women NOS, Organ transplant Exclusion criteria: Kidney Pancreas Transplant
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe	Setting: Setting not reported Jadad: 3	Inclusion criteria: Women otherwise undefined, Osteopenia T-score <= -1.0 NOS, Primary Biliary Cirrhosis Exclusion criteria: Renal insufficiency, Upper GI, Bisphosphonates, Fluoride, Estrogen agonists (including estrogen), Corticoids/Glucocorticoids, Bilirubin >10mg/dL

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Harris ST et al., 2004[22] Risedronate US, Canada	Setting: Multi-center Jadad: 3	Inclusion criteria: Post-menopausal >5 years, either spine T score <=-2.0 or hip T score <=-2.5, at least 3 evaluable lumbar vertebra without fx, age >50, ambulatory Exclusion criteria: Med known to affect skeleton, LS spine abnormalities prohibiting DEXA
Hay JE et al., 2001[23] Calcitonin US	Setting: Single center Jadad: 1	Inclusion criteria: Men, Pre-menopausal women, Post-menopausal women NOS, Organ transplant Exclusion criteria: Hypothyroidism, Hyperthyroidism, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Anticonvulsants, Hormone use, Corticoids/Glucocorticoids, Med known to affect skeleton, Survived 6mos after liver transplant
Hizmetli S et al., 1998[24] Calcitonin Turkey	Setting: Single center Jadad: 1	Inclusion criteria: Post-menopausal women NOS, Osteoporosis T-score <= -2.5 NOS Exclusion criteria: Med known to affect skeleton, Secondary Osteoporosis
Hochberg MC et al., 2005[25] Alendronate US FIT	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal >2 years, T score<= -1.6 at the femoral neck Exclusion criteria: Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Renal insufficiency, Malabsorption syndrome, Upper GI, Bisphosphonates, Calcitonin, Fluoride, Estrogen agonists (including estrogen), age >= 80, age <=55, life expectancy =<3yrs
Hooper MJ et al., 2005[26] Risedronate Australia/NZ	Setting: Multi-center Jadad: 3	Inclusion criteria: Post-menopausal >6 months, Osteoporosis T-score <= -2.5 spine, FSH>= 50, postmenopausal < 3 years Exclusion criteria: Hyperthyroidism, Hyperparathyroidism, Metabolic bone disorder other than osteoporosis, Serum estradiol >20, Med known to affect skeleton
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil	Setting: Multi-center Jadad: 5	Inclusion criteria: Post-menopausal >2 years, Osteoporosis T-score <= -2.5 hip, Osteoporosis T-score <= -2.5 spine, Hip and Spine Dexa <-2.0 Exclusion criteria: Hypothyroidism, Hyperthyroidism, Hypoparathyroidism, Metabolic bone disorder other than osteoporosis, Bisphosphonates, Fluoride, HRT, Estrogen agonists (including estrogen), Corticoids/Glucocorticoids, LS spine abnormalities prohibiting DEXA, Vitamin D deficient, Severe Upper GI symptoms, Severe Osteoporosis, age >90, age <60, Abnormal Urinary Calcium

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	Setting: Single center Jadad: 2	Inclusion criteria: Post-menopausal >5 years, Osteoporosis T-score <= -2.5 NOS, Osteoporosis/Fracture, ambulatory Exclusion criteria: Age > 75, Carcinoma or suspected carcinoma, Metabolic bone disorder other than osteoporosis, Med known to affect skeleton, bilateral hip fractures, mental condition that would preclude participation
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan	Setting: Multi-center Jadad: 1	Inclusion criteria: Women otherwise undefined, Osteoporosis/Fracture, Back Pain Exclusion criteria: Metabolic bone disorder other than osteoporosis, HRT, Estrogen agonists (including estrogen), Med known to affect skeleton
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal women NOS Exclusion criteria: Nephrolithiasis, Vitamin D, Corticoids/Glucocorticoids, age >= 80, Hypercalcemia, age <=50, life expectancy =<3yrs
Kanaji A et al., 2006[31] Risedronate Japan	Setting: Single center, Long Term Jadad: 4	Inclusion criteria: Men, leprosy Exclusion criteria: any medication that may alter bone and mineral metabolism
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland	Setting: Single center Jadad: 1	Inclusion criteria: Men, Women otherwise undefined, Organ transplant Exclusion criteria: Renal insufficiency, Myeloma

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	Setting: Multi-center, Community Jadad: 4	Inclusion criteria: Men, Osteoporosis T-score <= -2 hip, Osteoporosis T-score <= -2 spine Exclusion criteria: Age > 85, Carcinoma or suspected carcinoma, Hyperparathyroidism, Hypoparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Sprue, Inflammatory bowel disease, Malabsorption syndrome, Nephrolithiasis, Urolithiasis, Anticonvulsants, Aluminum, Bisphosphonates, Calcitonin, Calcium (includes antacids), Coumarins, Fluoride, Androgen, Estrogen agonists (including estrogen), Progestin, Estrogen antagonists, Anabolic steroids, Vitamin D, Corticoids/Glucocorticoids, Abnormal Urinary Calcium, nonambulatory, any medication that may alter bone and mineral metabolism, treatment with calcitriol analogues, age<30, Secondary Osteoporosis, Alcohol Abuse, LS spine abnormalities prohibiting DEXA, treatment with indandione derivatives, Hypercalcemia, Hypocalcemia, Major systemic Disease, drug abuse, Growth Hormone deficiency, poor intestinal calcium absorption
Kim SH et al., 2004[34] Pamidronate Asia	Setting: Single center Jadad: 2	Inclusion criteria: Men, Post-menopausal women NOS, Postmenopausal >18 months Exclusion criteria: Renal insufficiency, Bisphosphonates, bed rest
Kishimoto H et al., 2006[35] Risedronate Japan	Setting: Multi-center Jadad: 3	Inclusion criteria: Men, Women otherwise undefined, ambulatory, age >50, <70% YAM(young adult mean) spine or <80% YAM and fracture Exclusion criteria: Carcinoma or suspected carcinoma, Cardiovascular disease, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Gastrointestinal disease, Bisphosphonates, any medication that may alter bone and mineral metabolism, Drug Hypersensitivity, radiation therapy to lumbar spine or pelvis, LS spine abnormalities prohibiting DEXA
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	Setting: Multi-center Jadad: 4	Inclusion criteria: Men, Women otherwise undefined, Osteoporosis NOS, age >50, 1-4 vertebral fractures Exclusion criteria: Cardiovascular disease, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Gastrointestinal disease, treatment with Risedronate or Etidronate, Secondary Osteoporosis, radiographic findings that affect vertebral intensity, Med known to affect skeleton, malignancy under treatment with anti-tumor agents, radiation therapy to lumbar spine or pelvis

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY	Setting: Multi-center Jadad: 5	Inclusion criteria: Osteoporosis T-score <= -2 hip, Osteoporosis T-score <= -2 spine, Postmenopausal >18 months, Age >40, Age>25 if surgical menopause, Good health Exclusion criteria: Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Upper GI, Venous thromboembolic disease - Active, Venous thromboembolic disease - Ever, Bisphosphonates, Fluoride, Estrogen agonists (including estrogen), SERMS, Anabolic steroids, Corticoids/Glucocorticoids, LS spine abnormalities prohibiting DEXA, Immunosuppressants, Hypocalcemia, previous PTH use, Med known to affect skeleton, Breast Cancer, Uterine Cancer
McClung MR et al., 2006[38] Alendronate, AMG162 US	Setting: Multi-center Jadad: 2	Inclusion criteria: Post-menopausal women NOS, T score lumbar spine -1.8 to -4.0 or hip -1.8 to -3.5 Exclusion criteria: Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hypoparathyroidism, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Malabsorption syndrome, Bisphosphonates, Calcitonin, Fluoride, Androgen, Estrogen agonists (including estrogen), SERMS, Estrogen antagonists, Testosterone, Vitamin D, Corticoids/Glucocorticoids, age >= 80, Hypocalcemia, LS spine abnormalities prohibiting DEXA, previous PTH use, Long bone fracture, greater than one vertebral fracture, Osteoporotic fracture within 2yrs
Milgrom C et al., 2004[39] Risedronate Israel	Setting: Single center Jadad: 4	Inclusion criteria: Men Exclusion criteria: NR
Muscoso E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy	Setting: Setting not reported Jadad: 1	Inclusion criteria: Women otherwise undefined, Osteoporosis NOS Exclusion criteria: NR
Ninkovic M et al., 2002[41] Pamidronate UK	Setting: Setting not reported Jadad: 2	Inclusion criteria: Organ transplant Exclusion criteria: Renal insufficiency, Bisphosphonates, retransplantation

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Orwoll ES et al., 2003[42] PTH 1100101000	Setting: Multi-center Jadad: 4	Inclusion criteria: Men, Osteopenia T-score <= -2.0 NOS Exclusion criteria: Age > 85, Carcinoma or suspected carcinoma, Hyperparathyroidism, Hypoparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Sprue, Inflammatory bowel disease, Malabsorption syndrome, Nephrolithiasis, Urolithiasis, Anticonvulsants, Aluminum, Bisphosphonates, Calcitonin, Calcium (includes antacids), Coumarins, Fluoride, Estrogen agonists (including estrogen), Progestin, Estrogen antagonists, Anabolic steroids, Vitamin D, Corticoids/Glucocorticoids, age<30, Med known to affect skeleton, Alcohol Abuse, drug abuse, LS spine abnormalities prohibiting DEXA, Growth Hormone deficiency, treatment with indandione derivatives
Palomba S et al., 2005[43] Risedronate Italy	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal women NOS, Osteoporosis T-score <= -2.5 spine, Inflammatory bowel disease Exclusion criteria: Carcinoma or suspected carcinoma, Endocrine disease, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Bisphosphonates, Calcitonin, Fluoride, HRT, Anabolic steroids, Proton pump inhibitors, Corticoids/Glucocorticoids, Vitamin D deficient, Hypercalcemia, Hypocalcemia, Med known to affect skeleton, hydrochlorothiazide, active rheumatoid arthritis, tobacco abuse, extremes of BMI (either high or low), other medications that could cause GI irritation
Porthouse J et al., 2005[44] Calcium, Vitamin D UK	Setting: Multi-center, Community Jadad: 2	Inclusion criteria: Post-menopausal women NOS, at least one risk factor for osteoporotic fracture Exclusion criteria: Renal insufficiency, Nephrolithiasis, Urolithiasis, Calcium (includes antacids), age < 70, unable to give informed consent, Hypercalcemia, life expectancy <1/2 years
Prince RL et al., 2006[45] Calcium Australia/NZ	Setting: Setting not reported Jadad: 5	Inclusion criteria: Post-menopausal women NOS Exclusion criteria: age < 70, participation in another trial, Med known to affect skeleton, Life expectancy <5 years

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Quandt SA et al., 2005[46] Alendronate US FIT	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal >2 years, T score<= -1.6 at the femoral neck Exclusion criteria: Carcinoma or suspected carcinoma, Cardiovascular disease, Hyperparathyroidism, Hypoparathyroidism, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Malabsorption syndrome, Upper GI, Bisphosphonates, Calcitonin, Fluoride, Estrogen agonists (including estrogen), Progestin, Anabolic steroids, Corticoids/Glucocorticoids, BMD femoral neck < -3, noncompliance, history of bilateral hip replacement, nonambulatory, Alcohol Abuse, age <=55, age >= 80, Major systemic Disease, intending to move within four years, any vertebral deformity, recent major upper GI mucosal erosive disease, participation in another trial, unable to give informed consent, change in thyroid hormone dose, unexpected weight loss > 10% of ideal body weight in last 12 months
Ravn P et al., 1996[47] Ibandronate Western Europe	Setting: Single center Jadad: 3	Inclusion criteria: Post-menopausal >5 years, T-score at forearm <= -1.5, Body weight > 40 kg and not to exceed ideal body weight by >= 40% Exclusion criteria: Age > 75, Bisphosphonates, Calcitonin, HRT, Diseases, conditions or treatments known to interfere with calcium metabolism
Recker R et al., 2004[48] Ibandronate US, Western Europe	Setting: Multi-center Jadad: 3	Inclusion criteria: Post-menopausal >5 years, Osteoporosis T-score <= -2 spine, Osteoporosis/Fracture Exclusion criteria: Carcinoma or suspected carcinoma, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Gastrointestinal disease, Bisphosphonates, Calcitonin, Fluoride, HRT, Corticoids/Glucocorticoids, Alcohol Abuse, Med known to affect skeleton, Hypercalcemia, Hypocalcemia, Contraindication to Ca or Vitamin D, Cyclosporine
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal >2 years, Osteoporosis T-score <= -2 hip, ambulatory Exclusion criteria: Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hypoparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Upper GI, Venous thromboembolic disease, Bisphosphonates, Calcitonin, Fluoride, Androgen, Estrogen agonists (including estrogen), Progestin, SERMS, Estrogen antagonists, Anabolic steroids, Testosterone, Vitamin D, Corticoids/Glucocorticoids, any medication that may alter bone and mineral metabolism, Breast Cancer, previous PTH use, vaginal bleeding, age <=50, age > 80, T score<-4.0, fracture T4 to L4

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Reid IR et al., 1994[50] Pamidronate Australia/NZ	Setting: Single center Jadad: 4	Inclusion criteria: Post-menopausal women NOS, Osteoporosis/Fracture Exclusion criteria: Hypothyroidism, Hyperthyroidism, Hepatic insufficiency, Renal insufficiency, Anticonvulsants, Bisphosphonates, Calcitonin, Fluoride, HRT, Anabolic steroids, Corticoids/Glucocorticoids, Major systemic Disease, Hypercalcemia, Hypocalcemia
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia	Setting: Multi-center Jadad: 3	Inclusion criteria: Post-menopausal >5 years, Osteoporosis T-score <= -2 spine Exclusion criteria: Carcinoma or suspected carcinoma, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hypoparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Bisphosphonates, Fluoride, HRT, Estrogen agonists (including estrogen), >1 Fracture, Vitamin D deficient, Med known to affect skeleton
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	Setting: Multi-center Jadad: 2	Inclusion criteria: Post-menopausal women NOS, T>-2.5, <+2.0, hysterectomy <15 years prior Exclusion criteria: Hepatic insufficiency, Renal insufficiency, Venous thromboembolic disease - Ever, Anticonvulsants, Bisphosphonates, Calcitonin, Fluoride, Androgen, Estrogen agonists (including estrogen), Progestin, Lipid lowering agents, Vitamin D, Corticoids/Glucocorticoids, age <40, Endocrine disease requiring treatment except thyroid, FSH<40, excessive alcohol intake, >60 years, Breast Cancer, Estrogen Dependent CA, Any cancer except skin in last 5 years, Serious postmenopausal symptoms
Reid IR et al., 2006[53] Calcium Australia/NZ	Setting: Single center Jadad: 4	Inclusion criteria: Post-menopausal >5 years, Normal Lumbar Dexa Scan Exclusion criteria: Carcinoma or suspected carcinoma, Hypothyroidism, Hyperthyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Bisphosphonates, Calcium (includes antacids), HRT, Anabolic steroids, Corticoids/Glucocorticoids, age <=55, Med known to affect skeleton, Vitamin D deficient
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	Setting: Multi-center Jadad: 4	Inclusion criteria: Post-menopausal >6 months, Osteopenia T-score <= -2.0 NOS, Spine/Hip anatomy suitable for Dexa Exclusion criteria: Metabolic bone disorder other than osteoporosis, Upper GI, Bisphosphonates, Fluoride, HRT, Estrogen agonists (including estrogen), Anabolic steroids, Corticoids/Glucocorticoids, Immunosuppressants, previous PTH use, Inability to remain 30min upright, Vitamin D deficient

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Sato S et al., 2003[55] Etidronate Japan	Setting: Setting not reported Jadad: 1	Inclusion criteria: Men, Pre-menopausal women, Post-menopausal women NOS, Connective Tissue Disease, Glucocorticoids >7.5mg for >90days Exclusion criteria: Cardiovascular disease, Renal insufficiency, Med known to affect skeleton, LS spine abnormalities prohibiting DEXA
Sato Y et al., 2004[56] Etidronate Japan	Setting: Setting not reported Jadad: 4	Inclusion criteria: Post-menopausal women NOS, recent hip fracture Exclusion criteria: Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Renal insufficiency, Bisphosphonates, Calcitonin, Estrogen agonists (including estrogen), Vitamin D, Corticoids/Glucocorticoids, nonambulatory, Underlying neurologic disorder, Prior calcium use
Sato Y et al., 2005[57] Risedronate Japan	Setting: Single center Jadad: 4	Inclusion criteria: Men, Age > 65, first stroke >= 3 months prior to study start date, hemiplegia Exclusion criteria: Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Upper GI, >1 Fracture, Familial Osteoporosis, Use of any drug known to alter bone metabolism for 3 months or longer during the preceding 12 months
Sato Y et al., 2005[58] Risedronate Japan	Setting: Single center Jadad: 4	Inclusion criteria: Post-menopausal women NOS, dementia and probable Alzheimer's dementia Exclusion criteria: Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Anticonvulsants, Bisphosphonates, Calcitonin, Calcium (includes antacids), Estrogen agonists (including estrogen), Vitamin D, Corticoids/Glucocorticoids, age < 70, treatment with Vitamin K, Familial Osteoporosis
Sato Y et al., 2005[59] Vitamin D Japan	Setting: Single center Jadad: 4	Inclusion criteria: Women otherwise undefined, hemiplegia, stroke >2 years Exclusion criteria: Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Anticonvulsants, Calcium (includes antacids), Vitamin D, dementia, total disability, hospitalization less than 2yrs, history of previous fracture, Drugs affecting Vitamin D Metabolism, Use of any drug known to alter bone metabolism for 3 months or longer during the preceding 12 months

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Sato Y et al., 2005[60] Risedronate Japan	Setting: Single center Jadad: 4	Inclusion criteria: Post-menopausal women NOS, acute onset of hemiplegic stroke Exclusion criteria: Cardiovascular disease, Hepatic insufficiency, Renal insufficiency, age <65, Med known to affect skeleton, mental condition that would preclude participation, inability to stand, quadraparesis, artificial nutrition
Sato Y et al., 2006[61] Alendronate Japan	Setting: Single center Jadad: 5	Inclusion criteria: Post-menopausal women NOS, Age > 65, Parkinson's Exclusion criteria: Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Bisphosphonates, Calcitonin, Calcium (includes antacids), Estrogen agonists (including estrogen), Vitamin D, Corticoids/Glucocorticoids, treatment with Vitamin K, nonvertebral fracture, Stage 5 Parkinson's
Sato Y et al., 2006[62] Etidronate Japan	Setting: Multi-center Jadad: 4	Inclusion criteria: Men, Women otherwise undefined, ALS (amyotrophic lateral sclerosis) Exclusion criteria: Med known to affect skeleton
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	Setting: Multi-center Jadad: 2	Inclusion criteria: Post-menopausal >5 years, at least 2 vertebral fractures Exclusion criteria: Age > 85, Bisphosphonates, Calcitonin, Fluoride, Hormone use, Estrogen agonists (including estrogen), Progestin, Anabolic steroids, Vitamin D, LS spine abnormalities prohibiting DEXA, any medication that may alter bone and mineral metabolism, noncompliance
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy	Setting: Single center Jadad: 1	Inclusion criteria: Post-menopausal women NOS, Organ transplant Exclusion criteria: NR
Torres A et al., 2004[65] Calcium, Vitamin D Spain	Setting: Single center Jadad: 4	Inclusion criteria: Men, Pre-menopausal women, Post-menopausal women NOS, Organ transplant, age >20 Exclusion criteria: previous parathyroidectomy

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Toth E et al., 2005[66] Calcitonin Eastern Europe	Setting: Single center Jadad: 1	Inclusion criteria: Men, Osteoporosis T-score <= -2.5 hip, Osteoporosis T-score <= -2.5 spine Exclusion criteria: Carcinoma or suspected carcinoma, Endocrine disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hypoparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Malabsorption syndrome, Upper GI, Anticonvulsants, Bisphosphonates, Anabolic steroids, Vitamin D, Corticoids/Glucocorticoids, treatment with monofluorophosphate, any vertebral deformity, Secondary Osteoporosis, Hypogonadism, any significant lab abnormalities, any medication that may alter bone and mineral metabolism
Trovas GP et al., 2002[67] Calcitonin Greece	Setting: Setting not reported Jadad: 4	Inclusion criteria: Men, Osteoporosis T-score <= -2.5 hip, Osteoporosis T-score <= -2.5 spine Exclusion criteria: Metabolic bone disorder other than osteoporosis, Secondary Osteoporosis
Uchida S et al., 2005[68] Alendronate Japan	Setting: Multi-center Jadad: 3	Inclusion criteria: Men, Post-menopausal >2 years, ambulatory, age 43-90, <70% YAM(young adult mean) spine or <80% YAM and fracture Exclusion criteria: Bisphosphonates, >1 Fracture
Ushiroyama T et al., 2001[69] Calcitonin Japan	Setting: Single center Jadad: 1	Inclusion criteria: Post-menopausal >6 months, Osteopenia, Osteoporosis Exclusion criteria: Metabolic bone disorder other than osteoporosis, Renal insufficiency, Urolithiasis, HRT, Estrogen agonists (including estrogen), Contraceptive
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2	Setting: Multi-center Jadad: 3	Inclusion criteria: Post-menopausal >1 year, hysterectomy bilateral salpingo-oophorectomy, >55 with hysterectomy, <55 with hysterectomy and elevated FSH, 5-yr predicted risk of Breast CA >= 1.66 on Galle Scale Exclusion criteria: Carcinoma or suspected carcinoma, Diabetes, Venous thromboembolic disease - Ever, Coumarins, Androgen, HRT, Estrogen agonists (including estrogen), Progestin, Estrogen antagonists, Contraceptive, age <35, mental condition that would preclude participation, cholestyramine, Uncontrolled HTN, atrial fibrillation, performance status restricting activity

Author, Year, Drug, Country, Trial name	Setting, Quality (Jadad score)	Eligibility criteria
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK	Setting: Single center Jadad: 3	Inclusion criteria: Post-menopausal women NOS, Osteoporosis T-score <= -2 spine, Osteoporosis/Non-traumatic fracture Exclusion criteria: Metabolic bone disorder other than osteoporosis, Bisphosphonates, Calcitonin, Fluoride, HRT, Anabolic steroids, Corticoids/Glucocorticoids, oophorectomy, Med known to affect skeleton
Zein CO et al., 2005[72] Alendronate US	Setting: Single center Jadad: 5	Inclusion criteria: Men, Pre-menopausal women, Post-menopausal women NOS, Primary Biliary Cirrhosis, T <-1.5 of lumbar spine, estimated survival based on Mayo Risk score of >80% at 2 years Exclusion criteria: Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Renal insufficiency, Upper GI, Anticonvulsants, Calcitonin, Fluoride, Testosterone, Vitamin D, Corticoids/Glucocorticoids, heparin, Med known to affect skeleton, Vitamin D deficient, age >=70, age <18, starting estrogen within one year or discontinuing estrogen in the past

Author, Year, Drug, Country, Trial name	Interventions (drug, dose, duration)
Agrawal S et al., 2006[1] Risedronate US	Placebo weekly vs. Risedronate 30 mg weekly Duration: 3 months
Aris RM et al., 2000[2] Pamidronate US	Pamidronate 30 mg every 2 weeks vs. Control Duration: 24 months
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	Zoledronic acid 5 mg yearly vs Placebo yearly Duration: 36 months
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	Placebo and PTH 40 ug daily vs. Placebo and Alendronate 10 mg daily Duration: 14 months
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	Placebo daily vs. Placebo and Alendronate 10 mg daily vs. Placebo and Estrogen 0.625 mg daily vs. Alendronate 10 mg and Estrogen 0.625 mg daily Duration: 24 months
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	Alendronate 70 mg weekly vs. Risedronate 35 mg weekly Duration: 24 months
Boutsen Y et al., 1997[7] Pamidronate Western Europe	Pamidronate 90 mg daily and Pamidronate 30 mg every 3 months vs. Placebo Duration: 1 day
Brown JP et al., 2002[8] Risedronate US, Canada	Risedronate 5 mg daily vs. Risedronate 35 mg weekly vs. Risedronate 50 mg weekly Duration: 12 months

Author, Year, Drug, Country, Trial name	Interventions (drug, dose, duration)
Campbell IA et al., 2004[9] Etidronate UK	Control vs. Calcium 500 mg daily vs. Etidronate 400 mg daily for 14 days every 3 months vs. Etidronate 400 mg daily for 14 days every 3 months and Calcium 500 mg daily Duration: 60 months
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	Placebo daily vs. Alendronate 5-10 mg daily Duration: variable
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	Placebo daily vs. Alendronate 5-10 mg daily Duration: variable
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	Placebo daily vs. Ibandronate 2.5 mg daily vs. Placebo every other day for 12 doses followed by daily for the remainder of 3 mo and Ibandronate 20 mg every other day for 12 doses every 3 months Duration: 36 months
Coco M et al., 2003[12] Pamidronate US	Placebo vs. Pamidronate 60 mg at baseline and Pamidronate 30 mg at months 1, 2, 3 and 6 Duration: 12 months
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1	Placebo daily vs. Tamoxifen 20 mg daily Duration: variable
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	Risedronate 2.5 mg daily vs. Etidronate 200 mg daily for 14 days every 3 months Duration: 11 months

Author, Year, Drug, Country, Trial name	Interventions (drug, dose, duration)
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	Placebo daily vs. PTH 20 ug daily Duration: 19 months
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe	Calcitonin 100 I.U. daily vs. Etidronate 400 mg daily for 14 days every 2.5 months vs. Vitamin D 32000 I.U. weekly Duration: 18 months
Grant AM et al., 2005[17] Vitamin D UK	Placebo daily vs. Calcium 1000 mg and Vitamin D 800 I.U. daily vs. Placebo and Vitamin D 800 I.U. daily vs. Placebo and Calcium 1000 mg daily Duration: variable
Greenspan SL et al., 2003[18] Alendronate, Estrogen US	Placebo vs. Placebo and Estrogen 0.625 mg daily vs. Placebo and Alendronate 10 mg daily vs. Alendronate 10 mg and Estrogen 0.625 mg daily Duration: 36 months
Greenspan SL et al., 2006[19] Risedronate US	Risedronate 35 mg weekly vs. Placebo weekly Duration: 12 months
Grotz W et al., 2001[20] Ibandronate Germany	Control vs. Ibandronate 1 mg daily for 1 day and Ibandronate 2 mg every 3 months for 9 months
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe	Etidronate 400 mg daily for 14 days every 3 months vs. Alendronate 10 mg daily Duration: 24 months
Harris ST et al., 2004[22] Risedronate US, Canada	Risedronate 5 mg daily vs. Risedronate 35 mg weekly vs. Risedronate 50 mg weekly Duration: 24 months
Hay JE et al., 2001[23] Calcitonin US	Control vs. SQ Calcitonin 100 MRC units daily Duration: 6 months

Author, Year, Drug, Country, Trial name	Interventions (drug, dose, duration)
Hizmetli S et al., 1998[24] Calcitonin Turkey	Control vs. Calcitonin 50 I.U. daily vs. Calcitonin 100 I.U. daily Duration: 24 months
Hochberg MC et al., 2005[25] Alendronate US FIT	Placebo daily vs. Alendronate 5-10 mg daily Duration: variable
Hooper MJ et al., 2005[26] Risedronate Australia/NZ	Placebo daily vs. Risedronate 2.5 mg daily vs. Risedronate 5 mg daily Duration: 24 months
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil	Placebo daily and Placebo2 dosage not applicable weekly vs. Placebo weekly and Risedronate 5 mg daily vs. Placebo daily and Alendronate 70 mg weekly Duration: 12 months
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	Control daily vs. Estrogen 0.625 mg daily vs. Etidronate 200 mg daily for 2 weeks every 12 weeks vs. Calcitonin 20 I.U. weekly vs. Vitamin D 1 ug daily vs. Vitamin K 45 mg daily Duration: 24 months
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan	Etidronate 200 mg daily for 14 days every 3 months vs. Alendronate 5 mg daily Duration: 6 months
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI	Placebo daily vs. Calcium 1000 mg and Vitamin D 400 I.U. daily Duration: variable
Kanaji A et al., 2006[31] Risedronate Japan	Placebo daily vs. Risedronate 2.5 mg daily Duration: 8 months
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland	Control vs. Pamidronate 60 mg variable frequency Duration: 12 months

Author, Year, Drug, Country, Trial name	Interventions (drug, dose, duration)
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	Placebo daily vs. PTH 20 ug daily vs. PTH 40 ug daily Duration: 11 median months
Kim SH et al., 2004[34] Pamidronate Asia	Placebo every 3 months vs. Pamidronate 30 mg every 3 months Duration: 12 months
Kishimoto H et al., 2006[35] Risedronate Japan	Placebo daily and Risedronate 17.5 mg weekly vs. Placebo weekly and Risedronate 2.5 mg daily Duration: 11 months
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	Placebo daily for 2 weeks every 12 weeks and Risedronate 2.5 mg daily vs. Placebo daily and Etidronate 200 mg daily for 2 weeks every 12 weeks Duration: 22 months
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY	Alendronate 70 mg weekly vs. Raloxifene 60 mg daily Duration: 12 months
McClung MR et al., 2006[38] Alendronate, AMG162 US	Placebo vs. AMG 162 6 mg every 3 months vs. AMG 162 14 mg every 3 months vs. AMG 162 30 mg every 3 months vs. AMG 162 14 mg every 6 months vs. AMG 162 60 mg every 6 months vs. AMG 162 100 mg every 6 months vs. AMG 162 210 mg every 6 months vs. Alendronate 70 mg weekly Duration: 12 months
Milgrom C et al., 2004[39] Risedronate Israel	Placebo variable frequency vs. Risedronate variable dosage variable frequency Duration: 3 months
Muscoso E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy	Alendronate 10 mg daily vs. Clodronate 100 mg weekly vs. Risedronate 5 mg daily vs. Raloxifene 60 mg daily Duration: 24 months
Ninkovic M et al., 2002[41] Pamidronate UK	Control vs. Pamidronate 60 mg daily Duration: 1 day

Author, Year, Drug, Country, Trial name	Interventions (drug, dose, duration)
Orwoll ES et al., 2003[42] PTH 1100101000	Placebo daily vs. PTH 20 ug daily vs. PTH 40 ug daily Duration: variable
Palomba S et al., 2005[43] Risedronate Italy	Placebo weekly vs. Risedronate 35 mg weekly Duration: 12 months
Porthouse J et al., 2005[44] Calcium, Vitamin D UK	Control and Education vs. Calcium 1000 mg and Vitamin D 800 I.U. daily Duration: variable
Prince RL et al., 2006[45] Calcium Australia/NZ	Placebo daily vs. Calcium 1200 mg daily Duration: 60 months
Quandt SA et al., 2005[46] Alendronate US FIT	Alendronate 5 mg and Alendronate 10 mg daily vs. Placebo daily Duration: 24 months
Ravn P et al., 1996[47] Ibandronate Western Europe	Placebo daily vs. Ibandronate 0.25 mg daily vs. Ibandronate 0.5 mg daily vs. Ibandronate 1.0 mg daily vs. Ibandronate 25 mg daily vs. Ibandronate 5.0 mg daily Duration: 12 months
Recker R et al., 2004[48] Ibandronate US, Western Europe	Placebo every 3 months vs. Ibandronate 0.5 mg every 3 months vs. Ibandronate 1 mg every 3 months Duration: 36 months
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial	Placebo and Alendronate 10 mg daily vs. Placebo and Raloxifene 60 mg daily Duration: variable
Reid IR et al., 1994[50] Pamidronate Australia/NZ	Pamidronate 150 mg daily vs. Placebo daily Duration: 24 months

Author, Year, Drug, Country, Trial name	Interventions (drug, dose, duration)
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia	Zoledronic acid 0.25 mg every 3 months vs. Zoledronic acid 0.5 mg every 3 months vs. Zoledronic acid 1 mg every 3 months vs. Zoledronic acid 2 mg every 6 months vs. Zoledronic acid 4 mg yearly vs. Placebo every 3 months Duration: 12 months
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	Placebo vs. Raloxifene 60 mg daily vs. Raloxifene 150 mg daily vs. Estrogen 0.625 mg daily Duration: 36 months
Reid IR et al., 2006[53] Calcium Australia/NZ	Placebo daily vs. Calcium 1 g daily Duration: 60 months
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	Placebo and Alendronate 70 mg weekly vs. Placebo and Risedronate 35 mg weekly Duration: 12 months
Sato S et al., 2003[55] Etidronate Japan	Control vs. Etidronate 200 mg daily for 14 days every 3 months Duration: 33 months
Sato Y et al., 2004[56] Etidronate Japan	Placebo daily for 14days, off meds for 9wks, daily for 2wks vs. Etidronate 200 mg daily for 14days, off meds for 9wks, daily for 2wks Duration: 3 months
Sato Y et al., 2005[57] Risedronate Japan	Placebo daily vs. Risedronate 2.5 mg daily Duration: 18 months
Sato Y et al., 2005[58] Risedronate Japan	Risedronate 2.5 mg daily vs. Placebo daily Duration: 18 months
Sato Y et al., 2005[59] Vitamin D Japan	Placebo daily vs. Vitamin D 1000 I.U. daily Duration: 24 months

Author, Year, Drug, Country, Trial name	Interventions (drug, dose, duration)
Sato Y et al., 2005[60] Risedronate Japan	Placebo daily vs. Risedronate 2.5 mg daily Duration: 12 months
Sato Y et al., 2006[61] Alendronate Japan	Placebo and Vitamin D 1000 I.U. daily vs. Alendronate 5 mg and Vitamin D 1000 I.U. daily Duration: 24 months
Sato Y et al., 2006[62] Etidronate Japan	Placebo q.d x2wks then off 13wks vs. Etidronate 400 mg qd x2wks then off 13wks Duration: 24 months
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	Placebo daily vs. Risedronate 5 mg daily Duration: 60 months
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy	Control vs. Estradiol 2 mg daily and Dihydroprogesterone 10 mg every day for 14 days/month for 12 months vs. Risedronate 35 mg weekly for 12 months vs. Zoledronic acid 4 mg once every 28days every 3 months for 3 months
Torres A et al., 2004[65] Calcium, Vitamin D Spain	Placebo qod vs. Vitamin D 0.5 ug qod Duration: 3 months
Toth E et al., 2005[66] Calcitonin Eastern Europe	Control vs. Calcitonin 200 I.U. daily every other month Duration: 18 months
Trovas GP et al., 2002[67] Calcitonin Greece	Placebo daily vs. Calcitonin 200 I.U. daily Duration: 12 months
Uchida S et al., 2005[68] Alendronate Japan	Alendronate 5 mg daily vs. Alendronate 35 mg weekly Duration: 12 months

Author, Year, Drug, Country, Trial name	Interventions (drug, dose, duration)
Ushiroyama T et al., 2001[69] Calcitonin Japan	Control vs. SQ Calcitonin 10 I.U. every 2 weeks vs. Vitamin D 1 ug daily vs. Vitamin D 1 ug daily and SQ Calcitonin 10 I.U. every 2 weeks Duration: 24 months
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2	Tamoxifen 20 mg daily vs. Raloxifene 60 mg daily Duration: variable
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK	Control vs. Estrogen 0.625 mg and Norgestrel 150 ug daily vs. Etidronate 400 mg daily for 14 days every 3 months vs. Estrogen 0.625 mg daily, Etidronate 400 mg daily for 14 days every 3 months and Norgestrel 150 ug daily Duration: 48 months
Zein CO et al., 2005[72] Alendronate US	Placebo weekly vs. Alendronate 70 mg weekly Duration: 12 months

Author, Year, Drug, Country, Trial name	Interventions given to everyone	Run-in period Wash-out period	Allowed other medications/interventions
Agrawal S et al., 2006[1] Risedronate US	Calcium, Vitamin D	Run-in: None Wash-out: None	
Aris RM et al., 2000[2] Pamidronate US	Calcium, Vitamin D, Steroids	Run-in: None Wash-out: None	
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	Calcium, Vitamin D	Run-in: None Wash-out: None	
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	Calcium, Vitamin D	Run-in: 2 mo of Placebo, 2 mo of Control Wash-out: None	
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	Calcium	Run-in: None Wash-out: None	
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	Calcium, Vitamin D	Run-in: None Wash-out: None	
Boutsen Y et al., 1997[7] Pamidronate Western Europe	Calcium	Run-in: None Wash-out: None	
Brown JP et al., 2002[8] Risedronate US, Canada	Calcium	Run-in: None Wash-out: None	

Author, Year, Drug, Country, Trial name	Interventions given to everyone	Run-in period Wash-out period	Allowed other medications/interventions
Campbell IA et al., 2004[9] Etidronate UK	Steroids	Run-in: None Wash-out: None	
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	Calcium, Vitamin D	Run-in: None Wash-out: None	
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	Calcium, Vitamin D	Run-in: None Wash-out: None	
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	Calcium, Vitamin D	Run-in: None Wash-out: None	
Coco M et al., 2003[12] Pamidronate US	Calcium, Vitamin D	Run-in: None Wash-out: None	
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1		Run-in: None Wash-out: None	
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	Calcium	Run-in: None Wash-out: None	

Author, Year, Drug, Country, Trial name	Interventions given to everyone	Run-in period Wash-out period	Allowed other medications/interventions
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	Calcium, Vitamin D	Run-in: None Wash-out: None	
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe	Calcium, Steroids, Azathioprine, Cyclosporine	Run-in: None Wash-out: None	
Grant AM et al., 2005[17] Vitamin D UK	Steroids	Run-in: None Wash-out: None	
Greenspan SL et al., 2003[18] Alendronate, Estrogen US	Calcium, Vitamin D	Run-in: 3 mo of Placebo for Subjects that completed run-in randomized, 3 mo of Estrogen for Subjects that completed run-in randomized, 3 mo of Calcium for Subjects that completed run-in randomized Wash-out: None	Medroxyprogesterone (if necessary)
Greenspan SL et al., 2006[19] Risedronate US	Calcium, Vitamin D	Run-in: None Wash-out: None	
Grotz W et al., 2001[20] Ibandronate Germany	Calcium, Estrogen, Vitamin D, Steroids	Run-in: None Wash-out: None	
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe	Calcium, Vitamin D, Ursodeoxycholic Acid	Run-in: None Wash-out: None	
Harris ST et al., 2004[22] Risedronate US, Canada	Calcium	Run-in: None Wash-out: None	

Author, Year, Drug, Country, Trial name	Interventions given to everyone	Run-in period Wash-out period	Allowed other medications/interventions
Hay JE et al., 2001[23] Calcitonin US	Calcium, Vitamin D, Steroids	Run-in: None Wash-out: None	
Hochberg MC et al., 2005[25] Alendronate US FIT	Calcium, Vitamin D	Run-in: None Wash-out: None	
Hooper MJ et al., 2005[26] Risedronate Australia/NZ	Calcium	Run-in: None Wash-out: None	
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil	Calcium, Vitamin D	Run-in: None Wash-out: None	
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY		Run-in: None Wash-out: None	Medroxyprogesterone
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan		Run-in: None Wash-out: None	
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI	Calcium, Estrogen, Vitamin D	Run-in: None Wash-out: None	
Kanaji A et al., 2006[31] Risedronate Japan	Calcium, Vitamin D	Run-in: None Wash-out: None	
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland	Calcium, Estrogen, Testosterone, Vitamin D	Run-in: None Wash-out: None	

Author, Year, Drug, Country, Trial name	Interventions given to everyone	Run-in period Wash-out period	Allowed other medications/interventions
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	Calcium, Vitamin D	Run-in: 1 mo of Calcium, 1 mo of Vitamin D Wash-out: None	
Kim SH et al., 2004[34] Pamidronate Asia	Steroids	Run-in: None Wash-out: None	
Kishimoto H et al., 2006[35] Risedronate Japan	Calcium	Run-in: None Wash-out: None	
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	Calcium	Run-in: None Wash-out: None	
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY	Calcium, Vitamin D	Run-in: None Wash-out: None	
McClung MR et al., 2006[38] Alendronate, AMG162 US	Calcium, Vitamin D	Run-in: None Wash-out: None	
Milgrom C et al., 2004[39] Risedronate Israel		Run-in: None Wash-out: None	
Muscoso E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy	Calcium, Vitamin D	Run-in: None Wash-out: None	
Ninkovic M et al., 2002[41] Pamidronate UK	Steroids	Run-in: None Wash-out: None	

Author, Year, Drug, Country, Trial name	Interventions given to everyone	Run-in period Wash-out period	Allowed other medications/interventions
Orwoll ES et al., 2003[42] PTH 1100101000	Calcium, Vitamin D	Run-in: None Wash-out: None	
Palomba S et al., 2005[43] Risedronate Italy	Calcium, Vitamin D	Run-in: None Wash-out: None	
Porthouse J et al., 2005[44] Calcium, Vitamin D UK		Run-in: None Wash-out: None	
Prince RL et al., 2006[45] Calcium Australia/NZ		Run-in: None Wash-out: None	
Quandt SA et al., 2005[46] Alendronate US FIT		Run-in: None Wash-out: None	
Ravn P et al., 1996[47] Ibandronate Western Europe	Calcium	Run-in: None Wash-out: None	
Recker R et al., 2004[48] Ibandronate US, Western Europe	Calcium, Vitamin D	Run-in: None Wash-out: None	
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial	Calcium, Vitamin D	Run-in: None Wash-out: None	
Reid IR et al., 1994[50] Pamidronate Australia/NZ	Calcium	Run-in: None Wash-out: None	

Author, Year, Drug, Country, Trial name	Interventions given to everyone	Run-in period Wash-out period	Allowed other medications/interventions
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia	Calcium	Run-in: None Wash-out: None	
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	Calcium	Run-in: None Wash-out: None	
Reid IR et al., 2006[53] Calcium Australia/NZ		Run-in: None Wash-out: None	
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	Calcium, Vitamin D	Run-in: None Wash-out: None	
Sato S et al., 2003[55] Etidronate Japan	Calcium, Vitamin D, Steroids	Run-in: None Wash-out: None	
Sato Y et al., 2004[56] Etidronate Japan		Run-in: None Wash-out: None	
Sato Y et al., 2005[57] Risedronate Japan		Run-in: None Wash-out: None	
Sato Y et al., 2005[58] Risedronate Japan	Calcium, Vitamin D	Run-in: None Wash-out: None	
Sato Y et al., 2005[59] Vitamin D Japan		Run-in: None Wash-out: None	

Author, Year, Drug, Country, Trial name	Interventions given to everyone	Run-in period Wash-out period	Allowed other medications/interventions
Sato Y et al., 2005[60] Risedronate Japan		Run-in: None Wash-out: None	
Sato Y et al., 2006[61] Alendronate Japan		Run-in: None Wash-out: None	
Sato Y et al., 2006[62] Etidronate Japan	Vitamin D	Run-in: None Wash-out: None	
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	Calcium, Vitamin D	Run-in: None Wash-out: None	
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy	Calcium, Vitamin D, Steroids, Cyclosporine	Run-in: None Wash-out: None	
Torres A et al., 2004[65] Calcium, Vitamin D Spain	Calcium, Steroids	Run-in: None Wash-out: None	
Toth E et al., 2005[66] Calcitonin Eastern Europe	Calcium, Vitamin D	Run-in: None Wash-out: None	
Trovas GP et al., 2002[67] Calcitonin Greece	Calcium	Run-in: None Wash-out: None	
Uchida S et al., 2005[68] Alendronate Japan	Calcium, Vitamin D	Run-in: None Wash-out: None	

Appendix C2. Evidence Tables for Randomized Controlled Trials
Columns 5-7: Interventions given to everyone, Run-in/Wash-out, Allowed other meds

Author, Year, Drug, Country, Trial name	Interventions given to everyone	Run-in period Wash-out period	Allowed other medications/interventions
Ushiroyama T et al., 2001[69] Calcitonin Japan		Run-in: None Wash-out: None	
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2		Run-in: None Wash-out: None	
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK	Calcium, Vitamin D	Run-in: None Wash-out: None	
Zein CO et al., 2005[72] Alendronate US	Calcium, Vitamin D	Run-in: None Wash-out: None	

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Agrawal S et al., 2006[1] Risedronate US	Assessed at baseline, 6 wk, 12 wk: Total fractures	76/NR 77% male Not Reported
Aris RM et al., 2000[2] Pamidronate US	Assessed at baseline, 6 mo, 12 mo, 18 mo, 24 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture	28/18-38 50% male Not Reported
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	Assessed at baseline, 6 mo, 12 mo, 24 mo, 36 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Hip frac., Vertebral frac., Total fractures	73/NR 0% male 10110000
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	Assessed at baseline, 1 mo, 3 mo, 16 mo, 12 mo, 14 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Radial fracture	66/NR 0% male Caucasian, Hispanic, other
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	Assessed at baseline, 3 mo, 6 mo, 12 mo, 18 mo, 24 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Total fractures	62/42-82 0% male Caucasian, other
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	Assessed at baseline, 3 mo, 6 mo, 12 mo, 24 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Total fractures	65/NR 0% male Caucasian, African-American, Asian, other

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Boutsen Y et al., 1997[7] Pamidronate Western Europe	Assessed at baseline, 3 mo, 6 mo, 9 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture, Radiographic Vertebral Fractures	61/NR 18.5% male Not Reported
Brown JP et al., 2002[8] Risedronate US, Canada	Assessed at baseline, 3 mo, 6 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture, Total fractures, Radiographic Vertebral Fractures	68/NR 0% male Caucasian, other
Campbell IA et al., 2004[9] Etidronate UK	Assessed at baseline, 1 yr, 2 yr, 3 yr, 4 yr, 5 yr: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture, Total fractures, Radiographic Vertebral Fractures	60/NR 58% male Not Reported
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	Assessed at baseline, 997 yr: Vertebral fracture , Radiographic Vertebral Fractures	NR/55-80 0% male Not Reported
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	Assessed at baseline, 997 yr: Vertebral fracture , Radiographic Vertebral Fractures	NR/55-80 0% male Not Reported
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	Assessed at baseline, 6 mo, 12 mo, 18 mo, 24 mo, 30 mo, 36 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Total fractures, Symptomatic Vertebral Fractures, Radiographic Vertebral Fractures, Symptomatic Vertebral Fractures, Radiographic Vertebral Fractures	69/55-80 0% male Not Reported

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Coco M et al., 2003[12] Pamidronate US	Assessed at baseline, 1 mo, 2 mo, 3 mo, 4 mo, 5 mo, 6 mo, 7 mo, 8 mo, 9 mo, 10 mo, 11 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Hip fracture , Vertebral fracture	44/NR 50% male Caucasian, African-American, Hispanic, Asian
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1	Assessed at 997 mo: Hip fracture , Radial fracture , Vertebral fracture , Total fractures, Symptomatic Vertebral Fractures	NR/NR 0% male Caucasian, African-American, other
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	Assessed at baseline, 12 wk, 24 wk, 36 wk, 48 wk: BMD - DEXA-Spine, Vertebral fracture , Total fractures, Radiographic Vertebral Fractures	63/40-75 1% male Asian
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	Assessed at baseline, 1 mo, 3 mo, 6 mo, 9 mo, 12 mo, 15 mo, 18 mo, 21 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	70/NR 0% male Caucasian, other
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe	Assessed at baseline, 6 mo, 12 mo, 18 mo: BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	53/NR 95% male Not Reported
Grant AM et al., 2005[17] Vitamin D UK	Assessed at baseline, 62 mo: Hip fracture , Radial fracture , Vertebral fracture , Total fractures, Symptomatic Vertebral Fractures	77/NR 15% male Caucasian, other

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Greenspan SL et al., 2003[18] Alendronate, Estrogen US	Assessed at baseline, 0 mo, 6 mo, 12 mo, 18 mo, 24 mo, 30 mo, 36 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Total fractures	72/65-90 0% male Not Reported
Greenspan SL et al., 2006[19] Risedronate US	Assessed at baseline, 6 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Total fractures, Symptomatic Vertebral Fractures	50/NR 0% male Not Reported
Grotz W et al., 2001[20] Ibandronate Germany	Assessed at baseline, 6 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Total fractures, Radiographic Vertebral Fractures, Symptomatic Vertebral Fractures	43/20-60 67% male Not Reported
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe	Assessed at baseline, 6 mo, 12 mo, 18 mo, 24 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Total fractures, Radiographic Vertebral Fractures	59/41-77 0% male Not Reported
Harris ST et al., 2004[22] Risedronate US, Canada	Assessed at baseline, 3 mo, 6 mo, 12 mo, 24 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Total fractures, Radiographic Vertebral Fractures	68/NR 0% male Caucasian, other
Hay JE et al., 2001[23] Calcitonin US	Assessed at baseline, 4 mo, 12 mo: BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	51/NR 38% male Not Reported

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Hizmetli S et al., 1998[24] Calcitonin Turkey	Assessed at baseline, 6 mo, 12 mo, 24 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	58/NR 0% male Not Reported
Hochberg MC et al., 2005[25] Alendronate US FIT	Assessed at baseline, 997 yr: Hip fracture , Radial fracture , Vertebral fracture , Radiographic Vertebral Fractures	NR/55-80 0% male Not Reported
Hooper MJ et al., 2005[26] Risedronate Australia/NZ	Assessed at baseline, 3 mo, 6 mo, 12 mo, 18 mo, 24 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Symptomatic Vertebral Fractures, Radiographic Vertebral Fractures	53/42-63 0% male Caucasian, other
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil	Assessed at baseline, 1 mo, 3 mo, 6 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Total fractures, Symptomatic Vertebral Fractures	69/NR 0% male Caucasian, other
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	Assessed at baseline, 3 mo, 6 mo, 9 mo, 12 mo, 15 mo, 18 mo, 21 mo, 24 mo: Hip fracture , Radial fracture , Vertebral fracture	NR/50-75 0% male Not Reported
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan	Assessed at baseline, 3 mo, 6 mo: Vertebral fracture , Radiographic Vertebral Fractures	74/63-84 0% male Not Reported

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI	Assessed at 997 yr: BMD - DEXA-Hip, BMD - DEXA-Spine, Hip fracture , Radial fracture , Vertebral fracture , Total fractures, Symptomatic Vertebral Fractures	62/50-79 0% male Caucasian, African-American, Hispanic, Asian, Native American
Kanaji A et al., 2006[31] Risedronate Japan	Assessed at baseline, 6 mo, 12 mo: BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	NR/63-87 100% male Asian
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland	Assessed at baseline, 1 mo, 3 mo, 6 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	43/NR 50% male Not Reported
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	Assessed at baseline, 3 mo, 6 mo, 12 mo, 18 mo, 30 mo, 42 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	59/30-85 100% male Caucasian, other
Kim SH et al., 2004[34] Pamidronate Asia	Assessed at baseline, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Total fractures	49/NR 51% male Not Reported
Kishimoto H et al., 2006[35] Risedronate Japan	Assessed at baseline, 4 wk, 12 wk, 24 wk, 36 wk, 48 wk: BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	67/NR 3% male Asian

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	Assessed at baseline, 24 wk, 48 wk, 72 wk, 96 wk: Vertebral fracture	72/NR 4% male Not Reported
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY	Assessed at baseline, 6 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Hip fracture , Proximal humerus fracture , Radial fracture , Vertebral fracture , Total fractures	64/NR 0% male Caucasian, African-American, Asian, other
McClung MR et al., 2006[38] Alendronate, AMG162 US	Assessed at baseline, 1 mo, 2 mo, 3 mo, 4 mo, 5 mo, 6 mo, 7 mo, 8 mo, 9 mo, 10 mo, 11 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Proximal humerus fracture , Radial fracture , Vertebral fracture , Total fractures, Symptomatic Vertebral Fractures	63/NR 0% male Caucasian, African-American, Hispanic
Milgrom C et al., 2004[39] Risedronate Israel	Assessed at baseline, 15 wk: Total fractures	NR/18-28 100% male Not Reported
Mucosa E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy	Assessed at 12 mo, 24 mo: BMD - DEXA-Spine, Hip fracture , Radial fracture , Vertebral fracture , Symptomatic Vertebral Fractures	68/NR 0% male Not Reported
Nonionic M et al., 2002[41] Pamidronate UK	Assessed at baseline, 3 mo, 6 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Proximal humerus fracture , Vertebral fracture , Total fractures, Radiographic Vertebral Fractures, Symptomatic Vertebral Fractures	51/19-68 50% male Not Reported

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Orwell ES et al., 2003[42] PTH 1100101000	Assessed at baseline, 1 mo, 3 mo, 6 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Total fractures	59/NR 100% male Caucasian, other
Aplomb S et al., 2005[43] Risedronate Italy	Assessed at baseline, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Hip fracture , Radial fracture , Vertebral fracture , Total fractures, Radiographic Vertebral Fractures	52/NR 0% male Not Reported
Porthouse J et al., 2005[44] Calcium, Vitamin D UK	Assessed at baseline, 997 mo: Hip fracture , Radial fracture , Total fractures	77/NR 0% male Not Reported
Prince RL et al., 2006[45] Calcium Australia/NZ	Assessed at baseline, 60 mo: BMD - DEXA-Hip, Radial fracture , Vertebral fracture , Total fractures, Radiographic Vertebral Fractures, Symptomatic Vertebral Fractures	75/NR 0% male Not Reported
Quandt SA et al., 2005[46] Alendronate US FIT	Assessed at baseline, 6 mo, 12 mo, 18 mo, 24 mo, 30 mo, 36 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	69/55-80 0% male Caucasian, other
Ravn P et al., 1996[47] Ibandronate Western Europe	Assessed at baseline, 3 mo, 6 mo, 9 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Total fractures	65/NR 0% male Caucasian

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Recker R et al., 2004[48] Ibandronate US, Western Europe	Assessed at baseline, 6 mo, 12 mo, 18 mo, 24 mo, 30 mo, 36 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Hip fracture , Vertebral fracture , Total fractures, Radiographic Vertebral Fractures	67/55-76 0% male Not Reported
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial	Assessed at baseline, 997 days: BMD - DEXA-Hip, BMD - DEXA-Spine, Hip fracture , Radial fracture , Vertebral fracture , Total fractures, Radiographic Vertebral Fractures	66/NR 0% male Caucasian
Reid IR et al., 1994[50] Pamidronate Australia/NZ	Assessed at baseline, 1 yr, 2 yr: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	66/NR 0% male Not Reported
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia	Assessed at baseline, 3 mo, 6 mo, 9 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture	64/45-80 0% male Caucasian, other
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	Assessed at baseline, 3 mo, 6 mo, 9 mo, 12 mo, 15 mo, 18 mo, 21 mo, 24 mo, 30 mo, 36 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	53/NR 0% male Caucasian, other
Reid IR et al., 2006[53] Calcium Australia/NZ	Assessed at baseline, 997 NA: BMD - DEXA-Hip, BMD - DEXA-Spine, Hip fracture , Radial fracture , Vertebral fracture , Total fractures, Radiographic Vertebral Fractures	74/NR 0% male Not Reported

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	Assessed at baseline, 3 mo, 6 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Total fractures	65/NR 0% male Caucasian, African-American, Asian, other
Sato S et al., 2003[55] Etidronate Japan	Assessed at baseline, 24 wk, 48 wk, 144 wk: BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	45/21-73 999% male Asian
Sato Y et al., 2004[56] Etidronate Japan	Assessed at 13 wk: Total fractures	75/70-79 0% male Asian
Sato Y et al., 2005[57] Risedronate Japan	Assessed at baseline, 6 mo, 12 mo, 18 mo: Hip fracture	76/NR 100% male Not Reported
Sato Y et al., 2005[58] Risedronate Japan	Assessed at baseline, 4 wk, 8 wk, 12 wk, 16 wk, 20 wk, 24 wk, 28 wk, 32 wk, 36 wk, 40 wk, 44 wk, 48 wk, 52 wk, 56 wk, 60 wk, 64 wk, 68 wk, 72 wk: Hip fracture , Proximal humerus fracture	78/NR 0% male Not Reported
Sato Y et al., 2005[59] Vitamin D Japan	Assessed at baseline, 2 yr: Hip fracture	74/NR 0% male Asian

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Sato Y et al., 2005[60] Risedronate Japan	Assessed at 6 mo, 12 mo: Hip fracture	71/NR 0% male Asian
Sato Y et al., 2006[61] Alendronate Japan	Assessed at baseline, 997 yr: Hip fracture	72/65-85 0% male Asian
Sato Y et al., 2006[62] Etidronate Japan	Assessed at baseline, 1 yr, 2 yr: Proximal humerus fracture , Vertebral fracture , Symptomatic Vertebral Fractures	63/NR 57% male Asian
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	Assessed at baseline, 6 mo, 12 mo, 18 mo, 24 mo, 36 mo, 48 mo, 60 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Hip fracture , Proximal humerus fracture , Vertebral fracture , Total fractures, Radiographic Vertebral Fractures	71/NR 0% male Not Reported
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy	Assessed at baseline, 3 mo, 6 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	26/NR 0% male Not Reported
Torres A et al., 2004[65] Calcium, Vitamin D Spain	Assessed at baseline, 3 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Total fractures	49/NR 78% male Not Reported

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Toth E et al., 2005[66] Calcitonin Eastern Europe	Assessed at baseline, 3 mo, 6 mo, 9 mo, 12 mo, 15 mo, 18 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Proximal humerus fracture , Vertebral fracture , Symptomatic Vertebral Fractures, Radiographic Vertebral Fractures	59/40-76 100% male Not Reported
Trovas GP et al., 2002[67] Calcitonin Greece	Assessed at baseline, 3 mo, 6 mo, 9 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture , Radiographic Vertebral Fractures	53/27-74 100% male Not Reported
Uchida S et al., 2005[68] Alendronate Japan	Assessed at baseline, 12 wk, 24 wk, 52 wk: BMD - DEXA-Hip, BMD - DEXA-Spine, Total fractures	67/NR 4% male Asian
Ushiroyama T et al., 2001[69] Calcitonin Japan	Assessed at baseline, 6 mo, 12 mo, 18 mo, 24 mo: BMD - DEXA-Spine, Vertebral fracture , Total fractures, Symptomatic Vertebral Fractures	55/53-58 0% male Asian
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2	Assessed at 997 yr: Hip fracture , Radial fracture , Vertebral fracture , Total fractures, Symptomatic Vertebral Fractures	59/NR 0% male Caucasian, African-American, Hispanic, other

Author, Year, Drug, Country, Trial name	Method of outcome assessment Timing of assessment	Age (average/range) Gender Ethnicity
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK	Assessed at baseline, 2 yr, 4 yr: BMD - DEXA-Hip, BMD - DEXA-Spine, Vertebral fracture	65/58-72 0% male Caucasian
Zein CO et al., 2005[72] Alendronate US	Assessed at baseline, 6 mo, 12 mo: BMD - DEXA-Hip, BMD - DEXA-Spine, Hip fracture , Vertebral fracture , Radiographic Vertebral Fractures	61/NR 6% male Not Reported

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Agrawal S et al., 2006[1] Risedronate US	64/NR/60	7/0/53	Number of people with fracture not reported
Aris RM et al., 2000[2] Pamidronate US	44/37/37	3/0/34	Number of people with fracture: long bone fractures at 24 months: Pamidronate vs. Control 18.8% vs. 33.3% OR = 0.48 (95% CI 0.11, 2.17)
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	18421/9977/7765	NR/NR/7736	Number of people with fracture: Any clinical fracture at 36 months: Zoledronic Acid 5mg vs Placebo 8.4% vs 12.8% OR = 0.63 (95% CI 0.54, 0.73) - NNT=22.7 (95% CI 17.2-33.5)
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	265/149/149	37/1/143	Number of people with fracture: nonvertebral fractures (ankle) at 14 months: PTH vs. Alendronate 0.0% vs. 2.7% OR = 0.13 (95% CI 0.01, 2.15)
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	NR/NR/425	105/17/395	Number of people with fracture: any clinical fracture adverse effect (mostly nonvertebral fractures) at 24 months: Alendronate vs. Estrogen 5.0% vs. 7.0% OR = 0.77 (95% CI 0.26, 2.25) Alendronate vs. Placebo 5.0% vs. 8.0% OR = 0.65 (95% CI 0.16, 2.66) Alendronate+Estrogen vs. Alendronate 6.0% vs. 5.0% OR = 1.05 (95% CI 0.34, 3.30) Alendronate+Estrogen vs. Estrogen 6.0% vs. 7.0% OR = 0.81 (95% CI 0.31, 2.09) Alendronate+Estrogen vs. Placebo 6.0% vs. 8.0% OR = 0.68 (95% CI 0.18, 2.56) Estrogen vs. Placebo 7.0% vs. 8.0% OR = 0.86 (95% CI 0.25, 2.97)
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	1759/NR/1053	383/NR/750	Number of people with fracture: clinical fractures at 24 months: Alendronate vs. Risedronate 8.3% vs. 8.2% OR = 1.01 (95% CI 0.62, 1.66)
Boutsen Y et al., 1997[7] Pamidronate Western Europe	NR/NR/32	2/3/27	Number of people with fracture: vertebral fractures at 12 months: Pamidronate vs. Calcium 7.1% vs. 0.0% OR = 6.88 (95% CI 0.14, 347.7)

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Brown JP et al., 2002[8] Risedronate US, Canada	4972/NR/1468	259/NR/1456	Number of people with fracture: nonvertebral fractures at 24 months: Risedronate 35 mg vs. Risedronate 50 mg/wk 5.8% vs. 4.9% OR = 1.19 (95% CI 0.68, 2.08) Risedronate 5 mg vs. Risedronate 35 mg/wk 5.0% vs. 5.8% OR = 0.86 (95% CI 0.49, 1.50) Risedronate 5 mg vs. Risedronate 50 mg/wk 5.0% vs. 4.9% OR = 1.02 (95% CI 0.57, 1.83)
Campbell IA et al., 2004[9] Etidronate UK	NR/NR/352	NR/51/349	Number of people with fracture: new semi-quantitative vertebral fractures on spine radiographs at 60 months: Calcium vs. No treatment 12.9% vs. 15.8% OR = 0.80 (95% CI 0.35, 1.82) Etidronate vs. Calcium 11.1% vs. 12.9% OR = 0.84 (95% CI 0.33, 2.14) Etidronate vs. Etidronate +Calcium 11.1% vs. 8.0% OR = 1.44 (95% CI 0.52, 4.03) Etidronate vs. No treatment 11.1% vs. 15.8% OR = 0.67 (95% CI 0.28, 1.59) Etidronate+Calcium vs. Calcium 8.0% vs. 12.9% OR = 0.59 (95% CI 0.22, 1.56) Etidronate+Calcium vs. No treatment 8.0% vs. 15.8% OR = 0.48 (95% CI 0.20, 1.16)
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	NR/NR/1746	NR/NR/1746	Number of people with fracture not reported
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	NR/NR/1318	NR/NR/1318	Number of people with fracture not reported
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	18447/NR/2946	NR/NR/2929	Number of people with fracture: clinical osteoporotic nonvertebral fractures at 36 months: Ibandronate daily vs. Ibandronate intermittent 9.1% vs. 8.9% OR = 1.03 (95% CI 0.75, 1.40) Ibandronate daily vs. Placebo 9.1% vs. 8.2% OR = 1.00 (95% CI 0.73, 1.36) Ibandronate intermittent vs. Placebo 8.9% vs. 8.2% OR = 1.09 (95% CI 0.80, 1.50)
Coco M et al., 2003[12] Pamidronate US	112/98/72	13/NR/59	Number of people with fracture: nonvertebral fractures at 12 months: Pamidronate vs. Control 0.0% vs. 0.0% OR = NC

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1	98018/13954/13388	NR/212/13175	Number of people with fracture: hip fractures at 60 months: Tamoxifen vs. Placebo 0.2% vs. 0.3% OR = 0.56 (95% CI 0.28, 1.09)
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	362/NR/235	32/3/209	Number of people with fracture: nonvertebral fractures at 11.2 months: Etidronate vs. Risedronate 3.4% vs. 5.9% OR = 0.57 (95% CI 0.17, 1.91)
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	9347/NR/931	NR/NR/NR	Number of people with fracture: nonvertebral fractures at 21 months: Teriparatide vs. Placebo 6.4% vs. 9.9% OR = 0.63 (95% CI 0.39, 1.00)
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe	NR/NR/40	NR/NR/40	Number of people with fracture: vertebral fractures at 18 months: Calcidiol vs. Calcitonin 0.0% vs. 30.8% OR = 0.10 (95% CI 0.01, 0.83) Etidronate vs. Calcidiol 21.4% vs. 0.0% OR = 8.08 (95% CI 0.76, 85.33) Etidronate vs. Calcitonin 21.4% vs. 30.8% OR = 0.63 (95% CI 0.12, 3.39)
Grant AM et al., 2005[17] Vitamin D UK	15024/8827/5292	./NR/.	Number of people with fracture: clinical vertebral fractures at 62 months: Calcium vs. Placebo 0.2% vs. 0.1% OR = 2.77 (95% CI 0.39, 19.65) Calcium vs. Vitamin D3+Calcium 0.2% vs. 0.0% OR = 7.37 (95% CI 0.77, 70.93) Vitamin D3 vs. Calcium 0.3% vs. 0.2% OR = 0.77 (95% CI 0.17, 3.39) Vitamin D3 vs. Placebo 0.3% vs. 0.1% OR = 3.30 (95% CI 0.57, 19.07) Vitamin D3+Calcium vs. Placebo 0.0% vs. 0.1% OR = 0.14 (95% CI 0.00, 6.96) Vitamin D3+Calcium vs. Vitamin D3 0.3% vs. 0.0% OR = 7.62 (95% CI 1.07, 54.16)

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Greenspan SL et al., 2003[18] Alendronate, Estrogen US	573/548/373	26/8/373	Number of people with fracture: clinical fractures at 36 months: Alendronate vs. Estrogen 8.0% vs. 5.0% OR = 1.43 (95% CI 0.44, 4.58) Alendronate vs. Placebo 8.0% vs. 10.0% OR = 0.76 (95% CI 0.27, 2.12) Alendronate+Estrogen vs. Alendronate 4.0% vs. 8.0% OR = 0.56 (95% CI 0.16, 1.87) Alendronate+Estrogen vs. Estrogen 4.0% vs. 5.0% OR = 0.78 (95% CI 0.21, 2.98) Alendronate+Estrogen vs. Placebo 4.0% vs. 10.0% OR = 0.43 (95% CI 0.14, 1.34) Estrogen vs. Placebo 5.0% vs. 10.0% OR = 0.54 (95% CI 0.18, 1.60)
Greenspan SL et al., 2006[19] Risedronate US	106/94/87	5/4/87	Number of people with fracture: fractures at 12 months: Risedronate vs. Placebo 4.7% vs. 0.0% OR = 7.75 (95% CI 0.48, 125.9)
Grotz W et al., 2001[20] Ibandronate Germany	114/98/80	8/0/72	Number of people with fracture: arm fractures at 12 months: Ibandronate vs. Control 2.5% vs. 2.5% OR = 1.00 (95% CI 0.06, 16.27)
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe	NR/NR/32	6/0/26	Number of people with fracture: nonvertebral fractures at 24 months: Alendronate vs. Etidronate 15.4% vs. 7.7% OR = 2.06 (95% CI 0.19, 21.85)
Harris ST et al., 2004[22] Risedronate US, Canada	4972/NR/1468	341/24/1456	Number of people with fracture: vertebral fractures at 24 months: Risedronate 35 mg/wk vs. Risedronate 50 mg/wk 1.5% vs. 1.7% OR = 0.90 (95% CI 0.30, 2.68) Risedronate 5 mg vs. Risedronate 35 mg/wk 2.9% vs. 1.5% OR = 1.92 (95% CI 0.75, 4.88) Risedronate 5 mg vs. Risedronate 50 mg/wk 2.9% vs. 1.7% OR = 1.74 (95% CI 0.70, 4.32)
Hay JE et al., 2001[23] Calcitonin US	NR/NR/63	NR/NR/55	Number of people with fracture: other fractures at 12 months: Salmon calcitonin vs. No therapy 4.0% vs. 6.0% OR = 0.36 (95% CI 0.05, 2.71)
Hizmetli S et al., 1998[24] Calcitonin Turkey	NR/NR/107	20/NR/87	Number of people with fracture not reported
Hochberg MC et al., 2005[25] Alendronate US FIT	NR/NR/3658	NR/NR/3658	Number of people with fracture not reported

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Hooper MJ et al., 2005[26] Risedronate Australia/NZ	NR/NR/383	84/1/381	Number of people with fracture: nonvertebral fractures at 24 months: Risedronate 2.5 mg vs. Placebo 2.4% vs. 4.8% OR = 0.50 (95% CI 0.13, 1.90) Risedronate 2.5 mg vs. Risedronate 5 mg 2.4% vs. 3.9% OR = 0.60 (95% CI 0.15, 2.44) Risedronate 5 mg vs. Placebo 3.9% vs. 4.8% OR = 0.83 (95% CI 0.25, 2.76)
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil	1036/NR/549	107/3/NR	Number of people with fracture: vertebral or nonvertebral fractures at 12 months: Alendronate vs. Placebo 2.7% vs. 1.9% OR = 1.52 (95% CI 0.34, 6.67) Alendronate vs. Risedronate 2.7% vs. 2.7% OR = 1.04 (95% CI 0.33, 3.27) Risedronate vs. Placebo 2.7% vs. 1.9% OR = 1.47 (95% CI 0.33, 6.52)
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	739/NR/396	24/11/NR	Number of people with fracture: vertebral fractures at 24 months: Alfacalcidol vs. Control (no treatment) 16.7% vs. 25.8% OR = 0.58 (95% CI 0.25, 1.34) Alfacalcidol vs. Vitamin K 16.7% vs. 13.6% OR = 1.26 (95% CI 0.49, 3.26) Calcitonin vs. Alfacalcidol 12.1% vs. 16.7% OR = 0.69 (95% CI 0.26, 1.83) Calcitonin vs. Control (no treatment) 12.1% vs. 25.8% OR = 0.41 (95% CI 0.17, 0.99) - NNT=7.3 (95% CI 3.7-211.9) Calcitonin vs. Estrogen+Medroxyprogesterone 12.1% vs. 10.6% OR = 1.16 (95% CI 0.40, 3.39) Calcitonin vs. Vitamin K 12.1% vs. 13.6% OR = 0.87 (95% CI 0.32, 2.41) Control (no treatment) vs. Vitamin K 25.8% vs. 13.6% OR = 2.14 (95% CI 0.91, 5.03) Estrogen+Medroxyprogesterone vs. Alfacalcidol 10.6% vs. 16.7% OR = 0.60 (95% CI 0.22, 1.62) Estrogen+Medroxyprogesterone vs. Control (no treatment) 10.6% vs. 25.8% OR = 0.36 (95% CI 0.15, 0.88) - NNT=6.6 (95% CI 3.6-44.5) Estrogen+Medroxyprogesterone vs. Vitamin K 10.6% vs. 13.6% OR = 0.75 (95% CI 0.27, 2.14) Etidronate vs. Alfacalcidol 12.1% vs. 16.7% OR = 0.69 (95% CI 0.26, 1.83) Etidronate vs. Calcitonin 12.1% vs. 12.1% OR = 1.00 (95% CI 0.35, 2.83) Etidronate vs. Control (no treatment) 12.1% vs. 25.8% OR = 0.41 (95% CI 0.17, 0.99) - NNT=7.3 (95% CI 3.7-211.9) Etidronate vs. Estrogen+Medroxyprogesterone 12.1% vs. 10.6% OR = 1.16 (95% CI 0.40, 3.39) Etidronate vs. Vitamin K 12.1% vs. 13.6% OR = 0.87 (95% CI 0.32, 2.41)
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan	NR/NR/50	0/0/50	Number of people with fracture: vertebral fractures at 6 months: Alendronate vs. Etidronate 0.0% vs. 4.0% OR = 0.14 (95% CI 0.00, 6.82)

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI	68132/62528/36282	2235/296/36282	Number of people with fracture: clinical vertebral fractures at 84 months: Calcium+Vitamin D vs. Placebo 1.0% vs. 1.0% OR = 0.91 (95% CI 0.75, 1.12)
Kanaji A et al., 2006[31] Risedronate Japan	NR/NR/23	2/NR/21	Number of people with fracture: vertebral fractures at 12 months: Risedronate vs. Placebo 0.8% vs. 1.9% OR = NC
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland	115/108/99	33/0/72	Number of people with fracture: vertebral fractures at 12 months: Pamidronate vs. Control 8.6% vs. 13.2% OR = 0.57 (95% CI 0.13, 2.48)
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	959/437/355	NR/NR/279	Number of people with fracture: moderate or severe fractures at 30 months: Teriparatide 20 ug vs. Placebo 1.0% vs. 7.0% OR = 0.24 (95% CI 0.06, 0.97) - NNT=17.5 (95% CI 9.1-245.7) Teriparatide 20 ug vs. Teriparatide 40 ug 1.0% vs. 1.0% OR = 1.09 (95% CI 0.07, 17.56) Teriparatide 40 ug vs. Placebo 1.0% vs. 7.0% OR = 0.26 (95% CI 0.06, 1.06) Teriparatide combined vs. Placebo 1.0% vs. 7.0% OR = 0.16 (95% CI 0.04, 0.65) - NNT=17.7 (95% CI 9.3-180.7)
Kim SH et al., 2004[34] Pamidronate Asia	NR/NR/50	0/5/45	Number of people with fracture: vertebral fractures at 12 months: Pamidronate vs. Control 4.0% vs. 30.0% OR = 0.14 (95% CI 0.03, 0.72) - NNT=3.8 (95% CI 2.1-22.2)
Kishimoto H et al., 2006[35] Risedronate Japan	NR/NR/496	63/1/488	Number of people with fracture: vertebral fractures at 48 weeks: Risedronate 17.5 mg/wk+Calcium 200 mg/day vs. Risedronate 2.5 mg/day+Calcium 200 mg/day 2.2% vs. 2.7% OR = 0.81 (95% CI 0.25, 2.68)
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	NR/NR/547	157/17/433	Number of people with fracture: vertebral fractures at 24 weeks: Etidronate vs. Risedronate 6.0% vs. 8.8% OR = 0.66 (95% CI 0.32, 1.36)

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY	1200/508/456	76/8/405	Number of people with fracture: all clinical fractures at 12 months: Alendronate vs. Raloxifene 2.3% vs. 3.5% OR = 0.65 (95% CI 0.22, 1.95)
McClung MR et al., 2006[38] Alendronate, AMG162 US	NR/NR/412	43/NR/268	Number of people with fracture: clinical vertebral fractures at 12 months: Alendronate vs. Placebo 2.0% vs. 2.0% OR = 1.00 (95% CI 0.06, 16.23) Denosumab vs. Alendronate 4.0% vs. 2.0% OR = 1.60 (95% CI 0.31, 8.40) Denosumab vs. Placebo 4.0% vs. 2.0% OR = 1.60 (95% CI 0.31, 8.40)
Milgrom C et al., 2004[39] Risedronate Israel	473/473/324	216/0/324	Number of people with fracture: all stress fracture at 14 weeks: Risedronate vs. Placebo 14.5% vs. 13.2% OR = 1.12 (95% CI 0.60, 2.10)
Muscoso E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy	NR/NR/2000	NR/NR/NR	Number of people with fracture: femoral fractures at 12 months: Alendronate vs. Clodronate 0.1% vs. 0.0% OR = 6.05 (95% CI 0.12, 312.4) Alendronate vs. Raloxifene 0.1% vs. 0.0% OR = 3.00 (95% CI 0.00, 2746) Alendronate vs. Risedronate 0.1% vs. 0.0% OR = 3.00 (95% CI 0.00, 2746) Raloxifene vs. Clodronate 0.0% vs. 0.0% OR = NC Risedronate vs. Clodronate 0.0% vs. 0.0% OR = NC Risedronate vs. Raloxifene 0.0% vs. 0.0% OR = NC
Ninkovic M et al., 2002[41] Pamidronate UK	NR/NR/99	28/0/NR	Number of people with fracture: nonvertebral fractures at 12 months: Pamidronate vs. Placebo 2.9% vs. 2.4% OR = 1.21 (95% CI 0.07, 19.96)
Orwoll ES et al., 2003[42] PTH 1100101000	959/NR/437	81/NR/NR	Number of people with fracture: nonvertebral fractures at 11 months: Teriparatide 20 ug vs. Placebo 1.3% vs. 2.0% OR = 0.65 (95% CI 0.11, 3.79) Teriparatide 20 ug vs. Teriparatide 40 ug 1.3% vs. 0.7% OR = 1.80 (95% CI 0.19, 17.50) Teriparatide 40 ug vs. Placebo 0.7% vs. 2.0% OR = 0.38 (95% CI 0.05, 2.76)
Palomba S et al., 2005[43] Risedronate Italy	279/97/90	9/9/81	Number of people with fracture: nonvertebral fractures at 12 months: Risedronate vs. Placebo 0.0% vs. 10.0% OR = 0.13 (95% CI 0.02, 0.95) - NNT=10.2 (95% CI 5.3-148.4)

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Porthouse J et al., 2005[44] Calcium, Vitamin D UK	11022/7944/3454	NR/NR/NR	Number of people with fracture: all fractures at 24 months: Calcium+Vitamin D vs. control group (receiving only advice) equally allocated group 4.0% vs. 3.7% OR = 1.09 (95% CI 0.60, 1.96) Calcium+Vitamin D vs. control group (receiving only advice) unequally allocated group 4.8% vs. 5.0% OR = 0.96 (95% CI 0.63, 1.46)
Prince RL et al., 2006[45] Calcium Australia/NZ	4312/1510/1460	232/NR/1460	Number of people with fracture: any appendicular site fractures at 60 months: Calcium vs. Placebo 11.4% vs. 12.9% OR = 0.87 (95% CI 0.64, 1.19)
Quandt SA et al., 2005[46] Alendronate US FIT	NR/NR/3737	NR/NR/NR	Number of people with fracture: clinical vertebral fractures at 54 months: Alendronate vs. Placebo 0.6% vs. 1.6% OR = 0.43 (95% CI 0.23, 0.79) - NNT=108.6 (95% CI 62.9-396.4)
Ravn P et al., 1996[47] Ibandronate Western Europe	NR/821/180	39/2/180	Number of people with fracture: fractures at 12 months: Ibandronate 0.25 mg vs. Ibandronate 0.5 mg 0.0% vs. 0.0% OR = NC Ibandronate 0.25 mg vs. Ibandronate 1 mg 0.0% vs. 0.0% OR = NC Ibandronate 0.25 mg vs. Ibandronate 2.5 mg 0.0% vs. 0.0% OR = NC Ibandronate 0.25 mg vs. Ibandronate 5 mg 0.0% vs. 0.0% OR = NC Ibandronate 0.25 mg vs. Placebo 0.0% vs. 3.3% OR = 0.14 (95% CI 0.00, 6.82) Ibandronate 0.5 mg vs. Ibandronate 1 mg 0.0% vs. 0.0% OR = NC Ibandronate 0.5 mg vs. Ibandronate 2.5 mg 0.0% vs. 0.0% OR = NC Ibandronate 0.5 mg vs. Ibandronate 5 mg 0.0% vs. 0.0% OR = NC Ibandronate 0.5 mg vs. Placebo 0.0% vs. 3.3% OR = 0.14 (95% CI 0.00, 6.82) Ibandronate 1 mg vs. Ibandronate 2.5 mg 0.0% vs. 0.0% OR = NC Ibandronate 1 mg vs. Ibandronate 5 mg 0.0% vs. 0.0% OR = NC Ibandronate 1 mg vs. Placebo 0.0% vs. 3.3% OR = 0.14 (95% CI 0.00, 6.82) Ibandronate 2.5 mg vs. Ibandronate 5 mg 0.0% vs. 0.0% OR = NC Ibandronate 2.5 mg vs. Placebo 0.0% vs. 3.3% OR = 0.14 (95% CI 0.00, 6.82) Ibandronate 5 mg vs. Placebo 0.0% vs. 3.3% OR = 0.14 (95% CI 0.00, 6.82)
Recker R et al., 2004[48] Ibandronate US, Western Europe	16632/NR/2862	503/29/2860	Number of people with fracture: vertebral fractures at 36 months: Ibandronate 0.5 mg vs. Ibandronate 1 mg 8.7% vs. 9.2% OR = 0.96 (95% CI 0.69, 1.33) Ibandronate 0.5 mg vs. Placebo 8.7% vs. 10.7% OR = 0.78 (95% CI 0.57, 1.07) Ibandronate 1 mg vs. Placebo 9.2% vs. 10.7% OR = 0.82 (95% CI 0.60, 1.11)

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial	5531/1840/1423	222/28/1412	Number of people with fracture: hip fractures at 12 months: Alendronate vs. Raloxifene 0.1% vs. 0.3% OR = 0.50 (95% CI 0.05, 4.84)
Reid IR et al., 1994[50] Pamidronate Australia/NZ	NR/NR/61	13/0/48	Number of people with fracture: vertebral fractures at 24 months: Pamidronate vs. Placebo 26.9% vs. 45.5% OR = 0.45 (95% CI 0.14, 1.46)
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia	NR/NR/351	35/NR/351	Number of people with fracture: nonvertebral fractures at 12 months: Zoledronic acid 0.25 mg vs. Placebo 0.0% vs. 1.7% OR = 0.13 (95% CI 0.00, 6.71) Zoledronic acid 0.25 mg vs. Zoledronic acid 0.5 mg 0.0% vs. 1.7% OR = 0.13 (95% CI 0.00, 6.59) Zoledronic acid 0.25 mg vs. Zoledronic acid 1 mg 0.0% vs. 3.8% OR = 0.12 (95% CI 0.01, 1.89) Zoledronic acid 0.5 mg vs. Placebo 1.7% vs. 1.7% OR = 1.02 (95% CI 0.06, 16.46) Zoledronic acid 0.5 mg vs. Zoledronic acid 1 mg 1.7% vs. 3.8% OR = 0.46 (95% CI 0.05, 4.54) Zoledronic acid 1 mg vs. Placebo 3.8% vs. 1.7% OR = 2.20 (95% CI 0.22, 21.70) Zoledronic acid 2 mg vs. Placebo 1.6% vs. 1.7% OR = 0.97 (95% CI 0.06, 15.65) Zoledronic acid 2 mg vs. Zoledronic acid 0.25 mg 1.6% vs. 0.0% OR = 7.27 (95% CI 0.14, 366.4) Zoledronic acid 2 mg vs. Zoledronic acid 0.5 mg 1.6% vs. 1.7% OR = 0.95 (95% CI 0.06, 15.39) Zoledronic acid 2 mg vs. Zoledronic acid 1 mg 1.6% vs. 3.8% OR = 0.44 (95% CI 0.04, 4.32) Zoledronic acid 4 mg vs. Placebo 1.7% vs. 1.7% OR = 0.98 (95% CI 0.06, 15.91) Zoledronic acid 4 mg vs. Zoledronic acid 0.25 mg 1.7% vs. 0.0% OR = 7.39 (95% CI 0.15, 372.4) Zoledronic acid 4 mg vs. Zoledronic acid 0.5 mg 1.7% vs. 1.7% OR = 0.97 (95% CI 0.06, 15.64) Zoledronic acid 4 mg vs. Zoledronic acid 1 mg 1.7% vs. 3.8% OR = 0.45 (95% CI 0.05, 4.39) Zoledronic acid 4 mg vs. Zoledronic acid 2 mg 1.7% vs. 1.6% OR = 1.02 (95% CI 0.06, 16.45)

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	NR/1522/619	234/28/619	Number of people with fracture: vertebral fractures at 36 months: Estrogen vs. Placebo 1.0% vs. 1.1% OR = 0.88 (95% CI 0.05, 14.27) Raloxifene 150 mg vs. Estrogen 1.0% vs. 1.0% OR = 1.00 (95% CI 0.06, 16.10) Raloxifene 150 mg vs. Placebo 1.0% vs. 1.1% OR = 0.88 (95% CI 0.05, 14.27) Raloxifene 60 mg vs. Estrogen 3.3% vs. 1.0% OR = 3.11 (95% CI 0.43, 22.51) Raloxifene 60 mg vs. Placebo 3.3% vs. 1.1% OR = 2.73 (95% CI 0.38, 19.73) Raloxifene 60 mg vs. Raloxifene 150 mg 3.3% vs. 1.0% OR = 3.11 (95% CI 0.43, 22.51)
Reid IR et al., 2006[53] Calcium Australia/NZ	2421/1780/1471	216/153/1471	Number of people with fracture: distal forearm fractures at 60 months: Calcium vs. Placebo 4.0% vs. 6.0% OR = 0.62 (95% CI 0.39, 1.00)
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	1759/NR/1053	138/23/945	Number of people with fracture: fractures at 12 months: Alendronate vs. Risedronate 5.0% vs. 3.8% OR = 1.35 (95% CI 0.75, 2.43)
Sato S et al., 2003[55] Etidronate Japan	NR/NR/102	46/NR/61	Number of people with fracture: vertebral fractures at 144 weeks: Etidronate+Calcium+Alphacalcidol vs. Calcium+Alphacalcidol 0.0% vs. 6.5% OR = 0.14 (95% CI 0.01, 2.21)
Sato Y et al., 2004[56] Etidronate Japan	NR/NR/80	7/NR/73	Number of people with fracture: hip fractures at 3 months: Etidronate vs. Placebo 0.0% vs. 0.0% OR = NC
Sato Y et al., 2005[57] Risedronate Japan	312/287/280	9/4/267	Number of people with fracture: hip fractures at 18 months: Risedronate sodium vs. Placebo 1.0% vs. 7.0% OR = 0.25 (95% CI 0.08, 0.78) - NNT=16.6 (95% CI 9.1-91.2)
Sato Y et al., 2005[58] Risedronate Japan	658/510/500	33/6/500	Number of people with fracture: hip fractures at 18 months: Risedronate sodium vs. Placebo 2.0% vs. 8.0% OR = 0.29 (95% CI 0.13, 0.66) - NNT=10.9 (95% CI 7.1-23.5)
Sato Y et al., 2005[59] Vitamin D Japan	137/NR/96	11/NR/NR	Number of people with fracture: hip fractures at 24 months: Vitamin D vs. Placebo 0.0% vs. 16.7% OR = 0.12 (95% CI 0.02, 0.90) - NNT=6.0 (95% CI 3.2-56.9)

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Sato Y et al., 2005[60] Risedronate Japan	NR/NR/374	29/8/345	Number of people with fracture: hip fractures at 12 months: Risedronate vs. Placebo 0.6% vs. 4.0% OR = 0.22 (95% CI 0.05, 0.88) - NNT=28.9 (95% CI 15.1-316.0)
Sato Y et al., 2006[61] Alendronate Japan	558/NR/288	19/8/288	Number of people with fracture: hip fractures at 48 months: Alendronate+Vitamin D2 vs. Placebo+Vitamin D2 3.1% vs. 10.9% OR = 0.30 (95% CI 0.12, 0.78) - NNT=12.8 (95% CI 7.2-59.7)
Sato Y et al., 2006[62] Etidronate Japan	85/NR/82	7/0/82	Number of people with fracture: ankle fractures at 24 months: Etidronate vs. Placebo 0.0% vs. 2.0% OR = 0.14 (95% CI 0.00, 6.82)
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	4400/NR/1226	1006/NR/NR	Number of people with fracture: humerus fractures at 24 months: Risedronate 5 mg vs. Placebo 2.2% vs. 4.6% OR = 0.48 (95% CI 0.13, 1.81)
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy	NR/NR/60	0/0/60	Number of people with fracture: vertebral fractures at 12 months: HRT vs. Calcium+Vitamin D 6.0% vs. 13.0% OR = 0.49 (95% CI 0.05, 5.10) Risedronate vs. Calcium+Vitamin D 13.0% vs. 13.0% OR = 1.00 (95% CI 0.13, 7.92) Risedronate vs. HRT 13.0% vs. 6.0% OR = 2.05 (95% CI 0.20, 21.36) Risedronate vs. Zoledronic acid 13.0% vs. 20.0% OR = 0.63 (95% CI 0.10, 4.15) Zoledronic acid vs. Calcium+Vitamin D 20.0% vs. 13.0% OR = 1.59 (95% CI 0.24, 10.51) Zoledronic acid vs. HRT 20.0% vs. 6.0% OR = 3.05 (95% CI 0.38, 24.18)
Torres A et al., 2004[65] Calcium, Vitamin D Spain	NR/NR/90	11/8/71	Number of people with fracture: symptomatic fractures at 12 months: Calcitriol+Calcium vs. Calcium 0.0% vs. 0.0% OR = NC
Toth E et al., 2005[66] Calcitonin Eastern Europe	225/75/71	0/0/71	Number of people with fracture: vertebral fractures at 18 months: Calcitonin nasal spray+Vitamin D+Calcium vs. Vitamin D+Calcium 0.0% vs. 10.0% OR = 0.09 (95% CI 0.01, 0.96) - NNT=10.3 (95% CI 5.0-137.0)

Author, Year, Drug, Country, Trial name	Screened/Eligible/Enrolled	Withdrawn/Lost to FU/Analyzed	Results - 1
Trovas GP et al., 2002[67] Calcitonin Greece	NR/NR/28	0/0/28	Number of people with fracture: vertebral fractures at 12 months: Nasal salmon calcitonin vs. Placebo 8.0% vs. 18.2% OR = 0.40 (95% CI 0.04, 4.30)
Uchida S et al., 2005[68] Alendronate Japan	NR/NR/328	51/NR/297	Number of people with fracture not reported
Ushiroyama T et al., 2001[69] Calcitonin Japan	NR/NR/202	NR/NR/202	Number of people with fracture: vertebral fractures at 12 months: 1a-Hydroxycholecalciferol vs. Calcitonin +1a-Hydroxycholecalciferol 0.0% vs. 0.0% OR = NC 1a-Hydroxycholecalciferol vs. No treatment 0.0% vs. 3.8% OR = 0.14 (95% CI 0.01, 2.24) Calcitonin vs. 1a-Hydroxycholecalciferol 0.0% vs. 0.0% OR = NC Calcitonin vs. Calcitonin+1a-Hydroxycholecalciferol 0.0% vs. 0.0% OR = NC Calcitonin vs. No treatment 0.0% vs. 3.8% OR = 0.14 (95% CI 0.01, 2.28) Calcitonin+1a-Hydroxycholecalciferol vs. No treatment 0.0% vs. 3.8% OR = 0.14 (95% CI 0.01, 2.19)
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2	184460/20168/19747	NR/1137/19471	Number of people with fracture: osteoporotic fractures at 60 months: Tamoxifen vs. Raloxifene 1.0% vs. 1.0% OR = 1.09 (95% CI 0.82, 1.44)
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK	350/NR/72	13/1/58	Number of people with fracture: nonvertebral fractures at 48 months: Estrogen+Progesterone vs. Control 6.7% vs. 7.1% OR = 0.93 (95% CI 0.06, 15.69) Etidronate+Estrogen+Progesterone vs. Estrogen+Progesterone 6.7% vs. 6.7% OR = 1.00 (95% CI 0.06, 16.79) Etidronate vs. Control 7.1% vs. 7.1% OR = 1.00 (95% CI 0.06, 16.85) Etidronate vs. Estrogen+Progesterone 7.1% vs. 6.7% OR = 1.07 (95% CI 0.06, 18.10) Etidronate+Estrogen+Progesterone vs. Control 6.7% vs. 7.1% OR = 0.93 (95% CI 0.06, 15.69) Etidronate+Estrogen+Progesterone vs. Etidronate 6.7% vs. 7.1% OR = 0.93 (95% CI 0.06, 15.69)
Zein CO et al., 2005[72] Alendronate US	NR/NR/34	6/1/27	Number of people with fracture: new compression/vertebral fractures at 12 months: Alendronate vs. Placebo 7.0% vs. 0.0% OR = 6.88 (95% CI 0.14, 347.7)

Author, Year, Drug, Country, Trial name	Results - 2
Agrawal S et al., 2006[1] Risedronate US	
Aris RM et al., 2000[2] Pamidronate US	Number of people with fracture: vertebral fractures at 24 months: Pamidronate vs. Control 18.8% vs. 5.6% OR = 3.43 (95% CI 0.44, 26.92)
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	Number of people with fracture: Hip fracture at 36 months: Zoledronic Acid 5mg vs Placebo 1.4% vs 2.5% OR = 0.56 (95% CI 0.40, 0.78) - NNT=90.9 (95% CI 57.5-217.1) Number of people with fracture: Multiple (>=2) morphometric vertebral fractures at 36 months: Zoledronic Acid 5mg vs Placebo 0.2% vs 2.3% OR = 0.16 (95% CI 0.10, 0.25) - NNT=47.6 (95% CI 37.5-65.3)
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	Number of people with fracture: nonvertebral fractures (foot) at 14 months: PTH vs. Alendronate 1.4% vs. 1.4% OR = 1.00 (95% CI 0.06, 16.14) Number of people with fracture: nonvertebral fractures (other - toe) at 14 months: PTH vs. Alendronate 0.0% vs. 4.1% OR = 0.13 (95% CI 0.01, 1.29)
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	
Boutsen Y et al., 1997[7] Pamidronate Western Europe	
Brown JP et al., 2002[8] Risedronate US, Canada	Number of people with fracture: vertebral fractures at 24 months: Risedronate 35 mg vs. Risedronate 50 mg/wk 1.0% vs. 0.4% OR = 2.40 (95% CI 0.54, 10.60) Risedronate 5 mg vs. Risedronate 35 mg/wk 1.3% vs. 1.0% OR = 1.21 (95% CI 0.37, 3.98) Risedronate 5 mg vs. Risedronate 50 mg/wk 1.3% vs. 0.4% OR = 2.80 (95% CI 0.70, 11.26)

Author, Year, Drug, Country, Trial name	Results - 2
Campbell IA et al., 2004[9] Etidronate UK	Number of people with fracture: new symptomatic or semi-quantitative vertebral fractures at 60 months: Calcium vs. No treatment 17.6% vs. 20.0% OR = 0.86 (95% CI 0.41, 1.81) Etidronate vs. Calcium 16.0% vs. 17.6% OR = 0.89 (95% CI 0.40, 2.01) Etidronate vs. Etidronate +Calcium 16.0% vs. 15.9% OR = 1.01 (95% CI 0.44, 2.30) Etidronate vs. No treatment 16.0% vs. 20.0% OR = 0.77 (95% CI 0.36, 1.65) Etidronate+Calcium vs. Calcium 15.9% vs. 17.6% OR = 0.88 (95% CI 0.40, 1.96) Etidronate+Calcium vs. No treatment 15.9% vs. 20.0% OR = 0.76 (95% CI 0.36, 1.61) Number of people with fracture: new symptomatic vertebral and non-vertebral fractures at 60 months: Calcium vs. No treatment 8.2% vs. 7.4% OR = 1.13 (95% CI 0.38, 3.35) Etidronate vs. Calcium 6.2% vs. 8.2% OR = 0.74 (95% CI 0.23, 2.38) Etidronate vs. Etidronate +Calcium 6.2% vs. 10.2% OR = 0.59 (95% CI 0.20, 1.75) Etidronate vs. No treatment 6.2% vs. 7.4% OR = 0.83 (95% CI 0.26, 2.68) Etidronate+Calcium vs. Calcium 10.2% vs. 8.2% OR = 1.27 (95% CI 0.45, 3.53) Etidronate+Calcium vs. No treatment 10.2% vs. 7.4% OR = 1.43 (95% CI 0.51, 3.98)
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	Number of people with fracture: clinical vertebral fractures at 36 months: Ibandronate daily vs. Ibandronate intermittent 2.3% vs. 2.3% OR = 1.00 (95% CI 0.55, 1.82) Ibandronate daily vs. Placebo 2.3% vs. 4.2% OR = 0.54 (95% CI 0.32, 0.88) - NNT=51.2 (95% CI 28.4-258.2) Ibandronate intermittent vs. Placebo 2.3% vs. 4.2% OR = 0.54 (95% CI 0.32, 0.88) - NNT=51.2 (95% CI 28.4-258.2) Number of people with fracture: vertebral fractures at 36 months: Ibandronate daily vs. Ibandronate intermittent 3.8% vs. 4.0% OR = 0.95 (95% CI 0.60, 1.50) Ibandronate daily vs. Placebo 3.8% vs. 7.5% OR = 0.50 (95% CI 0.34, 0.73) - NNT=27.0 (95% CI 17.4-60.2) Ibandronate intermittent vs. Placebo 4.0% vs. 7.5% OR = 0.52 (95% CI 0.36, 0.77) - NNT=28.6 (95% CI 18.0-69.6)
Coco M et al., 2003[12] Pamidronate US	Number of people with fracture: vertebral fractures at 12 months: Pamidronate vs. Control 3.2% vs. 7.1% OR = 0.45 (95% CI 0.04, 4.52)

Author, Year, Drug, Country, Trial name	Results - 2
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1	Number of people with fracture: other lower radius fractures at 60 months: Tamoxifen vs. Placebo 1.0% vs. 1.0% OR = 1.05 (95% CI 0.74, 1.49) Number of people with fracture: radius, collies fracture at 60 months: Tamoxifen vs. Placebo 0.2% vs. 0.3% OR = 0.62 (95% CI 0.32, 1.17)
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	Number of people with fracture: vertebral fractures at 11.2 months: Etidronate vs. Risedronate 1.8% vs. 0.0% OR = 6.81 (95% CI 0.42, 110.0)
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	Number of people with fracture: vertebral fractures at 21 months: Teriparatide vs. Placebo 5.5% vs. 15.6% OR = 0.34 (95% CI 0.22, 0.54) - NNT=9.9 (95% CI 7.0-16.9)
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe	
Grant AM et al., 2005[17] Vitamin D UK	Number of people with fracture: confirmed fractures at 62 months: Calcium vs. Placebo 14.0% vs. 14.0% OR = 0.98 (95% CI 0.78, 1.21) Calcium vs. Vitamin D3+Calcium 14.0% vs. 14.0% OR = 1.03 (95% CI 0.83, 1.29) Calcium vs. Vitamin D3 16.0% vs. 14.0% OR = 1.12 (95% CI 0.90, 1.38) Vitamin D3 vs. Placebo 16.0% vs. 14.0% OR = 1.09 (95% CI 0.88, 1.35) Vitamin D3+Calcium vs. Placebo 14.0% vs. 14.0% OR = 0.94 (95% CI 0.76, 1.17) Vitamin D3+Calcium vs. Vitamin D3 14.0% vs. 16.0% OR = 0.87 (95% CI 0.70, 1.08) Number of people with fracture: distal forearm fractures at 62 months: Calcium vs. Placebo 2.5% vs. 2.1% OR = 1.20 (95% CI 0.72, 2.00) Calcium vs. Vitamin D3+Calcium 2.5% vs. 2.5% OR = 1.00 (95% CI 0.61, 1.62) Calcium vs. Vitamin D3 2.5% vs. 2.5% OR = 1.03 (95% CI 0.63, 1.67) Vitamin D3 vs. Placebo 2.5% vs. 2.1% OR = 1.17 (95% CI 0.71, 1.95) Vitamin D3+Calcium vs. Placebo 2.5% vs. 2.1% OR = 1.21 (95% CI 0.73, 2.01) Vitamin D3+Calcium vs. Vitamin D3 2.5% vs. 2.5% OR = 1.03 (95% CI 0.63, 1.68)

Author, Year, Drug, Country, Trial name	Results - 2
Greenspan SL et al., 2003[18] Alendronate, Estrogen US	
Greenspan SL et al., 2006[19] Risedronate US	
Grotz W et al., 2001[20] Ibandronate Germany	Number of people with fracture: vertebral fractures at 12 months: Ibandronate vs. Control 2.5% vs. 2.5% OR = 1.00 (95% CI 0.06, 16.27)
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe	Number of people with fracture: vertebral fractures at 24 months: Alendronate vs. Etidronate 0.0% vs. 0.0% OR = NC
Harris ST et al., 2004[22] Risedronate US, Canada	
Hay JE et al., 2001[23] Calcitonin US	Number of people with fracture: rib fractures at 12 months: Salmon calcitonin vs. No therapy 12.0% vs. 3.0% OR = 3.00 (95% CI 0.40, 22.53) Number of people with fracture: spine fractures at 12 months: Salmon calcitonin vs. No therapy 19.0% vs. 27.0% OR = 0.58 (95% CI 0.17, 1.99)
Hizmetli S et al., 1998[24] Calcitonin Turkey	
Hochberg MC et al., 2005[25] Alendronate US FIT	
Hooper MJ et al., 2005[26] Risedronate Australia/NZ	Number of people with fracture: vertebral fractures at 24 months: Risedronate 2.5 mg vs. Placebo 8.7% vs. 8.3% OR = 1.09 (95% CI 0.45, 2.66) Risedronate 2.5 mg vs. Risedronate 5 mg 8.7% vs. 7.7% OR = 1.13 (95% CI 0.46, 2.75) Risedronate 5 mg vs. Placebo 7.7% vs. 8.3% OR = 0.97 (95% CI 0.39, 2.40)

Author, Year, Drug, Country, Trial name	Results - 2
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil	
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan	
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI	Number of people with fracture: hip fractures at 84 months: Calcium+Vitamin D vs. Placebo 1.0% vs. 1.0% OR = 0.87 (95% CI 0.71, 1.07) Number of people with fracture: lower arm or wrist fractures at 84 months: Calcium+Vitamin D vs. Placebo 3.0% vs. 3.0% OR = 1.01 (95% CI 0.90, 1.14)
Kanaji A et al., 2006[31] Risedronate Japan	
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland	
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	Number of people with fracture: vertebral fractures at 30 months: Teriparatide 20 ug vs. Placebo 5.0% vs. 12.0% OR = 0.46 (95% CI 0.17, 1.24) Teriparatide 20 ug vs. Teriparatide 40 ug 5.0% vs. 6.0% OR = 0.91 (95% CI 0.25, 3.25) Teriparatide 40 ug vs. Placebo 6.0% vs. 12.0% OR = 0.50 (95% CI 0.19, 1.37) Teriparatide combined vs. Placebo 6.0% vs. 12.0% OR = 0.44 (95% CI 0.18, 1.09)
Kim SH et al., 2004[34] Pamidronate Asia	

Author, Year, Drug, Country, Trial name	Results - 2
Kishimoto H et al., 2006[35] Risedronate Japan	
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY	
McClung MR et al., 2006[38] Alendronate, AMG162 US	Number of people with fracture: humerus fractures at 12 months: Alendronate vs. Placebo 0.0% vs. 0.0% OR = NC Denosumab vs. Alendronate 0.3% vs. 0.0% OR = 3.15 (95% CI 0.01, 1116) Denosumab vs. Placebo 0.3% vs. 0.0% OR = 3.15 (95% CI 0.01, 1116) Number of people with fracture: lumbar vertebra fractures at 12 months: Alendronate vs. Placebo 0.0% vs. 0.0% OR = NC Denosumab vs. Alendronate 0.3% vs. 0.0% OR = 3.15 (95% CI 0.01, 1116) Denosumab vs. Placebo 0.3% vs. 0.0% OR = 3.15 (95% CI 0.01, 1116)
Milgrom C et al., 2004[39] Risedronate Israel	Number of people with fracture: femur fractures at 14 weeks: Risedronate vs. Placebo 6.7% vs. 6.3% OR = 1.06 (95% CI 0.44, 2.57) Number of people with fracture: metatarsus at 14 weeks: Risedronate vs. Placebo 4.8% vs. 2.5% OR = 1.92 (95% CI 0.61, 6.07)

Author, Year, Drug, Country, Trial name	Results - 2
Muscoso E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy	Number of people with fracture: radial fractures at 12 months: Alendronate vs. Clodronate 0.1% vs. 0.0% OR = 6.05 (95% CI 0.12, 312.4) Alendronate vs. Raloxifene 0.1% vs. 0.0% OR = 3.00 (95% CI 0.00, 2746) Alendronate vs. Risedronate 0.1% vs. 0.0% OR = 3.00 (95% CI 0.00, 2746) Raloxifene vs. Clodronate 0.0% vs. 0.0% OR = NC Risedronate vs. Clodronate 0.0% vs. 0.0% OR = NC Risedronate vs. Raloxifene 0.0% vs. 0.0% OR = NC Number of people with fracture: vertebral fractures at 12 months: Alendronate vs. Clodronate 0.2% vs. 0.4% OR = 0.53 (95% CI 0.09, 3.11) Alendronate vs. Raloxifene 0.2% vs. 0.0% OR = 3.01 (95% CI 0.02, 373.9) Alendronate vs. Risedronate 0.2% vs. 0.0% OR = 3.01 (95% CI 0.02, 373.9) Raloxifene vs. Clodronate 0.0% vs. 0.4% OR = 0.32 (95% CI 0.01, 11.91) Risedronate vs. Clodronate 0.0% vs. 0.4% OR = 0.32 (95% CI 0.01, 11.91) Risedronate vs. Raloxifene 0.0% vs. 0.0% OR = NC
Ninkovic M et al., 2002[41] Pamidronate UK	Number of people with fracture: vertebral fractures at 12 months: Pamidronate vs. Placebo 8.8% vs. 2.4% OR = 3.48 (95% CI 0.47, 25.98)
Orwoll ES et al., 2003[42] PTH 1100101000	
Palomba S et al., 2005[43] Risedronate Italy	Number of people with fracture: vertebral fractures at 12 months: Risedronate vs. Placebo 13.0% vs. 34.0% OR = 0.30 (95% CI 0.11, 0.84) - NNT=4.6 (95% CI 2.5-25.8)
Porthouse J et al., 2005[44] Calcium, Vitamin D UK	Number of people with fracture: hip and waist fractures at 24 months: Calcium+Vitamin D vs. control group (receiving only advice) equally allocated group 2.0% vs. 1.5% OR = 1.33 (95% CI 0.56, 3.14) Calcium+Vitamin D vs. control group (receiving only advice) unequally allocated group 2.4% vs. 3.2% OR = 0.76 (95% CI 0.44, 1.30) Number of people with fracture: hip fractures at 24 months: Calcium+Vitamin D vs. control group (receiving only advice) equally allocated group 0.8% vs. 0.3% OR = 2.35 (95% CI 0.53, 10.36) Calcium+Vitamin D vs. control group (receiving only advice) unequally allocated group 0.4% vs. 1.1% OR = 0.46 (95% CI 0.17, 1.23)
Prince RL et al., 2006[45] Calcium Australia/NZ	Number of people with fracture: any site fractures at 60 months: Calcium vs. Placebo 15.1% vs. 17.3% OR = 0.85 (95% CI 0.64, 1.12) Number of people with fracture: lower limb fractures at 60 months: Calcium vs. Placebo 2.5% vs. 4.2% OR = 0.59 (95% CI 0.34, 1.05)

Author, Year, Drug, Country, Trial name	Results - 2
Quandt SA et al., 2005[46] Alendronate US FIT	Number of people with fracture: radiographic vertebral fractures at 54 months: Alendronate vs. Placebo 2.7% vs. 4.6% OR = 0.58 (95% CI 0.41, 0.83) - NNT=52.5 (95% CI 31.8-149.6)
Ravn P et al., 1996[47] Ibandronate Western Europe	
Recker R et al., 2004[48] Ibandronate US, Western Europe	
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial	Number of people with fracture: nonvertebral fractures at 12 months: Alendronate vs. Raloxifene 2.0% vs. 2.1% OR = 0.94 (95% CI 0.44, 1.91) Number of people with fracture: vertebral fractures at 12 months: Alendronate vs. Raloxifene 1.1% vs. 0.7% OR = 1.56 (95% CI 0.52, 4.65)
Reid IR et al., 1994[50] Pamidronate Australia/NZ	
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia	Number of people with fracture: vertebral fractures at 12 months: Zoledronic acid 0.25 mg vs. Placebo 0.0% vs. 0.0% OR = NC Zoledronic acid 0.25 mg vs. Zoledronic acid 0.5 mg 0.0% vs. 0.0% OR = NC Zoledronic acid 0.25 mg vs. Zoledronic acid 1 mg 0.0% vs. 0.0% OR = NC Zoledronic acid 0.5 mg vs. Placebo 0.0% vs. 0.0% OR = NC Zoledronic acid 0.5 mg vs. Zoledronic acid 1 mg 0.0% vs. 0.0% OR = NC Zoledronic acid 1 mg vs. Placebo 0.0% vs. 0.0% OR = NC Zoledronic acid 2 mg vs. Placebo 0.0% vs. 0.0% OR = NC Zoledronic acid 2 mg vs. Zoledronic acid 0.25 mg 0.0% vs. 0.0% OR = NC Zoledronic acid 2 mg vs. Zoledronic acid 0.5 mg 0.0% vs. 0.0% OR = NC Zoledronic acid 2 mg vs. Zoledronic acid 1 mg 0.0% vs. 0.0% OR = NC Zoledronic acid 4 mg vs. Placebo 0.0% vs. 0.0% OR = NC Zoledronic acid 4 mg vs. Zoledronic acid 0.25 mg 0.0% vs. 0.0% OR = NC Zoledronic acid 4 mg vs. Zoledronic acid 0.5 mg 0.0% vs. 0.0% OR = NC Zoledronic acid 4 mg vs. Zoledronic acid 1 mg 0.0% vs. 0.0% OR = NC Zoledronic acid 4 mg vs. Zoledronic acid 2 mg 0.0% vs. 0.0% OR = NC
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	

Author, Year, Drug, Country, Trial name	Results - 2
Reid IR et al., 2006[53] Calcium Australia/NZ	Number of people with fracture: hip fractures at 60 months: Calcium vs. Placebo 2.3% vs. 0.7% OR = 3.00 (95% CI 1.29, 6.95) - NNT=61.8 (95% CI 35.1-261.3) Number of people with fracture: osteoporotic fractures at 60 months: Calcium vs. Placebo 14.0% vs. 16.0% OR = 0.84 (95% CI 0.63, 1.11)
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	
Sato S et al., 2003[55] Etidronate Japan	
Sato Y et al., 2004[56] Etidronate Japan	
Sato Y et al., 2005[57] Risedronate Japan	
Sato Y et al., 2005[58] Risedronate Japan	Number of people with fracture: nonvertebral fractures at 18 months: Risedronate sodium vs. Placebo 3.0% vs. 13.0% OR = 0.29 (95% CI 0.15, 0.57) - NNT=16.4 (95% CI 9.9-48.2)
Sato Y et al., 2005[59] Vitamin D Japan	
Sato Y et al., 2005[60] Risedronate Japan	
Sato Y et al., 2006[61] Alendronate Japan	

Author, Year, Drug, Country, Trial name	Results - 2
Sato Y et al., 2006[62] Etidronate Japan	Number of people with fracture: pelvis fractures at 24 months: Etidronate vs. Placebo 0.0% vs. 2.0% OR = 0.14 (95% CI 0.00, 6.82) Number of people with fracture: proximal humerus fractures at 24 months: Etidronate vs. Placebo 2.0% vs. 2.0% OR = 1.00 (95% CI 0.06, 16.27)
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	Number of people with fracture: nonvertebral fractures at 24 months: Risedronate 5 mg vs. Placebo 5.2% vs. 8.5% OR = 0.59 (95% CI 0.23, 1.54) Number of people with fracture: vertebral fractures at 24 months: Risedronate 5 mg vs. Placebo 13.8% vs. 28.2% OR = 0.42 (95% CI 0.22, 0.81) - NNT=6.9 (95% CI 4.0-28.1)
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy	
Torres A et al., 2004[65] Calcium, Vitamin D Spain	
Toth E et al., 2005[66] Calcitonin Eastern Europe	
Trovas GP et al., 2002[67] Calcitonin Greece	
Uchida S et al., 2005[68] Alendronate Japan	
Ushiroyama T et al., 2001[69] Calcitonin Japan	

Author, Year, Drug, Country, Trial name	Results - 2
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2	
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK	Number of people with fracture: vertebral fractures at 48 months: Estrogen+Progesterone vs. Control 13.3% vs. 35.7% OR = 0.31 (95% CI 0.06, 1.64) Etidronate+Estrogen+Progesterone vs. Estrogen+Progesterone 6.7% vs. 13.3% OR = 0.49 (95% CI 0.05, 5.10) Etidronate vs. Control 21.4% vs. 35.7% OR = 0.51 (95% CI 0.10, 2.55) Etidronate vs. Estrogen+Progesterone 21.4% vs. 13.3% OR = 1.73 (95% CI 0.26, 11.50) Etidronate+Estrogen+Progesterone vs. Control 6.7% vs. 35.7% OR = 0.18 (95% CI 0.03, 1.06) Etidronate+Estrogen+Progesterone vs. Etidronate 6.7% vs. 21.4% OR = 0.30 (95% CI 0.04, 2.40)
Zein CO et al., 2005[72] Alendronate US	Number of people with fracture: peripheral fractures at 12 months: Alendronate vs. Placebo 0.0% vs. 7.0% OR = 0.13 (95% CI 0.00, 6.33)

Author, Year, Drug, Country, Trial name	Results - 3
Agrawal S et al., 2006[1] Risedronate US	
Aris RM et al., 2000[2] Pamidronate US	
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	Number of people with fracture: Nonvertebral fracture at 36 months: Zoledronic Acid 5mg vs Placebo 8.0% vs 10.7% OR = 0.73 (95% CI 0.62, 0.85) - NNT=37.0 (95% CI 24.8-73.3) Number of people with fracture: clinical vertebral fracture at 36 months: Zoledronic Acid 5mg vs Placebo 0.5% vs 2.6% OR = 0.23 (95% CI 0.16, 0.35) - NNT=47.6 (95% CI 37.1-66.4)
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	Number of people with fracture: nonvertebral fractures (overall) at 14 months: PTH vs. Alendronate 4.1% vs. 13.7% OR = 0.31 (95% CI 0.10, 0.96) Number of people with fracture: nonvertebral fractures (radius) at 14 months: PTH vs. Alendronate 0.0% vs. 4.1% OR = 0.13 (95% CI 0.01, 1.29)
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	
Boutsen Y et al., 1997[7] Pamidronate Western Europe	
Brown JP et al., 2002[8] Risedronate US, Canada	

Author, Year, Drug, Country, Trial name	Results - 3
Campbell IA et al., 2004[9] Etidronate UK	
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	
Coco M et al., 2003[12] Pamidronate US	
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1	Number of people with fracture: spine fractures at 60 months: Tamoxifen vs. Placebo 0.3% vs. 0.5% OR = 0.75 (95% CI 0.44, 1.27)
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	

Author, Year, Drug, Country, Trial name	Results - 3
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe	
Grant AM et al., 2005[17] Vitamin D UK	Number of people with fracture: low-trauma fractures at 62 months: Calcium vs. Placebo 13.0% vs. 13.0% OR = 0.93 (95% CI 0.74, 1.17) Calcium vs. Vitamin D3+Calcium 13.0% vs. 13.0% OR = 1.00 (95% CI 0.80, 1.26) Vitamin D3 vs. Calcium 14.0% vs. 13.0% OR = 1.12 (95% CI 0.90, 1.40) Vitamin D3 vs. Placebo 14.0% vs. 13.0% OR = 1.05 (95% CI 0.84, 1.31) Vitamin D3+Calcium vs. Placebo 13.0% vs. 13.0% OR = 0.93 (95% CI 0.74, 1.17) Vitamin D3+Calcium vs. Vitamin D3 13.0% vs. 14.0% OR = 0.89 (95% CI 0.71, 1.11) Number of people with fracture: new fractures at 62 months: Calcium vs. Placebo 14.4% vs. 14.7% OR = 0.98 (95% CI 0.79, 1.21) Calcium vs. Vitamin D3+Calcium 14.0% vs. 14.0% OR = 1.03 (95% CI 0.83, 1.28) Vitamin D3 vs. Calcium 15.8% vs. 14.4% OR = 0.90 (95% CI 0.73, 1.11) Vitamin D3 vs. Placebo 15.8% vs. 14.7% OR = 1.09 (95% CI 0.88, 1.34) Vitamin D3+Calcium vs. Placebo 14.0% vs. 15.0% OR = 0.95 (95% CI 0.76, 1.18) Vitamin D3+Calcium vs. Vitamin D3 14.0% vs. 16.0% OR = 0.88 (95% CI 0.71, 1.08)
Greenspan SL et al., 2003[18] Alendronate, Estrogen US	
Greenspan SL et al., 2006[19] Risedronate US	
Grotz W et al., 2001[20] Ibandronate Germany	
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe	

Author, Year, Drug, Country, Trial name	Results - 3
Harris ST et al., 2004[22] Risedronate US, Canada	
Hay JE et al., 2001[23] Calcitonin US	Number of people with fracture: other fractures at 4 months: Salmon calcitonin vs. No therapy 4.0% vs. 6.0% OR = 0.52 (95% CI 0.05, 5.22) Number of people with fracture: rib fractures at 4 months: Salmon calcitonin vs. No therapy 4.0% vs. 7.0% OR = 0.52 (95% CI 0.05, 5.22)
Hizmetli S et al., 1998[24] Calcitonin Turkey	
Hochberg MC et al., 2005[25] Alendronate US FIT	
Hooper MJ et al., 2005[26] Risedronate Australia/NZ	
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil	
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan	

Author, Year, Drug, Country, Trial name	Results - 3
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI	Number of people with fracture: total fractures at 84 months: Calcium+Vitamin D vs. Placebo 12.0% vs. 12.0% OR = 0.97 (95% CI 0.91, 1.03)
Kanaji A et al., 2006[31] Risedronate Japan	
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland	
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	
Kim SH et al., 2004[34] Pamidronate Asia	
Kishimoto H et al., 2006[35] Risedronate Japan	
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY	

Author, Year, Drug, Country, Trial name	Results - 3
McClung MR et al., 2006[38] Alendronate, AMG162 US	Number of people with fracture: radius, ulna, or both at 12 months: Alendronate vs. Placebo 0.0% vs. 0.0% OR = NC Denosumab vs. Alendronate 1.0% vs. 0.0% OR = 3.17 (95% CI 0.11, 94.82) Denosumab vs. Placebo 1.0% vs. 0.0% OR = 3.17 (95% CI 0.11, 94.82) Number of people with fracture: sternum and ribs at 12 months: Alendronate vs. Placebo 0.0% vs. 0.0% OR = NC Denosumab vs. Alendronate 0.3% vs. 0.0% OR = 3.15 (95% CI 0.01, 1116) Denosumab vs. Placebo 0.3% vs. 0.0% OR = 3.15 (95% CI 0.01, 1116)
Milgrom C et al., 2004[39] Risedronate Israel	Number of people with fracture: tibia fracture at 14 weeks: Risedronate vs. Placebo 9.1% vs. 5.7% OR = 1.65 (95% CI 0.72, 3.78)
Muscoso E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy	Number of people with fracture: femoral fractures at 24 months: Alendronate vs. Clodronate 0.2% vs. 0.3% OR = 0.80 (95% CI 0.11, 5.75) Alendronate vs. Raloxifene 0.2% vs. 0.0% OR = 3.01 (95% CI 0.02, 373.9) Alendronate vs. Risedronate 0.2% vs. 0.0% OR = 3.01 (95% CI 0.02, 373.9) Raloxifene vs. Clodronate 0.0% vs. 0.3% OR = 0.32 (95% CI 0.00, 26.74) Risedronate vs. Clodronate 0.0% vs. 0.3% OR = 0.32 (95% CI 0.00, 26.74) Risedronate vs. Raloxifene 0.0% vs. 0.0% OR = NC Number of people with fracture: radial fractures at 24 months: Alendronate vs. Clodronate 0.0% vs. 0.0% OR = NC Alendronate vs. Raloxifene 0.0% vs. 0.0% OR = NC Alendronate vs. Risedronate 0.0% vs. 0.0% OR = NC Raloxifene vs. Clodronate 0.0% vs. 0.0% OR = NC Risedronate vs. Clodronate 0.0% vs. 0.0% OR = NC Risedronate vs. Raloxifene 0.0% vs. 0.0% OR = NC
Ninkovic M et al., 2002[41] Pamidronate UK	
Orwoll ES et al., 2003[42] PTH 1100101000	
Palomba S et al., 2005[43] Risedronate Italy	
Porthouse J et al., 2005[44] Calcium, Vitamin D UK	

Author, Year, Drug, Country, Trial name	Results - 3
Prince RL et al., 2006[45] Calcium Australia/NZ	Number of people with fracture: proximal femur fractures at 60 months: Calcium vs. Placebo 1.5% vs. 0.8% OR = 1.86 (95% CI 0.71, 4.83) Number of people with fracture: rib or pelvis fractures at 60 months: Calcium vs. Placebo 2.3% vs. 2.3% OR = 1.00 (95% CI 0.51, 1.97)
Quandt SA et al., 2005[46] Alendronate US FIT	
Ravn P et al., 1996[47] Ibandronate Western Europe	
Recker R et al., 2004[48] Ibandronate US, Western Europe	
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial	Number of people with fracture: vertebral or nonvertebral fractures at 12 months: Alendronate vs. Raloxifene 3.1% vs. 2.9% OR = 1.08 (95% CI 0.59, 2.00) Number of people with fracture: wrist fractures at 12 months: Alendronate vs. Raloxifene 0.8% vs. 1.1% OR = 0.74 (95% CI 0.26, 2.11)
Reid IR et al., 1994[50] Pamidronate Australia/NZ	
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia	
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	

Author, Year, Drug, Country, Trial name	Results - 3
Reid IR et al., 2006[53] Calcium Australia/NZ	Number of people with fracture: symptomatic fractures at 60 months: Calcium vs. Placebo 16.0% vs. 18.0% OR = 0.87 (95% CI 0.67, 1.14) Number of people with fracture: vertebral fractures at 60 months: Calcium vs. Placebo 4.0% vs. 5.0% OR = 0.70 (95% CI 0.42, 1.14)
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	
Sato S et al., 2003[55] Etidronate Japan	
Sato Y et al., 2004[56] Etidronate Japan	
Sato Y et al., 2005[57] Risedronate Japan	
Sato Y et al., 2005[58] Risedronate Japan	
Sato Y et al., 2005[59] Vitamin D Japan	
Sato Y et al., 2005[60] Risedronate Japan	
Sato Y et al., 2006[61] Alendronate Japan	

Author, Year, Drug, Country, Trial name	Results - 3
Sato Y et al., 2006[62] Etidronate Japan	Number of people with fracture: rib fractures at 24 months: Etidronate vs. Placebo 0.0% vs. 2.0% OR = 0.14 (95% CI 0.00, 6.82) Number of people with fracture: vertebral fractures at 24 months: Etidronate vs. Placebo 0.0% vs. 7.0% OR = 0.13 (95% CI 0.01, 1.27)
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy	
Torres A et al., 2004[65] Calcium, Vitamin D Spain	
Toth E et al., 2005[66] Calcitonin Eastern Europe	
Trovas GP et al., 2002[67] Calcitonin Greece	
Uchida S et al., 2005[68] Alendronate Japan	
Ushiroyama T et al., 2001[69] Calcitonin Japan	

Author, Year, Drug, Country, Trial name	Results - 3
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2	
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK	
Zein CO et al., 2005[72] Alendronate US	

Author, Year, Drug, Country, Trial name	Results - 4
Agrawal S et al., 2006[1] Risedronate US	
Aris RM et al., 2000[2] Pamidronate US	
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	Number of people with fracture: morphometric vertebral fractures at 36 months: Zoledronic Acid 5mg vs Placebo 3.3% vs 10.9% OR = 0.32 (95% CI 0.26, 0.39) - NNT=13.2 (95% CI 11.2-15.9)
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	Number of people with fracture: nonvertebral fractures (ribs) at 14 months: PTH vs. Alendronate 2.7% vs. 1.4% OR = 1.97 (95% CI 0.20, 19.20)
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	
Boutsen Y et al., 1997[7] Pamidronate Western Europe	
Brown JP et al., 2002[8] Risedronate US, Canada	

Author, Year, Drug, Country, Trial name	Results - 4
Campbell IA et al., 2004[9] Etidronate UK	
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	
Coco M et al., 2003[12] Pamidronate US	
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1	
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	

Author, Year, Drug, Country, Trial name	Results - 4
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe	
Grant AM et al., 2005[17] Vitamin D UK	Number of people with fracture: other arm fractures at 62 months: Calcium vs. Placebo 2.5% vs. 3.7% OR = 0.68 (95% CI 0.44, 1.05) Calcium vs. Vitamin D3+Calcium 2.5% vs. 3.5% OR = 0.71 (95% CI 0.45, 1.11) Vitamin D3 vs. Calcium 3.6% vs. 2.5% OR = 1.43 (95% CI 0.92, 2.22) Vitamin D3 vs. Placebo 3.6% vs. 3.7% OR = 0.97 (95% CI 0.65, 1.46) Vitamin D3+Calcium vs. Placebo 3.5% vs. 3.7% OR = 0.96 (95% CI 0.63, 1.44) Vitamin D3+Calcium vs. Vitamin D3 3.4% vs. 3.7% OR = 0.98 (95% CI 0.65, 1.49) Number of people with fracture: other fractures at 62 months: Calcium vs. Placebo 0.5% vs. 0.5% OR = 1.19 (95% CI 0.40, 3.53) Calcium vs. Vitamin D3+Calcium 0.5% vs. 0.2% OR = 2.22 (95% CI 0.64, 7.70) Vitamin D3 vs. Calcium 0.6% vs. 0.5% OR = 1.12 (95% CI 0.40, 3.08) Vitamin D3 vs. Placebo 0.6% vs. 0.5% OR = 1.32 (95% CI 0.46, 3.78) Vitamin D3+Calcium vs. Placebo 0.2% vs. 0.5% OR = 0.52 (95% CI 0.14, 1.93) Vitamin D3+Calcium vs. Vitamin D3 0.2% vs. 0.6% OR = 0.41 (95% CI 0.13, 1.35)
Greenspan SL et al., 2003[18] Alendronate, Estrogen US	
Greenspan SL et al., 2006[19] Risedronate US	
Grotz W et al., 2001[20] Ibandronate Germany	
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe	

Author, Year, Drug, Country, Trial name	Results - 4
Harris ST et al., 2004[22] Risedronate US, Canada	
Hay JE et al., 2001[23] Calcitonin US	Number of people with fracture: spine fractures at 4 months: Salmon calcitonin vs. No therapy 15.0% vs. 21.0% OR = 0.65 (95% CI 0.17, 2.51)
Hizmetli S et al., 1998[24] Calcitonin Turkey	
Hochberg MC et al., 2005[25] Alendronate US FIT	
Hooper MJ et al., 2005[26] Risedronate Australia/NZ	
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil	
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan	
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI	

Author, Year, Drug, Country, Trial name	Results - 4
Kanaji A et al., 2006[31] Risedronate Japan	
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland	
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	
Kim SH et al., 2004[34] Pamidronate Asia	
Kishimoto H et al., 2006[35] Risedronate Japan	
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY	

Author, Year, Drug, Country, Trial name	Results - 4
McClung MR et al., 2006[38] Alendronate, AMG162 US	Number of people with fracture: tarsus, metatarsus, or both at 12 months: Alendronate vs. Placebo 2.0% vs. 2.0% OR = 1.00 (95% CI 0.06, 16.23) Denosumab vs. Alendronate 1.0% vs. 2.0% OR = 0.52 (95% CI 0.04, 7.28) Denosumab vs. Placebo 1.0% vs. 2.0% OR = 0.52 (95% CI 0.04, 7.28) Number of people with fracture: tibia, fibula, or both at 12 months: Alendronate vs. Placebo 0.0% vs. 0.0% OR = NC Denosumab vs. Alendronate 1.0% vs. 0.0% OR = 3.17 (95% CI 0.11, 94.82) Denosumab vs. Placebo 1.0% vs. 0.0% OR = 3.17 (95% CI 0.11, 94.82)
Milgrom C et al., 2004[39] Risedronate Israel	
Muscoso E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy	Number of people with fracture: vertebral fractures at 24 months: Alendronate vs. Clodronate 0.4% vs. 0.4% OR = 1.07 (95% CI 0.24, 4.75) Alendronate vs. Raloxifene 0.4% vs. 0.0% OR = 3.01 (95% CI 0.10, 91.52) Alendronate vs. Risedronate 0.4% vs. 0.0% OR = 3.01 (95% CI 0.10, 91.52) Raloxifene vs. Clodronate 0.0% vs. 0.4% OR = 0.32 (95% CI 0.01, 11.91) Risedronate vs. Clodronate 0.0% vs. 0.4% OR = 0.32 (95% CI 0.01, 11.91) Risedronate vs. Raloxifene 0.0% vs. 0.0% OR = NC
Ninkovic M et al., 2002[41] Pamidronate UK	
Orwoll ES et al., 2003[42] PTH 1100101000	
Palomba S et al., 2005[43] Risedronate Italy	
Porthouse J et al., 2005[44] Calcium, Vitamin D UK	
Prince RL et al., 2006[45] Calcium Australia/NZ	Number of people with fracture: spine fractures at 60 months: Calcium vs. Placebo 5.2% vs. 5.3% OR = 0.98 (95% CI 0.62, 1.55) Number of people with fracture: upper limb fractures at 60 months: Calcium vs. Placebo 4.0% vs. 4.2% OR = 0.95 (95% CI 0.57, 1.59)

Author, Year, Drug, Country, Trial name	Results - 4
Quandt SA et al., 2005[46] Alendronate US FIT	
Ravn P et al., 1996[47] Ibandronate Western Europe	
Recker R et al., 2004[48] Ibandronate US, Western Europe	
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial	
Reid IR et al., 1994[50] Pamidronate Australia/NZ	
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia	
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	
Reid IR et al., 2006[53] Calcium Australia/NZ	
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	

Author, Year, Drug, Country, Trial name	Results - 4
Sato S et al., 2003[55] Etidronate Japan	
Sato Y et al., 2004[56] Etidronate Japan	
Sato Y et al., 2005[57] Risedronate Japan	
Sato Y et al., 2005[58] Risedronate Japan	
Sato Y et al., 2005[59] Vitamin D Japan	
Sato Y et al., 2005[60] Risedronate Japan	
Sato Y et al., 2006[61] Alendronate Japan	
Sato Y et al., 2006[62] Etidronate Japan	
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	

Author, Year, Drug, Country, Trial name	Results - 4
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy	
Torres A et al., 2004[65] Calcium, Vitamin D Spain	
Toth E et al., 2005[66] Calcitonin Eastern Europe	
Trovas GP et al., 2002[67] Calcitonin Greece	
Uchida S et al., 2005[68] Alendronate Japan	
Ushiroyama T et al., 2001[69] Calcitonin Japan	
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2	
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK	
Zein CO et al., 2005[72] Alendronate US	

Author, Year, Drug, Country, Trial name	Results - 5
Agrawal S et al., 2006[1] Risedronate US	
Aris RM et al., 2000[2] Pamidronate US	
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	
Boutsen Y et al., 1997[7] Pamidronate Western Europe	
Brown JP et al., 2002[8] Risedronate US, Canada	

Author, Year, Drug, Country, Trial name	Results - 5
Campbell IA et al., 2004[9] Etidronate UK	
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	
Coco M et al., 2003[12] Pamidronate US	
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1	
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	

Author, Year, Drug, Country, Trial name	Results - 5
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe	
Grant AM et al., 2005[17] Vitamin D UK	Number of people with fracture: other leg and pelvic fractures at 62 months: Calcium vs. Placebo 3.1% vs. 4.1% OR = 0.77 (95% CI 0.51, 1.15) Calcium vs. Vitamin D3+Calcium 3.1% vs. 2.8% OR = 1.11 (95% CI 0.71, 1.74) Calcium vs. Vitamin D3 3.6% vs. 3.1% OR = 0.87 (95% CI 0.57, 1.33) Vitamin D3 vs. Placebo 3.6% vs. 4.1% OR = 0.88 (95% CI 0.59, 1.30) Vitamin D3+Calcium vs. Placebo 2.8% vs. 4.1% OR = 0.69 (95% CI 0.46, 1.05) Vitamin D3+Calcium vs. Vitamin D3 2.8% vs. 3.6% OR = 0.79 (95% CI 0.51, 1.21) Number of people with fracture: proximal femur fractures at 62 months: Calcium vs. Placebo 3.7% vs. 3.1% OR = 1.22 (95% CI 0.80, 1.86) Calcium vs. Vitamin D3+Calcium 3.7% vs. 3.5% OR = 1.06 (95% CI 0.71, 1.60) Calcium vs. Vitamin D3 3.7% vs. 3.5% OR = 1.07 (95% CI 0.71, 1.06) Vitamin D3 vs. Placebo 3.5% vs. 3.1% OR = 1.14 (95% CI 0.75, 1.75) Vitamin D3+Calcium vs. Placebo 3.5% vs. 3.1% OR = 1.15 (95% CI 0.75, 1.76) Vitamin D3+Calcium vs. Vitamin D3 3.5% vs. 3.5% OR = 1.01 (95% CI 0.67, 1.52)
Greenspan SL et al., 2003[18] Alendronate, Estrogen US	
Greenspan SL et al., 2006[19] Risedronate US	
Grotz W et al., 2001[20] Ibandronate Germany	
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe	

Author, Year, Drug, Country, Trial name	Results - 5
Harris ST et al., 2004[22] Risedronate US, Canada	
Hay JE et al., 2001[23] Calcitonin US	
Hizmetli S et al., 1998[24] Calcitonin Turkey	
Hochberg MC et al., 2005[25] Alendronate US FIT	
Hooper MJ et al., 2005[26] Risedronate Australia/NZ	
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil	
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan	
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI	

Author, Year, Drug, Country, Trial name	Results - 5
Kanaji A et al., 2006[31] Risedronate Japan	
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland	
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	
Kim SH et al., 2004[34] Pamidronate Asia	
Kishimoto H et al., 2006[35] Risedronate Japan	
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY	
McClung MR et al., 2006[38] Alendronate, AMG162 US	

Author, Year, Drug, Country, Trial name	Results - 5
Milgrom C et al., 2004[39] Risedronate Israel	
Muscoso E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy	
Ninkovic M et al., 2002[41] Pamidronate UK	
Orwoll ES et al., 2003[42] PTH 1100101000	
Palomba S et al., 2005[43] Risedronate Italy	
Porthouse J et al., 2005[44] Calcium, Vitamin D UK	
Prince RL et al., 2006[45] Calcium Australia/NZ	Number of people with fracture: wrist or hand fractures at 60 months: Calcium vs. Placebo 2.9% vs. 2.7% OR = 1.08 (95% CI 0.58, 2.00)
Quandt SA et al., 2005[46] Alendronate US FIT	
Ravn P et al., 1996[47] Ibandronate Western Europe	

Author, Year, Drug, Country, Trial name	Results - 5
Recker R et al., 2004[48] Ibandronate US, Western Europe	
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial	
Reid IR et al., 1994[50] Pamidronate Australia/NZ	
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia	
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	
Reid IR et al., 2006[53] Calcium Australia/NZ	
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	
Sato S et al., 2003[55] Etidronate Japan	
Sato Y et al., 2004[56] Etidronate Japan	

Author, Year, Drug, Country, Trial name	Results - 5
Sato Y et al., 2005[57] Risedronate Japan	
Sato Y et al., 2005[58] Risedronate Japan	
Sato Y et al., 2005[59] Vitamin D Japan	
Sato Y et al., 2005[60] Risedronate Japan	
Sato Y et al., 2006[61] Alendronate Japan	
Sato Y et al., 2006[62] Etidronate Japan	
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy	
Torres A et al., 2004[65] Calcium, Vitamin D Spain	

Author, Year, Drug, Country, Trial name	Results - 5
Toth E et al., 2005[66] Calcitonin Eastern Europe	
Trovas GP et al., 2002[67] Calcitonin Greece	
Uchida S et al., 2005[68] Alendronate Japan	
Ushiroyama T et al., 2001[69] Calcitonin Japan	
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2	
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK	
Zein CO et al., 2005[72] Alendronate US	

Author, Year, Drug, Country, Trial name	Results - 6	Methods of adverse events assessment
Agrawal S et al., 2006[1] Risedronate US		Monitored, reported by patient
Aris RM et al., 2000[2] Pamidronate US		Monitored, elicited by investigator
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon		Monitored, elicited by investigator, reported by patient
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel		Monitored, elicited by investigator
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP		Bone histology
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT		Monitored, elicited by investigator, reported by patient
Boutsen Y et al., 1997[7] Pamidronate Western Europe		Monitored
Brown JP et al., 2002[8] Risedronate US, Canada		Monitored, reported by patient
Campbell IA et al., 2004[9] Etidronate UK		Reported by patient

Author, Year, Drug, Country, Trial name	Results - 6	Methods of adverse events assessment
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT		Monitored, elicited by investigator, reported by patient
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT		Monitored, elicited by investigator, reported by patient
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE		Monitored
Coco M et al., 2003[12] Pamidronate US		NR
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1		Monitored, elicited by investigator, reported by patient
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH		Monitored, reported by patient
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL		Reported by patient

Author, Year, Drug, Country, Trial name	Results - 6	Methods of adverse events assessment
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe		NR
Grant AM et al., 2005[17] Vitamin D UK		Elicited by investigator, reported by patient
Greenspan SL et al., 2003[18] Alendronate, Estrogen US		NR
Greenspan SL et al., 2006[19] Risedronate US		Reported by patient
Grotz W et al., 2001[20] Ibandronate Germany		Monitored, reported by patient
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe		NR
Harris ST et al., 2004[22] Risedronate US, Canada		Monitored, reported by patient
Hay JE et al., 2001[23] Calcitonin US		Monitored, reported by patient
Hizmetli S et al., 1998[24] Calcitonin Turkey		NR
Hochberg MC et al., 2005[25] Alendronate US FIT		Monitored, elicited by investigator, reported by patient

Author, Year, Drug, Country, Trial name	Results - 6	Methods of adverse events assessment
Hooper MJ et al., 2005[26] Risedronate Australia/NZ		Elicited by investigator, reported by patient
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil		Monitored, elicited by investigator, reported by patient
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY		NR
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan		NR
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI		Monitored, elicited by investigator, reported by patient
Kanaji A et al., 2006[31] Risedronate Japan		Monitored
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland		NR
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden		Reported by patient
Kim SH et al., 2004[34] Pamidronate Asia		NR

Author, Year, Drug, Country, Trial name	Results - 6	Methods of adverse events assessment
Kishimoto H et al., 2006[35] Risedronate Japan		Monitored, reported by patient
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP		Monitored, reported by patient
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY		Elicited by investigator, reported by patient
McClung MR et al., 2006[38] Alendronate, AMG162 US		Monitored, reported by patient
Milgrom C et al., 2004[39] Risedronate Israel		Elicited by investigator
Muscoso E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy		NR
Ninkovic M et al., 2002[41] Pamidronate UK		NR
Orwoll ES et al., 2003[42] PTH 1100101000		Monitored, reported by patient
Palomba S et al., 2005[43] Risedronate Italy		Monitored, reported by patient

Author, Year, Drug, Country, Trial name	Results - 6	Methods of adverse events assessment
Porthouse J et al., 2005[44] Calcium, Vitamin D UK		NR
Prince RL et al., 2006[45] Calcium Australia/NZ		Monitored, reported by patient
Quandt SA et al., 2005[46] Alendronate US FIT		Monitored, elicited by investigator, reported by patient
Ravn P et al., 1996[47] Ibandronate Western Europe		Monitored, reported by patient
Recker R et al., 2004[48] Ibandronate US, Western Europe		Monitored
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial		Monitored, elicited by investigator, reported by patient
Reid IR et al., 1994[50] Pamidronate Australia/NZ		Monitored
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia		NR
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa		Elicited by investigator

Author, Year, Drug, Country, Trial name	Results - 6	Methods of adverse events assessment
Reid IR et al., 2006[53] Calcium Australia/NZ		Reported by patient
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI		Monitored, elicited by investigator, reported by patient
Sato S et al., 2003[55] Etidronate Japan		NR
Sato Y et al., 2004[56] Etidronate Japan		Monitored, reported by patient
Sato Y et al., 2005[57] Risedronate Japan		Monitored, elicited by investigator, reported by patient
Sato Y et al., 2005[58] Risedronate Japan		Reported by patient
Sato Y et al., 2005[59] Vitamin D Japan		Monitored, elicited by investigator
Sato Y et al., 2005[60] Risedronate Japan		Monitored, reported by patient
Sato Y et al., 2006[61] Alendronate Japan		Monitored, elicited by investigator, reported by patient
Sato Y et al., 2006[62] Etidronate Japan		Monitored, elicited by investigator, reported by patient

Author, Year, Drug, Country, Trial name	Results - 6	Methods of adverse events assessment
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT		Monitored, reported by patient
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy		Monitored
Torres A et al., 2004[65] Calcium, Vitamin D Spain		Monitored
Toth E et al., 2005[66] Calcitonin Eastern Europe		Elicited by investigator, reported by patient
Trovas GP et al., 2002[67] Calcitonin Greece		Monitored, reported by patient
Uchida S et al., 2005[68] Alendronate Japan		Monitored, reported by patient
Ushiroyama T et al., 2001[69] Calcitonin Japan		Monitored, reported by patient
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2		Monitored, reported by patient

Author, Year, Drug, Country, Trial name	Results - 6	Methods of adverse events assessment
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK		Monitored
Zein CO et al., 2005[72] Alendronate US		Monitored, elicited by investigator, reported by patient

Author, Year, Drug, Country, Trial name	Total withdrawals and Withdrawals due to adverse events
Agrawal S et al., 2006[1] Risedronate US	Placebo vs. Risedronate: Withdrawals: 13.8%(4/29) vs. 9.7%(3/31) Withdrawals due to adverse events: 6.9%(2/29) vs. 6.5%(2/31)
Aris RM et al., 2000[2] Pamidronate US	Control vs. Pamidronate: Withdrawals: Not reported Withdrawals due to adverse events: Not reported
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	Placebo vs Zoledronic acid: Withdrawals: 15.7%(607/3876) vs 16.5%(641/3889) Withdrawals due to adverse events: 1.8%(70/3876) vs 2.1%(80/3889)
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	Alendronate vs. PTH: Withdrawals: 21.9%(16/73) vs. 30.1%(22/73) Withdrawals due to adverse events: 9.6%(7/73) vs. 19.2%(14/73)
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	Alendronate vs. Estrogen vs. Alendronate, Estrogen vs. Placebo: Withdrawals: 15.2%(14/92) vs. 15.4%(22/143) vs. 13.6%(19/140) vs. 18.0%(9/50) Withdrawals due to adverse events: 6.5%(6/92) vs. 9.8%(14/143) vs. 9.3%(13/140) vs. 10.0%(5/50)
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	Alendronate vs. Risedronate: Withdrawals: 35.2%(183/520) vs. 37.5%(200/533) Withdrawals due to adverse events: Not reported
Boutsen Y et al., 1997[7] Pamidronate Western Europe	Calcium vs. Pamidronate: Withdrawals: 30.8%(4/13) vs. 35.7%(5/14) Withdrawals due to adverse events: 7.7%(1/13) vs. 0.0%(0/14)
Brown JP et al., 2002[8] Risedronate US, Canada	Risedronate 35 mg vs. Risedronate 5 mg vs. Risedronate 50 mg: Withdrawals: 18.6%(90/485) vs. 16.0%(77/480) vs. 16.3%(80/491) Withdrawals due to adverse events: 11.5%(56/485) vs. 11.9%(57/480) vs. 8.8%(43/491)
Campbell IA et al., 2004[9] Etidronate UK	Etidronate, Calcium vs. Calcium vs. Etidronate vs. Placebo: Withdrawals: 35.2%(31/88) vs. 24.7%(21/85) vs. 21.0%(17/81) vs. 10.5%(10/95) Withdrawals due to adverse events: 19.3%(17/88) vs. 5.9%(5/85) vs. 11.1%(9/81) vs. 0.0%(0/95)

Author, Year, Drug, Country, Trial name	Total withdrawals and Withdrawals due to adverse events
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	Alendronate vs. Placebo: Withdrawals: Not reported Withdrawals due to adverse events: Not reported
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	Alendronate vs. Placebo: Withdrawals: Not reported Withdrawals due to adverse events: Not reported
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	Ibandronate 2.5mg vs. Ibandronate 20mg vs. Placebo: Withdrawals: 34.2%(334/977) vs. 32.8%(320/977) vs. 36.3%(354/975) Withdrawals due to adverse events: 17.9%(175/977) vs. 18.2%(178/977) vs. 18.5%(180/975)
Coco M et al., 2003[12] Pamidronate US	Calcium vs. Pamidronate: Withdrawals: 22.2%(8/36) vs. 13.9%(5/36) Withdrawals due to adverse events: Not reported
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1	Placebo vs. Tamoxifen: Withdrawals: 1.6%(108/6707) vs. 1.6%(104/6681) Withdrawals due to adverse events: Not reported
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	Etidronate vs. Risedronate: Withdrawals: 12.8%(15/117) vs. 16.9%(20/118) Withdrawals due to adverse events: 6.0%(7/117) vs. 6.8%(8/118)
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	Placebo vs. PTH: Withdrawals: Not reported Withdrawals due to adverse events: Not reported
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe	Calcidiol vs. Calcitonin vs. Etidronate: Withdrawals: Not reported Withdrawals due to adverse events: Not reported

Author, Year, Drug, Country, Trial name	Total withdrawals and Withdrawals due to adverse events
Grant AM et al., 2005[17] Vitamin D UK	Calcium vs. Placebo vs. Vitamin D vs. Calcium, Vitamin D: Withdrawals: 1.7%(22/1311) vs. 1.1%(14/1332) vs. 1.1%(15/1343) vs. 1.2%(16/1306) Withdrawals due to adverse events: Not reported
Greenspan SL et al., 2003[18] Alendronate, Estrogen US	Alendronate vs. Estrogen vs. Alendronate, Estrogen vs. Placebo: Withdrawals: 8.6%(8/93) vs. 9.7%(9/93) vs. 9.6%(9/94) vs. 10.8%(10/93) Withdrawals due to adverse events: 2.2%(2/93) vs. 2.2%(2/93) vs. 0.0%(0/94) vs. 2.2%(2/93)
Greenspan SL et al., 2006[19] Risedronate US	Placebo vs. Risedronate: Withdrawals: 2.3%(1/44) vs. 9.3%(4/43) Withdrawals due to adverse events: Not reported
Grotz W et al., 2001[20] Ibandronate Germany	Ibandronate vs. Placebo: Withdrawals: 10.0%(4/40) vs. 10.0%(4/40) Withdrawals due to adverse events: 7.5%(3/40) vs. 5.0%(2/40)
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe	Alendronate vs. Etidronate: Withdrawals: 18.8%(3/16) vs. 18.8%(3/16) Withdrawals due to adverse events: 6.3%(1/16) vs. 18.8%(3/16)
Harris ST et al., 2004[22] Risedronate US, Canada	Risedronate 35 mg once a week vs. Risedronate 50mg once a week vs. Risedronate 5mg daily: Withdrawals: 23.7%(115/485) vs. 22.8%(112/491) vs. 21.3%(102/480) Withdrawals due to adverse events: 15.5%(75/485) vs. 12.2%(60/491) vs. 15.6%(75/480)
Hay JE et al., 2001[23] Calcitonin US	Placebo vs. Calcitonin: Withdrawals: 5.9%(2/34) vs. 24.1%(7/29) Withdrawals due to adverse events: 2.9%(1/34) vs. 10.3%(3/29)
Hizmetli S et al., 1998[24] Calcitonin Turkey	Calcitonin 100 iu & calcium + Vitamin D 1000 mg/d vs. Calcitonin 50 iu & calcium + Vitamin D 1000 mg/d vs. Calcium, Vitamin D: Withdrawals: 14.6%(6/41) vs. 17.1%(6/35) vs. 25.8%(8/31) Withdrawals due to adverse events: Not reported
Hochberg MC et al., 2005[25] Alendronate US FIT	Alendronate vs. Placebo: Withdrawals: Not reported Withdrawals due to adverse events: Not reported
Hooper MJ et al., 2005[26] Risedronate Australia/NZ	Placebo vs. Risedronate 2.5mg/d vs. Risedronate 5mg/d: Withdrawals: 26.2%(33/126) vs. 21.9%(28/128) vs. 20.2%(26/129) Withdrawals due to adverse events: 6.3%(8/126) vs. 9.4%(12/128) vs. 5.4%(7/129)

Author, Year, Drug, Country, Trial name	Total withdrawals and Withdrawals due to adverse events
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil	Alendronate vs. Placebo vs. Risedronate: Withdrawals: 21.5%(47/219) vs. 17.6%(19/108) vs. 19.8%(44/222) Withdrawals due to adverse events: 14.2%(31/219) vs. 11.1%(12/108) vs. 14.0%(31/222)
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	Vitamin D vs. Calcitonin vs. Control vs. Etidronate vs. Estrogen vs. Vitamin K: Withdrawals: 4.5%(3/66) vs. 6.1%(4/66) vs. 9.1%(6/66) vs. 6.1%(4/66) vs. 6.1%(4/66) vs. 4.5%(3/66) Withdrawals due to adverse events: 0.0%(0/66) vs. 0.0%(0/66) vs. 0.0%(0/66) vs. 1.5%(1/66) vs. 4.5%(3/66) vs. 0.0%(0/66)
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan	Alendronate vs. Etidronate: Withdrawals: 0.0%(0/25) vs. 0.0%(0/25) Withdrawals due to adverse events: 0.0%(0/25) vs. 0.0%(0/25)
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI	Calcium, Vitamin D vs. Placebo: Withdrawals: 6.8%(1240/18176) vs. 7.1%(1291/18106) Withdrawals due to adverse events: Not reported
Kanaji A et al., 2006[31] Risedronate Japan	Placebo vs. Risedronate: Withdrawals: 0.0%(0/11) vs. 16.7%(2/12) Withdrawals due to adverse events: 0.0%(0/11) vs. 0.0%(0/12)
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland	Estrogen, Calcium, Vitamin D vs. Pamidronate: Withdrawals: 32.7%(16/49) vs. 34.0%(17/50) Withdrawals due to adverse events: 30.6%(15/49) vs. 30.0%(15/50)
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	Placebo vs. Teriparitide 20ug vs. Teriparitide 40ug: Withdrawals: Not reported Withdrawals due to adverse events: Not reported
Kim SH et al., 2004[34] Pamidronate Asia	Pamidronate vs. Placebo: Withdrawals: 0.0%(0/25) vs. 20.0%(5/25) Withdrawals due to adverse events: Not reported
Kishimoto H et al., 2006[35] Risedronate Japan	Risedronate 17.5 mg/week vs. Risedronate 2.5 mg/d: Withdrawals: 9.2%(23/249) vs. 16.2%(40/247) Withdrawals due to adverse events: 5.2%(13/249) vs. 10.1%(25/247)

Author, Year, Drug, Country, Trial name	Total withdrawals and Withdrawals due to adverse events
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	Etidronate vs. Risedronate: Withdrawals: 30.7%(84/274) vs. 26.7%(73/273) Withdrawals due to adverse events: 21.2%(58/274) vs. 13.9%(38/273)
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY	Alendronate vs. Raloxifene: Withdrawals: 19.7%(44/223) vs. 17.2%(40/233) Withdrawals due to adverse events: 11.2%(25/223) vs. 10.3%(24/233)
McClung MR et al., 2006[38] Alendronate, AMG162 US	Alendronate vs. AMG 162 vs. Placebo: Withdrawals: Not reported Withdrawals due to adverse events: 0.0%(0/46) vs. 2.2%(7/314) vs. 2.2%(1/46)
Milgrom C et al., 2004[39] Risedronate Israel	Placebo vs. Risedronate: Withdrawals: 64.8%(103/159) vs. 68.5%(113/165) Withdrawals due to adverse events: 7.5%(12/159) vs. 15.2%(25/165)
Muscoso E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy	Alendronate vs. Clodronate vs. Raloxifene vs. Risedronate: Withdrawals: Not reported Withdrawals due to adverse events: Not reported
Ninkovic M et al., 2002[41] Pamidronate UK	Control vs. Pamidronate: Withdrawals: 29.6%(16/54) vs. 26.7%(12/45) Withdrawals due to adverse events: 25.9%(14/54) vs. 13.3%(6/45)
Orwoll ES et al., 2003[42] PTH 1100101000	Placebo vs. Teriparatide 20 mg vs. Teriparatide 40 mg: Withdrawals: 11.6%(17/147) vs. 18.5%(28/151) vs. 25.9%(36/139) Withdrawals due to adverse events: 4.8%(7/147) vs. 9.3%(14/151) vs. 12.9%(18/139)
Palomba S et al., 2005[43] Risedronate Italy	Placebo vs. Risedronate: Withdrawals: 8.9%(4/45) vs. 11.1%(5/45) Withdrawals due to adverse events: 0.0%(0/45) vs. 0.0%(0/45)
Porthouse J et al., 2005[44] Calcium, Vitamin D UK	Calcium, Vitamin D vs. Control: Withdrawals: 8.3%(109/1321) vs. 6.6%(131/1993) Withdrawals due to adverse events: Not reported
Prince RL et al., 2006[45] Calcium Australia/NZ	Calcium vs. Placebo: Withdrawals: 15.5%(113/730) vs. 16.3%(119/730) Withdrawals due to adverse events: Not reported

Author, Year, Drug, Country, Trial name	Total withdrawals and Withdrawals due to adverse events
Quandt SA et al., 2005[46] Alendronate US FIT	Alendronate vs. Placebo: Withdrawals: Not reported Withdrawals due to adverse events: Not reported
Ravn P et al., 1996[47] Ibandronate Western Europe	Ibandronate 0.25mg vs. Ibandronate 0.5mg vs. Ibandronate 1.0mg vs. Ibandronate 2.5mg vs. Ibandronate 5.0mg vs. Placebo: Withdrawals: 13.3%(4/30) vs. 26.7%(8/30) vs. 13.3%(4/30) vs. 20.0%(6/30) vs. 40.0%(12/30) vs. 16.7%(5/30) Withdrawals due to adverse events: 6.7%(2/30) vs. 10.0%(3/30) vs. 3.3%(1/30) vs. 3.3%(1/30) vs. 3.3%(1/30) vs. 13.3%(4/30)
Recker R et al., 2004[48] Ibandronate US, Western Europe	Ibandronate 0.5 mg vs. Ibandronate 1 mg vs. Placebo: Withdrawals: 16.1%(153/950) vs. 19.5%(187/961) vs. 17.2%(163/949) Withdrawals due to adverse events: 8.1%(77/950) vs. 10.9%(105/961) vs. 7.5%(71/949)
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial	Alendronate vs. Raloxifene: Withdrawals: 14.2%(102/716) vs. 13.0%(92/707) Withdrawals due to adverse events: 6.0%(43/716) vs. 5.2%(37/707)
Reid IR et al., 1994[50] Pamidronate Australia/NZ	Pamidronate vs. Placebo: Withdrawals: 19.2%(5/26) vs. 36.4%(8/22) Withdrawals due to adverse events: 11.5%(3/26) vs. 22.7%(5/22)
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia	Placebo vs. Zoledronic acid 1x 4 mg vs. Zoledronic acid 2x 2 mg vs. Zoledronic acid 4x 0.25 mg vs. Zoledronic acid 4x 0.50 mg vs. Zoledronic acid 4x 1 mg: Withdrawals: Not reported Withdrawals due to adverse events: 1.7%(1/59) vs. 3.3%(2/60) vs. 3.3%(2/61) vs. 6.7%(4/60) vs. 3.4%(2/58) vs. 5.7%(3/53)
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	Estrogen vs. Placebo vs. Raloxifene 150mg/d vs. Raloxifene 60mg/d: Withdrawals: 35.4%(56/158) vs. 40.8%(62/152) vs. 35.0%(55/157) vs. 40.1%(61/152) Withdrawals due to adverse events: 15.8%(25/158) vs. 16.4%(25/152) vs. 19.1%(30/157) vs. 19.1%(29/152)
Reid IR et al., 2006[53] Calcium Australia/NZ	Calcium vs. Placebo: Withdrawals: 45.9%(336/732) vs. 40.1%(296/739) Withdrawals due to adverse events: 18.2%(133/732) vs. 14.2%(105/739)

Author, Year, Drug, Country, Trial name	Total withdrawals and Withdrawals due to adverse events
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	Alendronate vs. Risedronate: Withdrawals: 15.8%(82/520) vs. 14.8%(79/533) Withdrawals due to adverse events: 6.3%(33/520) vs. 6.4%(34/533)
Sato S et al., 2003[55] Etidronate Japan	Control vs. Etidronate: Withdrawals: 43.1%(22/51) vs. 47.1%(24/51) Withdrawals due to adverse events: 7.8%(4/51) vs. 3.9%(2/51)
Sato Y et al., 2004[56] Etidronate Japan	Etidronate vs. Placebo: Withdrawals: Not reported Withdrawals due to adverse events: Not reported
Sato Y et al., 2005[57] Risedronate Japan	Placebo vs. Risedronate: Withdrawals: 5.0%(7/140) vs. 4.3%(6/140) Withdrawals due to adverse events: 1.4%(2/140) vs. 0.7%(1/140)
Sato Y et al., 2005[58] Risedronate Japan	Control vs. Risedronate: Withdrawals: 8.0%(20/250) vs. 7.6%(19/250) Withdrawals due to adverse events: 4.0%(10/250) vs. 4.0%(10/250)
Sato Y et al., 2005[59] Vitamin D Japan	Placebo vs. Vitamin D: Withdrawals: 12.5%(6/48) vs. 10.4%(5/48) Withdrawals due to adverse events: 0.0%(0/48) vs. 0.0%(0/48)
Sato Y et al., 2005[60] Risedronate Japan	Placebo vs. Risedronate: Withdrawals: 7.5%(14/187) vs. 8.0%(15/187) Withdrawals due to adverse events: 0.0%(0/187) vs. 0.0%(0/187)
Sato Y et al., 2006[61] Alendronate Japan	Alendronate vs. Placebo: Withdrawals: 9.0%(13/144) vs. 9.7%(14/144) Withdrawals due to adverse events: 2.8%(4/144) vs. 2.8%(4/144)
Sato Y et al., 2006[62] Etidronate Japan	Etidronate vs. Placebo: Withdrawals: 9.8%(4/41) vs. 7.3%(3/41) Withdrawals due to adverse events: 2.4%(1/41) vs. 0.0%(0/41)
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	Placebo vs. Risedronate: Withdrawals: 19.2%(25/130) vs. 14.8%(20/135) Withdrawals due to adverse events: 12.3%(16/130) vs. 7.4%(10/135)

Author, Year, Drug, Country, Trial name	Total withdrawals and Withdrawals due to adverse events
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy	Calcium, Vitamin D vs. Estradiol + dihydroprogesterone + calcium vs. Estradiol 2 mg & dihydroprogesterone 10 vs. Risedronate, Calcium, Vitamin D vs. Zoledronic acid, Calcium, Vitamin D vs. Zoledronic acid, C: Withdrawals: 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/15) Withdrawals due to adverse events: 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/15) vs. 0.0%(0/15)
Torres A et al., 2004[65] Calcium, Vitamin D Spain	Calcium, Vitamin D vs. Placebo, Calcium: Withdrawals: 0.0%(0/45) vs. 8.9%(4/45) Withdrawals due to adverse events: 0.0%(0/45) vs. 4.4%(2/45)
Toth E et al., 2005[66] Calcitonin Eastern Europe	Calcium, Vitamin D vs. Calcitonin, Calcium, Vitamin D: Withdrawals: 0.0%(0/31) vs. 0.0%(0/40) Withdrawals due to adverse events: 0.0%(0/31) vs. 0.0%(0/40)
Trovas GP et al., 2002[67] Calcitonin Greece	Calcitonin vs. Placebo: Withdrawals: 0.0%(0/15) vs. 0.0%(0/13) Withdrawals due to adverse events: 0.0%(0/15) vs. 0.0%(0/13)
Uchida S et al., 2005[68] Alendronate Japan	Alendronate 35mg / weekly vs. Alendronate 5mg / day: Withdrawals: 16.1%(27/168) vs. 15.0%(24/160) Withdrawals due to adverse events: 5.4%(9/168) vs. 8.1%(13/160)
Ushiroyama T et al., 2001[69] Calcitonin Japan	Vitamin D vs. Calcitonin vs. Calcitonin, Vitamin D vs. Placebo: Withdrawals: Not reported Withdrawals due to adverse events: Not reported
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2	Raloxifene vs. Tamoxifen: Withdrawals: 1.3%(128/9875) vs. 1.5%(146/9872) Withdrawals due to adverse events: Not reported
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK	Control vs. Etidronate vs. Estrogen vs. Estrogen, Etidronate: Withdrawals: 22.2%(4/18) vs. 17.6%(3/17) vs. 16.7%(3/18) vs. 21.1%(4/19) Withdrawals due to adverse events: 16.7%(3/18) vs. 17.6%(3/17) vs. 16.7%(3/18) vs. 21.1%(4/19)
Zein CO et al., 2005[72] Alendronate US	Alendronate vs. Placebo: Withdrawals: 11.8%(2/17) vs. 23.5%(4/17) Withdrawals due to adverse events: 5.9%(1/17) vs. 11.8%(2/17)

Author, Year, Drug, Country, Trial name	Screener notes	Long form notes
Agrawal S et al., 2006[1] Risedronate US		
Aris RM et al., 2000[2] Pamidronate US		DROPOUTS DESCRIBED BUT NEVER STATED WHICH ARM THEY BELONG TO.
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon		STUDY POPULATION=HIGH RISK FOR FRACTURE
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel		STUDY ENDED EARLY SECONDARY ADVERSE EVENTS (OSTEOSARCOMA) IN RATS
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP		
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT		
Boutsen Y et al., 1997[7] Pamidronate Western Europe		ARM 1 - PATIENT RECEIVED LOADING DOSE STUDY DURATION LASTED AS LONG AS PT WAS ON CORTICOSTEROIDS - VARIABLE
Brown JP et al., 2002[8] Risedronate US, Canada		

Author, Year, Drug, Country, Trial name	Screener notes	Long form notes
Campbell IA et al., 2004[9] Etidronate UK		
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT		
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT		
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE		
Coco M et al., 2003[12] Pamidronate US		CALCITRIOL AND CALCIUM GIVEN TO MAINTAIN SERUM CALCIUM BETWEEN 8.5 AND 10.5 MG IDL
Fisher B et al., 1998[13] Tamoxifen US, Canada NSABP-P1		
Fukunaga M et al., 2002[14] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH		

Author, Year, Drug, Country, Trial name	Screener notes	Long form notes
Gallagher JC et al., 2005[15] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL		2 COUNTRIES WERE NOT REPORTED. STUDY DURATION MEDIAN IN ABSTRACT STATES 21 MOS WHEN IN THE METHODS STATES 19 MOS
Garcia-Delgado I et al., 1997[16] Calcitonin, Etidronate Western Europe	SPECIAL POPULATION CARDIAC TRANSPLANTS	
Grant AM et al., 2005[17] Vitamin D UK	Vit D	
Greenspan SL et al., 2003[18] Alendronate, Estrogen US		
Greenspan SL et al., 2006[19] Risedronate US		
Grotz W et al., 2001[20] Ibandronate Germany		IBANDRONATE GROUP GIVEN ONE DOSE OF 1 MG PRIOR TO TRANSPLANT THEN 2 MG AT 3, 6 AND 9 MONTHS
Guanabens N et al., 2003[21] Alendronate, Etidronate Western Europe	#4 PRIMARY BILIARY CIRRHOSIS	
Harris ST et al., 2004[22] Risedronate US, Canada		

Author, Year, Drug, Country, Trial name	Screener notes	Long form notes
Hay JE et al., 2001[23] Calcitonin US	Only patients with low vitamin D levels, hypocalcemia, increased PTH or low urinary, calcium in regimen, vitamin D in both arms	
Hizmetli S et al., 1998[24] Calcitonin Turkey		
Hochberg MC et al., 2005[25] Alendronate US FIT	subgroup analyses	
Hooper MJ et al., 2005[26] Risedronate Australia/NZ		VERTEBRAL AND NONVERTEBRAL FRACTURES WERE MONITORED AS ADVERSE EVENTS
Hosking D et al., 2003[27] Alendronate, Risedronate UK, Western Europe, Brazil		
Ishida Y et al., 2004[28] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY		
Iwamoto J et al., 2003[29] Alendronate, Etidronate Japan		
Jackson RD et al., 2006[30] Calcium, Vitamin D US WHI		

Author, Year, Drug, Country, Trial name	Screener notes	Long form notes
Kanaji A et al., 2006[31] Risedronate Japan		
Kananen K et al., 2005[32] Estrogen, Pamidronate, Testosterone Finland		
Kaufman JM et al., 2005[33] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden		NO ADDITIONAL INFORMATION ABOUT ADHERENCE. THIS WAS A FOLLOW-UP STUDY. 1 COUNTRY WAS NOT REPORTED. THIS STUDY WAS DISCONTINUED EARLY SUBJECTS IN ANALYSIS VOLUNTEERED TO FOLLOW-UP.
Kim SH et al., 2004[34] Pamidronate Asia		
Kishimoto H et al., 2006[35] Risedronate Japan		
Kushida K et al., 2004[36] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP		
Luckey M et al., 2004[37] Alendronate, Raloxifene US THE EFFECT STUDY		
McClung MR et al., 2006[38] Alendronate, AMG162 US		

Author, Year, Drug, Country, Trial name	Screener notes	Long form notes
Milgrom C et al., 2004[39] Risedronate Israel		
Muscoso E et al., 2004[40] Alendronate, Raloxifene, Risedronate Italy		
Ninkovic M et al., 2002[41] Pamidronate UK		PAMIDRONATE GIVEN AS ONE TIME ONLY DOSE, THEN PATIENTS FOLLOWED FOR 12 MONTHS
Orwoll ES et al., 2003[42] PTH 1100101000		
Palomba S et al., 2005[43] Risedronate Italy		
Porthouse J et al., 2005[44] Calcium, Vitamin D UK		
Prince RL et al., 2006[45] Calcium Australia/NZ		
Quandt SA et al., 2005[46] Alendronate US FIT		TABS COUNTED @ EACH VISITS ALENDRONATE GROUP RECEIVED 2 YRS OF 5MG QD THEN 10MG QD FOR VARIABLE PERIOD OF TIME (UP TO 2.5YRS)
Ravn P et al., 1996[47] Ibandronate Western Europe		

Author, Year, Drug, Country, Trial name	Screener notes	Long form notes
Recker R et al., 2004[48] Ibandronate US, Western Europe		
Recker RR et al., 2006[49] Alendronate, Raloxifene US, Canada EVA trial		
Reid IR et al., 1994[50] Pamidronate Australia/NZ		
Reid IR et al., 2002[51] Zoledronic acid Western Europe, Australia		
Reid IR et al., 2004[52] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa		
Reid IR et al., 2006[53] Calcium Australia/NZ	calcium versus placebo;	
Rosen CJ et al., 2005[54] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI		
Sato S et al., 2003[55] Etidronate Japan		
Sato Y et al., 2004[56] Etidronate Japan		

Author, Year, Drug, Country, Trial name	Screener notes	Long form notes
Sato Y et al., 2005[57] Risedronate Japan		NO ADDITIONAL INFORMATION FOR ADHERENCE QS HIP FRACTURE WAS THE PRIMARY OUTCOME
Sato Y et al., 2005[58] Risedronate Japan		NONVERTEBRAL FRACTURES MEASURED AS ADVERSE EVENTS
Sato Y et al., 2005[59] Vitamin D Japan		
Sato Y et al., 2005[60] Risedronate Japan		
Sato Y et al., 2006[61] Alendronate Japan		
Sato Y et al., 2006[62] Etidronate Japan	note: only those low in vitamin D based on blood tests received vitamin D supplementation	
Sorensen OH et al., 2003[63] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	1. This is the followup study for ID # 3168; 2. put a footnote in table: *this is the 2 year extension study of #3168 and not all of the 1226 subjects enrolled in the initial study wither chose to participate in the extension or were eligible to participate	
Tauchmanova L et al., 2006[64] Estrogen, Risedronate, Zoledronic acid Italy		
Torres A et al., 2004[65] Calcium, Vitamin D Spain		

Author, Year, Drug, Country, Trial name	Screener notes	Long form notes
Toth E et al., 2005[66] Calcitonin Eastern Europe		THE INCIDENCE OF VERTEBRAL AND NONVERTEBRAL FRACTURES WAS A SECONDARY OUTCOME
Trovas GP et al., 2002[67] Calcitonin Greece		
Uchida S et al., 2005[68] Alendronate Japan		
Ushiroyama T et al., 2001[69] Calcitonin Japan		
Vogel VG et al., 2006[70] Raloxifene, Tamoxifen US, Canada STAR P-2	Breast Cancer	
Wimalawansa SJ, 1998[71] Estrogen, Etidronate UK		INTERVENTIONS - NUMBER COMPLETING/ ANALYZED IS FOR 4 YEAR DATA (2 YEAR DIFFERENT)
Zein CO et al., 2005[72] Alendronate US		

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Appendix C3. Quality Tables for Randomized Controlled Trials
Columns 1-9: Article, Randomization, Concealment, Similar, Eligibility, Assessors, Providers, Patient, Adhere

Author, Year, Drug, Country, Trial name	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcomes assessors masked?	Care provider masked?	Patient masked?	Reporting of adherence and contamination?
Agrawal S et al., 2006[1] Risedronate US	Not described	Not described	Yes	Yes	NR	Yes	Yes	Yes/Yes
Aris RM et al., 2000[2] Pamidronate US	Yes	Not described	Yes	Yes	Yes	No	No	NR/NR
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	Yes	Not described	Yes	Yes	Yes	NR	Yes, but not described	Yes/NR
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	Not described	Not described	Yes	Yes	Yes, but not described	Yes, but not described	Yes, but not described	Yes/NR
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	Yes	Not described	Yes	Yes	NR	Yes, but not described	Yes, but not described	NR/NR
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	Yes	Not described	Yes	Yes	Yes	Yes	Yes	NR/NR
Boutsen Y et al., 1997[7] Pamidronate Western Europe	Yes	Not described	Yes	Yes	NR	NR	NR	NR/NR
Brown JP et al., 2002[8] Risedronate US, Canada	Not described	Not described	Yes	Yes	Yes	Yes	Yes	Yes/NR

Author, Year, Drug, Country, Trial name	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcomes assessors masked?	Care provider masked?	Patient masked?	Reporting of adherence and contamination?
Campbell IA et al., 2004[9] Etidronate UK	Yes	No	Yes	Yes	NR	No	No	NR/NR
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes/NR
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes/NR
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	Yes	Not described	Yes	Yes	NR	Yes	Yes	NR/NR
Coco M et al., 2003[12] Pamidronate US	Yes	Not described	Yes	Yes	NR	NR	NR	NR/NR
Cosman F et al., 2001[13] Estrogen, PTH US	Yes	Not described	Yes	Yes	Yes	NR	NR	NR/NR
Cosman F et al., 2005[14] Alendronate, PTH US	Yes	Not described	Yes	Yes	Yes	No	No	Yes/NR

Author, Year, Drug, Country, Trial name	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcomes assessors masked?	Care provider masked?	Patient masked?	Reporting of adherence and contamination?
Fisher B et al., 1998[15] Tamoxifen US, Canada NSABP-P1	Yes	Yes	NR	Yes	NR	Yes, but not described	Yes, but not described	NR/NR
Fukunaga M et al., 2002[16] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	Not described	Not described	Yes	Yes	Yes	Yes	Yes	NR/NR
Gallagher JC et al., 2005[17] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	Not described	Not described	Yes	Yes	Yes	Yes, but not described	Yes, but not described	NR/NR
Garcia-Delgado I et al., 1997[18] Calcitonin, Etidronate Western Europe	Not described	Not described	Yes	Yes	NR	NR	NR	NR/NR
Grant AM et al., 2005[19] Vitamin D UK	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes/NR
Greenspan SL et al., 2003[20] Alendronate, Estrogen US	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NR/NR
Greenspan SL et al., 2006[21] Risedronate US	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes/NR
Grotz W et al., 2001[22] Ibandronate Germany	Not described	No	Yes	Yes	Yes	NR	No	Yes/NR

Author, Year, Drug, Country, Trial name	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcomes assessors masked?	Care provider masked?	Patient masked?	Reporting of adherence and contamination?
Guanabens N et al., 2003[23] Alendronate, Etidronate Western Europe	Yes	Not described	Yes	Yes	Yes	NR	NR	NR/NR
Harris ST et al., 2001[24] Estrogen, Risedronate US	Not described	Not described	Yes	Yes	NR	NR	NR	Yes/NR
Harris ST et al., 2004[25] Risedronate US, Canada	Not described	Not described	Yes	Yes	Yes	Yes	Yes	Yes/NR
Hay JE et al., 2001[26] Calcitonin US	Not described	No	Yes	Yes	NR	No	No	NR/Yes
Henderson S et al., 2006[27] Risedronate Australia/NZ	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NR/NR
Hizmetli S et al., 1998[28] Calcitonin Turkey	Not described	No	Yes	Yes	NR	No	No	NR/NR
Hochberg MC et al., 2005[29] Alendronate US FIT	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NR/NR
Hodsman AB et al., 1997[30] Calcitonin, Raloxifene Canada	Not described	Not described	Yes	Yes	NR	NR	NR	NR/NR
Hooper MJ et al., 2005[31] Risedronate Australia/NZ	Yes	Not described	Yes	Yes	NR	NR	NR	NR/NR

Author, Year, Drug, Country, Trial name	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcomes assessors masked?	Care provider masked?	Patient masked?	Reporting of adherence and contamination?
Hosking D et al., 2003[32] Alendronate, Risedronate UK, Western Europe, Brazil	Yes	Yes	Yes	Yes	NR	Yes	Yes	NR/NR
Ishida Y et al., 2004[33] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	Not described	Not described	Yes	Yes	Yes	NR	NR	NR/NR
Iwamoto J et al., 2003[34] Alendronate, Etidronate Japan	Not described	Not described	Yes	Yes	NR	NR	No	NR/NR
Iwamoto J et al., 2003[35] Alendronate, Etidronate Japan	Not described	Not described	Yes	Yes	NR	NR	No	NR/NR
Jackson RD et al., 2006[36] Calcium, Vitamin D US WHI	Yes	Not described	Yes	Yes	Yes	Yes	Yes	Yes/Yes
Kanaji A et al., 2006[37] Risedronate Japan	Not described	Not described	Yes	Yes	NR	Yes	Yes	NR/NR
Kananen K et al., 2005[38] Estrogen, Pamidronate, Testosterone Finland	Not described	Not described	Yes	Yes	NR	No	No	NR/Yes
Kaufman JM et al., 2005[39] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	Yes	Not described	Yes	Yes	NR	Yes	NR	Yes/NR

Author, Year, Drug, Country, Trial name	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcomes assessors masked?	Care provider masked?	Patient masked?	Reporting of adherence and contamination?
Kim SH et al., 2004[40] Pamidronate Asia	Not described	Not described	Yes	Yes	NR	NR	NR	NR/NR
Kishimoto H et al., 2006[41] Risedronate Japan	Not described	Not described	Yes	Yes	Yes	Yes	Yes	NR/NR
Kushida K et al., 2004[42] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	Not described	Not described	Yes	Yes	Yes	NR	Yes	NR/NR
Lindsay R et al., 1997[43] Estrogen, PTH US	Yes	Yes	Yes	Yes	Yes	NR	No	Yes/NR
Lindsay R et al., 1999[44] Alendronate, Estrogen US	Not described	Not described	Yes	Yes	NR	NR	NR	NR/NR
Luckey M et al., 2004[45] Alendronate, Raloxifene US THE EFFECT STUDY	Yes	Yes	Yes	Yes	Yes	NR	Yes	NR/NR
McClung MR et al., 2006[46] Alendronate, AMG162 US	Yes	Not described	Yes	Yes	Yes	No	No	NR/NR
Milgrom C et al., 2004[47] Risedronate Israel	Not described	Not described	Yes	Yes	NR	Yes	Yes	Yes/Yes
Muscoso E et al., 2004[48] Alendronate, Raloxifene, Risedronate Italy	Not described	Not described	NR	Yes	NR	No	No	NR/NR

Author, Year, Drug, Country, Trial name	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcomes assessors masked?	Care provider masked?	Patient masked?	Reporting of adherence and contamination?
Ninkovic M et al., 2002[49] Pamidronate UK	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes/Yes
Orwoll ES et al., 2003[50] PTH 1100101000	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes/NR
Palomba S et al., 2005[51] Risedronate Italy	Yes	Not described	Yes	Yes	Yes	Yes	Yes	NR/NR
Porthouse J et al., 2005[52] Calcium, Vitamin D UK	Yes	Yes	Yes	Yes	No	No	No	Yes/Yes
Prince RL et al., 2006[53] Calcium Australia/NZ	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes/NR
Quandt SA et al., 2005[54] Alendronate US FIT	Yes	Not described	Yes	Yes	Yes	Yes	Yes	Yes/NR
Ravn P et al., 1996[55] Ibandronate Western Europe	Not described	Not described	Yes	Yes	NR	NR	NR	NR/NR
Recker R et al., 2004[56] Ibandronate US, Western Europe	Yes	Not described	Yes	Yes	Yes	Yes, but not described	Yes, but not described	NR/NR
Recker RR et al., 2006[57] Alendronate, Raloxifene US, Canada EVA trial	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes/NR

Author, Year, Drug, Country, Trial name	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcomes assessors masked?	Care provider masked?	Patient masked?	Reporting of adherence and contamination?
Reginster JY et al., 2006[58] Ibandronate US, Canada, Latin Amer, UK, Western Europe, Eastern Europe, Australia/NZ, South Africa MOBILE	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes/NR
Reid IR et al., 1994[59] Pamidronate Australia/NZ	Not described	Not described	Yes	Yes	NR	Yes	Yes	Yes/NR
Reid IR et al., 2002[60] Zoledronic acid Western Europe, Australia	Not described	Yes	Yes	Yes	Yes	Yes	Yes	NR/NR
Reid IR et al., 2004[61] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	Yes	Not described	Yes	Yes	Yes	NR	NR	NR/NR
Reid IR et al., 2006[62] Calcium Australia/NZ	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes/NR
Ringe JD et al., 2006[63] Risedronate Germany	Not described	Not described	Yes	Yes	Yes	No	No	NR/NR
Rosen CJ et al., 2005[64] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	Yes	Not described	Yes	Yes	Yes	Yes	Yes	NR/NR
Sato S et al., 2003[65] Etidronate Japan	Not described	Not described	Yes	Yes	Yes	No	No	NR/NR

Author, Year, Drug, Country, Trial name	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcomes assessors masked?	Care provider masked?	Patient masked?	Reporting of adherence and contamination?
Sato Y et al., 2004[66] Etidronate Japan	Yes	Not described	NR	Yes	NR	Yes, but not described	Yes, but not described	NR/NR
Sato Y et al., 2005[67] Risedronate Japan	Yes	Yes	Yes	Yes	NR	NR	NR	Yes/NR
Sato Y et al., 2005[68] Risedronate Japan	Yes	Yes	Yes	Yes	Yes	Yes	Yes, but not described	Yes/NR
Sato Y et al., 2005[69] Vitamin D Japan	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NR/NR
Sato Y et al., 2005[70] Risedronate Japan	Yes	No	Yes	Yes	NR	Yes, but not described	Yes, but not described	NR/NR
Sato Y et al., 2005[71] Calcium, Vitamin D Japan	Yes	Yes	Yes	Yes	Yes	NR	No	NR/NR
Sato Y et al., 2006[72] Alendronate Japan	Yes	Yes	Yes	Yes	Yes	NR	Yes	NR/NR
Sato Y et al., 2006[73] Etidronate Japan	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NR/NR
Sorensen OH et al., 2003[74] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	Not described	Not described	Yes	Yes	Yes	Yes, but not described	Yes, but not described	NR/NR

Author, Year, Drug, Country, Trial name	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcomes assessors masked?	Care provider masked?	Patient masked?	Reporting of adherence and contamination?
Tauchmanova L et al., 2006[75] Estrogen, Risedronate, Zoledronic acid Italy	Not described	Not described	Yes	Yes	NR	NR	No	NR/NR
Torres A et al., 2004[76] Calcium, Vitamin D Spain	Not described	Not described	Yes	Yes	NR	Yes	Yes	NR/NR
Toth E et al., 2005[77] Calcitonin Eastern Europe	Not described	Not described	Yes	Yes	NR	No	No	NR/NR
Trovas GP et al., 2002[78] Calcitonin Greece	Not described	Not described	Yes	Yes	NR	Yes	Yes	NR/NR
Uchida S et al., 2005[79] Alendronate Japan	Yes	Yes	Yes	Yes	Yes, but not described	Yes, but not described	Yes, but not described	NR/NR
Ushiroyama T et al., 2001[80] Calcitonin Japan	Not described	No	Yes	Yes	NR	No	No	NR/NR
Vogel VG et al., 2006[81] Raloxifene, Tamoxifen US, Canada STAR P-2	Yes	Not described	NR	Yes	Yes, but not described	Yes, but not described	Yes, but not described	Yes/NR
Wimalawansa SJ, 1998[82] Estrogen, Etidronate UK	Yes	Yes	Yes	Yes	Yes	NR	No	NR/NR
Zein CO et al., 2005[83] Alendronate US	Yes	No	Yes	Yes	Yes	Yes	Yes	NR/NR

Author, Year, Drug, Country, Trial name	Loss to follow-up: differential/high?	Intention-to-treat (ITT) analysis?	Quality rating (Jadad score)	Number screened/eligible/enrolled
Agrawal S et al., 2006[1] Risedronate US	No	No	4	64/NR/60
Aris RM et al., 2000[2] Pamidronate US	No	Yes	3	44/37/37
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	NR	Yes	4	18421/9977/7765
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	No	Yes	4	265/149/149
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	No	Yes	4	NR/NR/425
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	NR	Yes	4	1759/NR/1053
Boutsen Y et al., 1997[7] Pamidronate Western Europe	No	No	3	NR/NR/32
Brown JP et al., 2002[8] Risedronate US, Canada	NR	Yes	3	4972/NR/1468
Campbell IA et al., 2004[9] Etidronate UK	No	Yes	2	NR/NR/352

Author, Year, Drug, Country, Trial name	Loss to follow-up: differential/high?	Intention-to-treat (ITT) analysis?	Quality rating (Jadad score)	Number screened/eligible/enrolled
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	NR	No	4	NR/NR/1746
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	NR	No	4	NR/NR/1318
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	NR	Yes	4	18447/NR/2946
Coco M et al., 2003[12] Pamidronate US	NR	No	2	112/98/72
Cosman F et al., 2001[13] Estrogen, PTH US	No	No	3	280/174/52
Cosman F et al., 2005[14] Alendronate, PTH US	No	No	3	1345/131/126
Fisher B et al., 1998[15] Tamoxifen US, Canada NSABP-P1	No	No	3	98018/13954/13388

Author, Year, Drug, Country, Trial name	Loss to follow-up: differential/high?	Intention-to-treat (ITT) analysis?	Quality rating (Jadad score)	Number screened/eligible/enrolled
Fukunaga M et al., 2002[16] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	No	No	3	362/NR/235
Gallagher JC et al., 2005[17] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	NR	No	2	9347/NR/931
Garcia-Delgado I et al., 1997[18] Calcitonin, Etidronate Western Europe	NR	Yes	1	NR/NR/40
Grant AM et al., 2005[19] Vitamin D UK	NR	Yes	4	15024/8827/5292
Greenspan SL et al., 2003[20] Alendronate, Estrogen US	No	Yes	5	573/548/373
Greenspan SL et al., 2006[21] Risedronate US	No	Yes	5	106/94/87
Grotz W et al., 2001[22] Ibandronate Germany	No	No	2	114/98/80
Guanabens N et al., 2003[23] Alendronate, Etidronate Western Europe	No	No	3	NR/NR/32
Harris ST et al., 2001[24] Estrogen, Risedronate US	NR	Yes	2	NR/NR/524

Author, Year, Drug, Country, Trial name	Loss to follow-up: differential/high?	Intention-to-treat (ITT) analysis?	Quality rating (Jadad score)	Number screened/eligible/enrolled
Harris ST et al., 2004[25] Risedronate US, Canada	No	Yes	3	4972/NR/1468
Hay JE et al., 2001[26] Calcitonin US	NR	Yes	1	NR/NR/63
Henderson S et al., 2006[27] Risedronate Australia/NZ	No	No	5	NR/NR/61
Hizmetli S et al., 1998[28] Calcitonin Turkey	NR	No	1	NR/NR/107
Hochberg MC et al., 2005[29] Alendronate US FIT	NR	Yes	4	NR/NR/3658
Hodsman AB et al., 1997[30] Calcitonin, Raloxifene Canada	No	No	2	NR/NR/39
Hooper MJ et al., 2005[31] Risedronate Australia/NZ	No	Yes	3	NR/NR/383
Hosking D et al., 2003[32] Alendronate, Risedronate UK, Western Europe, Brazil	No	Yes	5	1036/NR/549
Ishida Y et al., 2004[33] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	No	Yes	2	739/NR/396

Author, Year, Drug, Country, Trial name	Loss to follow-up: differential/high?	Intention-to-treat (ITT) analysis?	Quality rating (Jadad score)	Number screened/eligible/enrolled
Iwamoto J et al., 2003[34] Alendronate, Etidronate Japan	No	Yes	1	NR/NR/50
Iwamoto J et al., 2003[35] Alendronate, Etidronate Japan	NR	No	1	NR/NR/40
Jackson RD et al., 2006[36] Calcium, Vitamin D US WHI	No	Yes	4	68132/62528/36282
Kanaji A et al., 2006[37] Risedronate Japan	NR	No	4	NR/NR/23
Kananen K et al., 2005[38] Estrogen, Pamidronate, Testosterone Finland	No	No	1	115/108/99
Kaufman JM et al., 2005[39] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	NR	No	4	959/437/355
Kim SH et al., 2004[40] Pamidronate Asia	No	Yes	2	NR/NR/50
Kishimoto H et al., 2006[41] Risedronate Japan	No	Yes	3	NR/NR/496
Kushida K et al., 2004[42] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	No	No	4	NR/NR/547

Author, Year, Drug, Country, Trial name	Loss to follow-up: differential/high?	Intention-to-treat (ITT) analysis?	Quality rating (Jadad score)	Number screened/eligible/enrolled
Lindsay R et al., 1997[43] Estrogen, PTH US	No	Yes	3	NR/NR/40
Lindsay R et al., 1999[44] Alendronate, Estrogen US	No	Yes	1	1855/565/428
Luckey M et al., 2004[45] Alendronate, Raloxifene US THE EFFECT STUDY	No	Yes	5	1200/508/456
McClung MR et al., 2006[46] Alendronate, AMG162 US	NR	Yes	2	NR/NR/412
Milgrom C et al., 2004[47] Risedronate Israel	No	Yes	4	473/473/324
Muscoso E et al., 2004[48] Alendronate, Raloxifene, Risedronate Italy	NR	No	1	NR/NR/2000
Ninkovic M et al., 2002[49] Pamidronate UK	No	No	2	NR/NR/99
Orwoll ES et al., 2003[50] PTH 1100101000	NR	Yes	4	959/NR/437
Palomba S et al., 2005[51] Risedronate Italy	No	No	4	279/97/90

Author, Year, Drug, Country, Trial name	Loss to follow-up: differential/high?	Intention-to-treat (ITT) analysis?	Quality rating (Jadad score)	Number screened/eligible/enrolled
Porthouse J et al., 2005[52] Calcium, Vitamin D UK	NR	Yes	2	11022/7944/3454
Prince RL et al., 2006[53] Calcium Australia/NZ	NR	Yes	5	4312/1510/1460
Quandt SA et al., 2005[54] Alendronate US FIT	NR	No	4	NR/NR/3737
Ravn P et al., 1996[55] Ibandronate Western Europe	No	No	3	NR/821/180
Recker R et al., 2004[56] Ibandronate US, Western Europe	No	No	3	16632/NR/2862
Recker RR et al., 2006[57] Alendronate, Raloxifene US, Canada EVA trial	No	Yes	4	5531/1840/1423
Reginster JY et al., 2006[58] Ibandronate US, Canada, Latin Amer, UK, Western Europe, Eastern Europe, Australia/NZ, South Africa MOBILE	No	Yes	4	2410/NR/1609
Reid IR et al., 1994[59] Pamidronate Australia/NZ	No	No	4	NR/NR/61

Author, Year, Drug, Country, Trial name	Loss to follow-up: differential/high?	Intention-to-treat (ITT) analysis?	Quality rating (Jadad score)	Number screened/eligible/enrolled
Reid IR et al., 2002[60] Zoledronic acid Western Europe, Australia	NR	Yes	3	NR/NR/351
Reid IR et al., 2004[61] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	No	Yes	2	NR/1522/619
Reid IR et al., 2006[62] Calcium Australia/NZ	No	Yes	4	2421/1780/1471
Ringe JD et al., 2006[63] Risedronate Germany	NR	Yes	1	580/NR/316
Rosen CJ et al., 2005[64] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	No	Yes	4	1759/NR/1053
Sato S et al., 2003[65] Etidronate Japan	NR	Yes	1	NR/NR/102
Sato Y et al., 2004[66] Etidronate Japan	NR	No	4	NR/NR/80
Sato Y et al., 2005[67] Risedronate Japan	No	Yes	4	312/287/280
Sato Y et al., 2005[68] Risedronate Japan	No	Yes	4	658/510/500

Author, Year, Drug, Country, Trial name	Loss to follow-up: differential/high?	Intention-to-treat (ITT) analysis?	Quality rating (Jadad score)	Number screened/eligible/enrolled
Sato Y et al., 2005[69] Vitamin D Japan	NR	No	4	137/NR/96
Sato Y et al., 2005[70] Risedronate Japan	No	No	4	NR/NR/374
Sato Y et al., 2005[71] Calcium, Vitamin D Japan	NR	No	2	NR/NR/200
Sato Y et al., 2006[72] Alendronate Japan	No	Yes	5	558/NR/288
Sato Y et al., 2006[73] Etidronate Japan	No	Yes	4	85/NR/82
Sorensen OH et al., 2003[74] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	NR	No	2	4400/NR/1226
Tauchmanova L et al., 2006[75] Estrogen, Risedronate, Zoledronic acid Italy	No	Yes	1	NR/NR/60
Torres A et al., 2004[76] Calcium, Vitamin D Spain	No	No	4	NR/NR/90
Toth E et al., 2005[77] Calcitonin Eastern Europe	No	Yes	1	225/75/71

Author, Year, Drug, Country, Trial name	Loss to follow-up: differential/high?	Intention-to-treat (ITT) analysis?	Quality rating (Jadad score)	Number screened/eligible/enrolled
Trovas GP et al., 2002[78] Calcitonin Greece	No	Yes	4	NR/NR/28
Uchida S et al., 2005[79] Alendronate Japan	NR	No	3	NR/NR/328
Ushiroyama T et al., 2001[80] Calcitonin Japan	NR	Yes	1	NR/NR/202
Vogel VG et al., 2006[81] Raloxifene, Tamoxifen US, Canada STAR P-2	No	Yes	3	184460/20168/19747
Wimalawansa SJ, 1998[82] Estrogen, Etidronate UK	No	No	3	350/NR/72
Zein CO et al., 2005[83] Alendronate US	No	No	5	NR/NR/34

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Agrawal S et al., 2006[1] Risedronate US	Carcinoma or suspected carcinoma, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Med known to affect skeleton, age <65, any significant lab abnormalities, Osteoporotic fracture within 2yrs	NR NR	Not reported
Aris RM et al., 2000[2] Pamidronate US	Pregnancy, Renal insufficiency, Life expectancy <5 years, Graft Failure	NR NR	Not reported
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	Bisphosphonates, Fluoride, Anabolic steroids, Corticoids/Glucocorticoids, Hypercalcemia, Hypocalcemia, previous PTH use, >2+ protein on urine dipstick, bisphosphonate use for >=48 weeks within 2 years prior to study, Growth Hormone use, strontium use, calculated creatinine clearance , 30.0 ml/min	NR NR	No
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	Age > 85, Carcinoma or suspected carcinoma, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Malabsorption syndrome, Urolithiasis, Bisphosphonates, Calcitonin, Fluoride, Androgen, Estrogen agonists (including estrogen), Anabolic steroids, Corticoids/Glucocorticoids, Alcohol Abuse, Allergy to PTH, age<30, LS spine abnormalities prohibiting DEXA, previous PTH use	Run-in period reported NR	Yes
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	Cardiovascular disease, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Venous thromboembolic disease - Active, Venous thromboembolic disease - Ever, Bisphosphonates, Calcitonin, Fluoride, Vitamin D deficient, recent major upper GI mucosal erosive disease, Increased risk of breast cancer, Unexplained genital bleeding x 1 year, Fasting triglycerides >400mg/dL, Contraindication to HRT, HRT within last 6 months	NR NR	Not reported
Bonnick S et al., 2006[6] Alendronate, Risedronate US FACT	Metabolic bone disorder other than osteoporosis, Upper GI, Bisphosphonates, Fluoride, HRT, Estrogen agonists (including estrogen), Anabolic steroids, Corticoids/Glucocorticoids, Vitamin D deficient, previous PTH use, Hypocalcemia, Immunosuppressants	NR NR	Not reported
Boutsen Y et al., 1997[7] Pamidronate Western Europe	Carcinoma or suspected carcinoma, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Renal insufficiency, Urolithiasis, Bisphosphonates, Fluoride, Previous Glucocorticoids	NR NR	Yes

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Brown JP et al., 2002[8] Risedronate US, Canada	Med known to affect skeleton, LS spine abnormalities prohibiting DEXA	NR NR	Not reported
Campbell IA et al., 2004[9] Etidronate UK	Hysterectomy, age <=50, age >=70	NR NR	Not reported
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Renal insufficiency, Malabsorption syndrome, Upper GI, Bisphosphonates, Calcitonin, Fluoride, Estrogen agonists (including estrogen), age >= 80, age <=55, life expectancy =<3yrs	NR NR	Yes
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Renal insufficiency, Malabsorption syndrome, Upper GI, Bisphosphonates, Calcitonin, Fluoride, Estrogen agonists (including estrogen), age >= 80, age <=55, life expectancy =<3yrs	NR NR	Yes
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	Metabolic bone disorder other than osteoporosis, Renal insufficiency, Bisphosphonates, Fluoride, Med known to affect skeleton, Diseases known to affect skeleton, > 2 fractures lumbar spine, Contraindication to Ca or Vitamin D, Hypercalcemia, Hypocalcemia, age <=55, age >= 80, T score<-5.0	NR NR	Yes
Coco M et al., 2003[12] Pamidronate US	Pregnancy	NR NR	Not reported
Cosman F et al., 2001[13] Estrogen, PTH US	Metabolic bone disorder other than osteoporosis, Nephrolithiasis	NR Washout period reported	Not reported

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Cosman F et al., 2005[14] Alendronate, PTH US	Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hypoparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Nephrolithiasis, Anticonvulsants, Estrogen agonists (including estrogen), Corticoids/Glucocorticoids, Abnormal Urinary Calcium, Abnormal CBC	NR NR	No
Fisher B et al., 1998[15] Tamoxifen US, Canada NSABP-P1	Pregnancy, Hepatic insufficiency, Renal insufficiency, Venous thromboembolic disease, Estrogen agonists (including estrogen), Progestin, Contraceptive, Breast Cancer, Abnormal CBC	NR NR	Not reported
Fukunaga M et al., 2002[16] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH	Age > 75, Carcinoma or suspected carcinoma, Cardiovascular disease, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Upper GI, LS spine abnormalities prohibiting DEXA, Med known to affect skeleton, Drug Hypersensitivity, History of Radiotherapy	NR NR	Not reported
Gallagher JC et al., 2005[17] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	Hepatic insufficiency, Renal insufficiency, Urolithiasis, nonambulatory, Alcohol Abuse, drug abuse, any medication that may alter bone and mineral metabolism, illnesses that affect bone and calcium metabolism	NR NR	Not reported
Garcia-Delgado I et al., 1997[18] Calcitonin, Etidronate Western Europe	Med known to affect skeleton, Hypogonadism	NR NR	Not reported
Grant AM et al., 2005[19] Vitamin D UK	Carcinoma or suspected carcinoma, Nephrolithiasis, Bisphosphonates, Calcitonin, Calcium (includes antacids), Fluoride, HRT, SERMS, Vitamin D, age < 70, nonambulatory, mental condition that would preclude participation, Hypercalcemia, life expectancy <1/2 years, fracture associated with bone abnormality	NR NR	Not reported

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Greenspan SL et al., 2003[20] Alendronate, Estrogen US	Carcinoma or suspected carcinoma, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Renal insufficiency, Anticonvulsants, Bisphosphonates, Calcitonin, Hormone use, Corticoids/Glucocorticoids, Med known to affect skeleton, Contraindication to HRT, Contraindication to alendronate, BMD hip T score >0.0	Run-in period reported NR	Not reported
Greenspan SL et al., 2006[21] Risedronate US	Carcinoma or suspected carcinoma, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Malabsorption syndrome, age <18, Stage IV breast cancer, any medication that may alter bone and mineral metabolism	NR NR	Not reported
Grotz W et al., 2001[22] Ibandronate Germany	Kidney Pancreas Transplant	NR NR	Not reported
Guanabens N et al., 2003[23] Alendronate, Etidronate Western Europe	Renal insufficiency, Upper GI, Bisphosphonates, Fluoride, Estrogen agonists (including estrogen), Corticoids/Glucocorticoids, Bilirubin >10mg/dL	NR NR	Yes
Harris ST et al., 2001[24] Estrogen, Risedronate US	Metabolic bone disorder other than osteoporosis, HRT, Med known to affect skeleton, Major systemic Disease, Abnormal Pap, Significant Psychiatric disease, LS spine abnormalities prohibiting DEXA	NR NR	Not reported
Harris ST et al., 2004[25] Risedronate US, Canada	Med known to affect skeleton, LS spine abnormalities prohibiting DEXA	NR NR	Not reported
Hay JE et al., 2001[26] Calcitonin US	Hypothyroidism, Hyperthyroidism, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Anticonvulsants, Hormone use, Corticoids/Glucocorticoids, Med known to affect skeleton, Survived 6mos after liver transplant	NR NR	Not reported
Henderson S et al., 2006[27] Risedronate Australia/NZ	Pregnancy, Hepatic insufficiency, Bisphosphonates, HRT, Vitamin D deficient, Osteoporotic fracture, breast feeding, Hypercalcemia, Hypocalcemia	NR NR	Yes
Hizmetli S et al., 1998[28] Calcitonin Turkey	Med known to affect skeleton, Secondary Osteoporosis	NR NR	Yes

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Hochberg MC et al., 2005[29] Alendronate US FIT	Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Renal insufficiency, Malabsorption syndrome, Upper GI, Bisphosphonates, Calcitonin, Fluoride, Estrogen agonists (including estrogen), age >= 80, age <=55, life expectancy =<3yrs	NR NR	Yes
Hodsman AB et al., 1997[30] Calcitonin, Raloxifene Canada	Endocrine disease, Metabolic bone disorder other than osteoporosis, Bisphosphonates, Calcitonin, Corticoids/Glucocorticoids	NR NR	Not reported
Hooper MJ et al., 2005[31] Risedronate Australia/NZ	Hyperthyroidism, Hyperparathyroidism, Metabolic bone disorder other than osteoporosis, Serum estradiol >20, Med known to affect skeleton	NR NR	Not reported
Hosking D et al., 2003[32] Alendronate, Risedronate UK, Western Europe, Brazil	Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Metabolic bone disorder other than osteoporosis, Bisphosphonates, Fluoride, HRT, Estrogen agonists (including estrogen), Corticoids/Glucocorticoids, LS spine abnormalities prohibiting DEXA, Vitamin D deficient, Severe Upper GI symptoms, Severe Osteoporosis, age >90, age <60, Abnormal Urinary Calcium	NR NR	Not reported
Ishida Y et al., 2004[33] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	Age > 75, Carcinoma or suspected carcinoma, Metabolic bone disorder other than osteoporosis, Med known to affect skeleton, bilateral hip fractures, mental condition that would preclude participation	NR NR	Not reported
Iwamoto J et al., 2003[34] Alendronate, Etidronate Japan	Metabolic bone disorder other than osteoporosis, HRT, Estrogen agonists (including estrogen), Med known to affect skeleton	NR NR	Yes
Iwamoto J et al., 2003[35] Alendronate, Etidronate Japan	Metabolic bone disorder other than osteoporosis, HRT, Estrogen agonists (including estrogen), Med known to affect skeleton, any lumbar vertebral fractures	NR NR	Yes
Jackson RD et al., 2006[36] Calcium, Vitamin D US WHI	Nephrolithiasis, Vitamin D, Corticoids/Glucocorticoids, age >= 80, Hypercalcemia, age <=50, life expectancy =<3yrs	NR NR	No

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Kanaji A et al., 2006[37] Risedronate Japan	any medication that may alter bone and mineral metabolism	NR NR	Not reported
Kananen K et al., 2005[38] Estrogen, Pamidronate, Testosterone Finland	Renal insufficiency, Myeloma	NR NR	Not reported
Kaufman JM et al., 2005[39] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	Age > 85, Carcinoma or suspected carcinoma, Hyperparathyroidism, Hypoparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Sprue, Inflammatory bowel disease, Malabsorption syndrome, Nephrolithiasis, Urolithiasis, Anticonvulsants, Aluminum, Bisphosphonates, Calcitonin, Calcium (includes antacids), Coumarins, Fluoride, Androgen, Estrogen agonists (including estrogen), Progestin, Estrogen antagonists, Anabolic steroids, Vitamin D, Corticoids/Glucocorticoids, Abnormal Urinary Calcium, nonambulatory, any medication that may alter bone and mineral metabolism, treatment with calcitriol analogues, age<30, Secondary Osteoporosis, Alcohol Abuse, LS spine abnormalities prohibiting DEXA, treatment with indandione derivatives, Hypercalcemia, Hypocalcemia, Major systemic Disease, drug abuse, Growth Hormone deficiency, poor intestinal calcium absorption	Run-in period reported NR	Not reported
Kim SH et al., 2004[40] Pamidronate Asia	Renal insufficiency, Bisphosphonates, bed rest	NR NR	Not reported
Kishimoto H et al., 2006[41] Risedronate Japan	Carcinoma or suspected carcinoma, Cardiovascular disease, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Gastrointestinal disease, Bisphosphonates, any medication that may alter bone and mineral metabolism, Drug Hypersensitivity, radiation therapy to lumbar spine or pelvis, LS spine abnormalities prohibiting DEXA	NR NR	Not reported

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Kushida K et al., 2004[42] Etidronate, Risedronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	Cardiovascular disease, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Gastrointestinal disease, treatment with Risedronate or etidronate, Secondary Osteoporosis, radiographic findings that affect vertebral intensity, Med known to affect skeleton, malignancy under treatment with anti-tumor agents, radiation therapy to lumbar spine or pelvis	NR NR	Not reported
Lindsay R et al., 1997[43] Estrogen, PTH US	Hypothyroidism, Hyperthyroidism, Hepatic insufficiency, Renal insufficiency, Nephrolithiasis, Secondary Osteoporosis	Run-in period reported NR	Not reported
Lindsay R et al., 1999[44] Alendronate, Estrogen US	Hyperthyroidism, Metabolic bone disorder other than osteoporosis, Upper GI, Bisphosphonates, Calcitonin	Run-in period reported NR	Not reported
Luckey M et al., 2004[45] Alendronate, Raloxifene US THE EFFECT STUDY	Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Upper GI, Venous thromboembolic disease - Active, Venous thromboembolic disease - Ever, Bisphosphonates, Fluoride, Estrogen agonists (including estrogen), SERMS, Anabolic steroids, Corticoids/Glucocorticoids, LS spine abnormalities prohibiting DEXA, Immunosuppressants, Hypocalcemia, previous PTH use, Med known to affect skeleton, Breast Cancer, Uterine Cancer	NR NR	Not reported
McClung MR et al., 2006[46] Alendronate, AMG162 US	Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hypoparathyroidism, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Malabsorption syndrome, Bisphosphonates, Calcitonin, Fluoride, Androgen, Estrogen agonists (including estrogen), SERMS, Estrogen antagonists, Testosterone, Vitamin D, Corticoids/Glucocorticoids, age >= 80, Hypocalcemia, LS spine abnormalities prohibiting DEXA, previous PTH use, Long bone fracture, greater than one vertebral fracture, Osteoporotic fracture within 2yrs	NR NR	Not reported
Milgrom C et al., 2004[47] Risedronate Israel	NR	NR NR	Not reported
Muscoso E et al., 2004[48] Alendronate, Raloxifene, Risedronate Italy	NR	NR NR	Not reported

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Ninkovic M et al., 2002[49] Pamidronate UK	Renal insufficiency, Bisphosphonates, retransplantation	NR NR	Yes
Orwoll ES et al., 2003[50] PTH 1100101000	Age > 85, Carcinoma or suspected carcinoma, Hyperparathyroidism, Hypoparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Sprue, Inflammatory bowel disease, Malabsorption syndrome, Nephrolithiasis, Urolithiasis, Anticonvulsants, Aluminum, Bisphosphonates, Calcitonin, Calcium (includes antacids), Coumarins, Fluoride, Estrogen agonists (including estrogen), Progestin, Estrogen antagonists, Anabolic steroids, Vitamin D, Corticoids/Glucocorticoids, age<30, Med known to affect skeleton, Alcohol Abuse, drug abuse, LS spine abnormalities prohibiting DEXA, Growth Hormone deficiency, treatment with indandione derivatives	NR NR	Yes
Palomba S et al., 2005[51] Risedronate Italy	Carcinoma or suspected carcinoma, Endocrine disease, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Bisphosphonates, Calcitonin, Fluoride, HRT, Anabolic steroids, Proton pump inhibitors, Corticoids/Glucocorticoids, Vitamin D deficient, Hypercalcemia, Hypocalcemia, Med known to affect skeleton, hydrochlorothiazide, active rheumatoid arthritis, tobacco abuse, extremes of BMI (either high or low), other medications that could cause GI irritation	NR NR	Not reported
Porthouse J et al., 2005[52] Calcium, Vitamin D UK	Renal insufficiency, Nephrolithiasis, Urolithiasis, Calcium (includes antacids), age < 70, unable to give informed consent, Hypercalcemia, life expectancy <1/2 years	NR NR	Not reported
Prince RL et al., 2006[53] Calcium Australia/NZ	age < 70, participation in another trial, Med known to affect skeleton, Life expectancy <5 years	NR NR	Not reported

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Quandt SA et al., 2005[54] Alendronate US FIT	Carcinoma or suspected carcinoma, Cardiovascular disease, Hyperparathyroidism, Hypoparathyroidism, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Malabsorption syndrome, Upper GI, Bisphosphonates, Calcitonin, Fluoride, Estrogen agonists (including estrogen), Progestin, Anabolic steroids, Corticoids/Glucocorticoids, BMD femoral neck < -3, noncompliance, history of bilateral hip replacement, nonambulatory, Alcohol Abuse, age <=55, age >= 80, Major systemic Disease, intending to move within four years, any vertebral deformity, recent major upper GI mucosal erosive disease, participation in another trial, unable to give informed consent, change in thyroid hormone dose, unexpected weight loss > 10% of ideal body weight in last 12 months	NR NR	No
Ravn P et al., 1996[55] Ibandronate Western Europe	Age > 75, Bisphosphonates, Calcitonin, HRT, Diseases, conditions or treatments known to interfere with calcium metabolism	NR NR	Not reported
Recker R et al., 2004[56] Ibandronate US, Western Europe	Carcinoma or suspected carcinoma, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Gastrointestinal disease, Bisphosphonates, Calcitonin, Fluoride, HRT, Corticoids/Glucocorticoids, Alcohol Abuse, Med known to affect skeleton, Hypercalcemia, Hypocalcemia, Contraindication to Ca or Vitamin D, Cyclosporine	NR NR	Not reported
Recker RR et al., 2006[57] Alendronate, Raloxifene US, Canada EVA trial	Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hypoparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Upper GI, Venous thromboembolic disease, Bisphosphonates, Calcitonin, Fluoride, Androgen, Estrogen agonists (including estrogen), Progestin, SERMS, Estrogen antagonists, Anabolic steroids, Testosterone, Vitamin D, Corticoids/Glucocorticoids, any medication that may alter bone and mineral metabolism, Breast Cancer, previous PTH use, vaginal bleeding, age <=50, age > 80, T score<-4.0, fracture T4 to L4	NR NR	Not reported
Reginster JY et al., 2006[58] Ibandronate US, Canada, Latin Amer, UK, Western Europe, Eastern Europe, Australia/NZ, South Africa MOBILE	Metabolic bone disorder other than osteoporosis, Renal insufficiency, Upper GI, Bisphosphonates, Fluoride, age > 80, Contraindication to Ca or Vitamin D	NR NR	Yes

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Reid IR et al., 1994[59] Pamidronate Australia/NZ	Hypothyroidism, Hyperthyroidism, Hepatic insufficiency, Renal insufficiency, Anticonvulsants, Bisphosphonates, Calcitonin, Fluoride, HRT, Anabolic steroids, Corticoids/Glucocorticoids, Major systemic Disease, Hypercalcemia, Hypocalcemia	NR NR	Yes
Reid IR et al., 2002[60] Zoledronic acid Western Europe, Australia	Carcinoma or suspected carcinoma, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hypoparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Bisphosphonates, Fluoride, HRT, Estrogen agonists (including estrogen), >1 Fracture, Vitamin D deficient, Med known to affect skeleton	NR NR	Yes
Reid IR et al., 2004[61] Estrogen, Raloxifene US, Canada, Western Europe, Australia/NZ, South Africa	Hepatic insufficiency, Renal insufficiency, Venous thromboembolic disease - Ever, Anticonvulsants, Bisphosphonates, Calcitonin, Fluoride, Androgen, Estrogen agonists (including estrogen), Progestin, Lipid lowering agents, Vitamin D, Corticoids/Glucocorticoids, age <40, Endocrine disease requiring treatment except thyroid, FSH<40, excessive alcohol intake, >60 years, Breast Cancer, Estrogen Dependent CA, Any cancer except skin in last 5 years, Serious postmenopausal symptoms	NR NR	No
Reid IR et al., 2006[62] Calcium Australia/NZ	Carcinoma or suspected carcinoma, Hypothyroidism, Hyperthyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Bisphosphonates, Calcium (includes antacids), HRT, Anabolic steroids, Corticoids/Glucocorticoids, age <=55, Med known to affect skeleton, Vitamin D deficient	NR NR	Not reported
Ringe JD et al., 2006[63] Risedronate Germany	Renal insufficiency, Bisphosphonates, Fluoride, Hypocalcemia, Drug Hypersensitivity	NR NR	Not reported
Rosen CJ et al., 2005[64] Alendronate, Risedronate US FOSAMAX ACTONEL COMPARISON TRI	Metabolic bone disorder other than osteoporosis, Upper GI, Bisphosphonates, Fluoride, HRT, Estrogen agonists (including estrogen), Anabolic steroids, Corticoids/Glucocorticoids, Immunosuppressants, previous PTH use, Inability to remain 30min upright, Vitamin D deficient	NR NR	Not reported
Sato S et al., 2003[65] Etidronate Japan	Cardiovascular disease, Renal insufficiency, Med known to affect skeleton, LS spine abnormalities prohibiting DEXA	NR NR	Not reported

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Sato Y et al., 2004[66] Etidronate Japan	Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Renal insufficiency, Bisphosphonates, Calcitonin, Estrogen agonists (including estrogen), Vitamin D, Corticoids/Glucocorticoids, nonambulatory, Underlying neurologic disorder, Prior calcium use	NR NR	Not reported
Sato Y et al., 2005[67] Risedronate Japan	Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Upper GI, >1 Fracture, Familial Osteoporosis, Use of any drug known to alter bone metabolism for 3 months or longer during the preceding 12 months	NR NR	Not reported
Sato Y et al., 2005[68] Risedronate Japan	Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Anticonvulsants, Bisphosphonates, Calcitonin, Calcium (includes antacids), Estrogen agonists (including estrogen), Vitamin D, Corticoids/Glucocorticoids, age < 70, treatment with Vitamin K, Familial Osteoporosis	NR NR	Not reported
Sato Y et al., 2005[69] Vitamin D Japan	Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Anticonvulsants, Calcium (includes antacids), Vitamin D, dementia, total disability, hospitalization less than 2yrs, history of previous fracture, Drugs affecting Vitamin D Metabolism, Use of any drug known to alter bone metabolism for 3 months or longer during the preceding 12 months	NR NR	Not reported
Sato Y et al., 2005[70] Risedronate Japan	Cardiovascular disease, Hepatic insufficiency, Renal insufficiency, age <65, Med known to affect skeleton, mental condition that would preclude participation, inability to stand, quadraparesis, artificial nutrition	NR NR	Yes
Sato Y et al., 2005[71] Calcium, Vitamin D Japan	Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Renal insufficiency, Bisphosphonates, Calcitonin, Calcium (includes antacids), Estrogen agonists (including estrogen), Vitamin D, Corticoids/Glucocorticoids, age < 70, treatment with Vitamin K, nonambulatory, Diseases known to affect skeleton, nonvertebral fracture	NR NR	Not reported
Sato Y et al., 2006[72] Alendronate Japan	Cardiovascular disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Bisphosphonates, Calcitonin, Calcium (includes antacids), Estrogen agonists (including estrogen), Vitamin D, Corticoids/Glucocorticoids, treatment with Vitamin K, nonvertebral fracture, Stage 5 Parkinson's	NR NR	Not reported

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Sato Y et al., 2006[73] Etidronate Japan	Med known to affect skeleton	NR NR	Not reported
Sorensen OH et al., 2003[74] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	Age > 85, Bisphosphonates, Calcitonin, Fluoride, Hormone use, Estrogen agonists (including estrogen), Progestin, Anabolic steroids, Vitamin D, LS spine abnormalities prohibiting DEXA, any medication that may alter bone and mineral metabolism, noncompliance	NR NR	Not reported
Tauchmanova L et al., 2006[75] Estrogen, Risedronate, Zoledronic acid Italy	NR	NR NR	Yes
Torres A et al., 2004[76] Calcium, Vitamin D Spain	previous parathyroidectomy	NR NR	Not reported
Toth E et al., 2005[77] Calcitonin Eastern Europe	Carcinoma or suspected carcinoma, Endocrine disease, Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Hypoparathyroidism, Hepatic insufficiency, Metabolic bone disorder other than osteoporosis, Renal insufficiency, Malabsorption syndrome, Upper GI, Anticonvulsants, Bisphosphonates, Anabolic steroids, Vitamin D, Corticoids/Glucocorticoids, treatment with monofluorophosphate, any vertebral deformity, Secondary Osteoporosis, Hypogonadism, any significant lab abnormalities, any medication that may alter bone and mineral metabolism	NR NR	Not reported
Trovas GP et al., 2002[78] Calcitonin Greece	Metabolic bone disorder other than osteoporosis, Secondary Osteoporosis	NR NR	Not reported
Uchida S et al., 2005[79] Alendronate Japan	Bisphosphonates, >1 Fracture	NR NR	Not reported
Ushiroyama T et al., 2001[80] Calcitonin Japan	Metabolic bone disorder other than osteoporosis, Renal insufficiency, Urolithiasis, HRT, Estrogen agonists (including estrogen), Contraceptive	NR NR	Not reported

Author, Year, Drug, Country, Trial name	Exclusion criteria	Run-in/Washout	Class naive patients only?
Vogel VG et al., 2006[81] Raloxifine, Tamoxifen US, Canada STAR P-2	Carcinoma or suspected carcinoma, Diabetes, Venous thromboembolic disease - Ever, Coumarins, Androgen, HRT, Estrogen agonists (including estrogen), Progestin, Estrogen antagonists, Contraceptive, age <35, mental condition that would preclude participation, cholestyramine, Uncontrolled HTN, atrial fibrillation, preformance status restricting activity	NR NR	Not reported
Wimalawansa SJ, 1998[82] Estrogen, Etidronate UK	Metabolic bone disorder other than osteoporosis, Bisphosphonates, Calcitonin, Fluoride, HRT, Anabolic steroids, Corticoids/Glucocorticoids, oopherectomy, Med known to affect skeleton	NR NR	Yes
Zein CO et al., 2005[83] Alendronate US	Hypothyroidism, Hyperthyroidism, Hyperparathyroidism, Renal insufficiency, Upper GI, Anticonvulsants, Calcitonin, Fluoride, Testosterone, Vitamin D, Corticoids/Glucocorticoids, heparin, Med known to affect skeleton, Vitamin D deficient, age >=70, age <18, starting estrogen within one year or discontinuing estrogen in the past	NR NR	Not reported

Author, Year, Drug, Country, Trial name	Control group standard of care?	Funding	Relevance?
Agrawal S et al., 2006[1] Risedronate US	Yes	Source: Industry; Role: described	Limited
Aris RM et al., 2000[2] Pamidronate US	Yes	Source: Government & Private; Role: NR	Limited
Black DM et al., 2007[3] Zoledronic acid US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Asia Horizon	Yes	Source: Industry; Role: described	Yes
Body JJ et al., 2002[4] Alendronate, PTH US, Canada, Latin America, Western Europe, Israel	Yes	Source: Industry; Role: NR	Yes
Bone HG et al., 2000[5] Alendronate, Estrogen US ALENDRONATE ESTROGEN STUDY GRP	No	Source: Industry; Role: NR	Yes
Bonnick S et al., 2006[6] Alendronate, Resindronate US FACT	Yes	Source: Industry; Role: NR	Yes
Boutsen Y et al., 1997[7] Pamidronate Western Europe	No	Source: Not reported	Yes
Brown JP et al., 2002[8] Risedronate US, Canada	Yes	Source: Industry; Role: NR	Yes
Campbell IA et al., 2004[9] Etidronate UK	No	Source: Industry; Role: NR	Yes

Author, Year, Drug, Country, Trial name	Control group standard of care?	Funding	Relevance?
Chapurlat RD et al., 2005[10] [Hip] Alendronate US FIT	Yes	Source: Industry; Role: NR	Yes
Chapurlat RD et al., 2005[10] [Spine] Alendronate US FIT	Yes	Source: Industry; Role: NR	Yes
Chesnut CH et al., 2004[11] Ibandronate US, Canada, UK, Western Europe, Eastern Europe BONE	Yes	Source: Industry; Role: NR	Yes
Coco M et al., 2003[12] Pamidronate US	Yes	Source: Not reported	Yes
Cosman F et al., 2001[13] Estrogen, PTH US	Yes	Source: Government; Role: NR	Yes
Cosman F et al., 2005[14] Alendronate, PTH US	No	Source: Government; Role: described	Yes
Fisher B et al., 1998[15] Tamoxifen US, Canada NSABP-P1	Yes	Source: Government; Role: NR	Yes
Fukunaga M et al., 2002[16] Etidronate, Resindronate Japan RESIDRONATE PHASE III RESEARCH	No	Source: Industry; Role: NR	Yes

Author, Year, Drug, Country, Trial name	Control group standard of care?	Funding	Relevance?
Gallagher JC et al., 2005[17] PTH US, Canada, Latin Amer, Western Europe, Eastern Europe, Australia/NZ, Finland, Denmark, Italy, Israel FRACTURE PREVENTION TRIAL	Yes	Source: Industry; Role: NR	Yes
Garcia-Delgado I et al., 1997[18] Calcitonin, Etidronate Western Europe	Yes	Source: Government; Role: NR	No
Grant AM et al., 2005[19] Vitamin D UK	No	Source: Government & Industry; Role: described	Yes
Greenspan SL et al., 2003[20] Alendronate, Estrogen US	Yes	Source: Government; Role: described	Yes
Greenspan SL et al., 2006[21] Risedronate US	Yes	Source: 11110; Role: described	Yes
Grotz W et al., 2001[22] Ibandronate Germany	No	Source: Not reported	Limited
Guanabens N et al., 2003[23] Alendronate, Etidronate Western Europe	Yes	Source: Government; Role: described	No
Harris ST et al., 2001[24] Estrogen, Resindronate US	Yes	Source: Industry; Role: NR	Yes
Harris ST et al., 2004[25] Risedronate US, Canada	Yes	Source: Industry; Role: NR	Yes

Author, Year, Drug, Country, Trial name	Control group standard of care?	Funding	Relevance?
Hay JE et al., 2001[26] Calcitonin US	Yes	Source: Industry; Role: NR	Yes
Henderson S et al., 2006[27] Risedronate Australia/NZ	Yes	Source: Industry; Role: NR	Yes
Hizmetli S et al., 1998[28] Calcitonin Turkey	Yes	Source: Not reported	Yes
Hochberg MC et al., 2005[29] Alendronate US FIT	Yes	Source: Industry; Role: NR	Yes
Hodsman AB et al., 1997[30] Calcitonin, Raloxifine Canada	No	Source: Government & Industry; Role: NR	Yes
Hooper MJ et al., 2005[31] Risedronate Australia/NZ	No	Source: Industry; Role: NR	Yes
Hosking D et al., 2003[32] Alendronate, Resindronate UK, Western Europe, Brazil	No	Source: Industry; Role: NR	Yes
Ishida Y et al., 2004[33] Calcitonin, Estrogen, Etidronate Japan YAMAGUCHI OP PREVENTION STUDY	No	Source: Not reported	Yes
Iwamoto J et al., 2003[34] Alendronate, Etidronate Japan	No	Source: Not reported	Yes

Author, Year, Drug, Country, Trial name	Control group standard of care?	Funding	Relevance?
Iwamoto J et al., 2003[35] Alendronate, Etidronate Japan	No	Source: Not reported	Yes
Jackson RD et al., 2006[36] Calcium, Vitamin D US WHI	Yes	Source: Government & Industry; Role: described	Yes
Kanaji A et al., 2006[37] Risedronate Japan	Yes	Source: Not reported	Limited
Kananen K et al., 2005[38] Estrogen, Pamidronate, Testosterone Finland	Yes	Source: Hospital, Industry & Private; Role: NR	Limited
Kaufman JM et al., 2005[39] PTH US, Canada, Australia/NZ, Netherlands, Italy, Belgium, France, Spain, Sweden	Yes	Source: Industry; Role: NR	Yes
Kim SH et al., 2004[40] Pamidronate Asia	Yes	Source: Unclear; Role: NR	Limited
Kishimoto H et al., 2006[41] Risedronate Japan	Yes	Source: Industry; Role: NR	Yes
Kushida K et al., 2004[42] Etidronate, Resindronate Japan RESIDRONATE PHASE III RESEARCH III RESEARCH GROUP	Yes	Source: Industry & Private; Role: NR	Yes
Lindsay R et al., 1997[43] Estrogen, PTH US	No	Source: Government & Industry; Role: described	Yes

Author, Year, Drug, Country, Trial name	Control group standard of care?	Funding	Relevance?
Lindsay R et al., 1999[44] Alendronate, Estrogen US	Yes	Source: Industry; Role: NR	Yes
Luckey M et al., 2004[45] Alendronate, Raloxifine US THE EFFECT STUDY	Yes	Source: Industry; Role: NR	Yes
McClung MR et al., 2006[46] Alendronate, AMG162 US	Yes	Source: Industry; Role: described	Yes
Milgrom C et al., 2004[47] Risedronate Israel	Yes	Source: Government & Industry; Role: NR	Limited
Muscoso E et al., 2004[48] Alendronate, Raloxifine, Resindronate Italy	Yes	Source: Not reported	Yes
Ninkovic M et al., 2002[49] Pamidronate UK	No	Source: Not reported	Limited
Orwoll ES et al., 2003[50] PTH 1100101000	Yes	Source: Industry; Role: NR	Yes
Palomba S et al., 2005[51] Risedronate Italy	Yes	Source: Not reported	Yes
Porthouse J et al., 2005[52] Calcium, Vitamin D UK	No	Source: Government & Industry; Role: described	Yes

Author, Year, Drug, Country, Trial name	Control group standard of care?	Funding	Relevance?
Prince RL et al., 2006[53] Calcium Australia/NZ	No	Source: Government; Role: described	Yes
Quandt SA et al., 2005[54] Alendronate US FIT	No	Source: Industry; Role: NR	Yes
Ravn P et al., 1996[55] Ibandronate Western Europe	Yes	Source: Not reported	Yes
Recker R et al., 2004[56] Ibandronate US, Western Europe	Yes	Source: Industry; Role: NR	Yes
Recker RR et al., 2006[57] Alendronate, Raloxifine US, Canada EVA trial	Yes	Source: Industry; Role: described	Yes
Reginster JY et al., 2006[58] Ibandronate US, Canada, Latin Amer, UK, Western Europe, Eastern Europe, Australia/NZ, South Africa MOBILE	Yes	Source: Industry; Role: NR	Yes
Reid IR et al., 1994[59] Pamidronate Australia/NZ	No	Source: Government, Industry & Private; Role: NR	Yes
Reid IR et al., 2002[60] Zoledronic acid Western Europe, Australia	No	Source: Industry; Role: described	Yes
Reid IR et al., 2004[61] Estrogen, Raloxifine US, Canada, Western Europe, Australia/NZ, South Africa	No	Source: Industry; Role: NR	Yes

Author, Year, Drug, Country, Trial name	Control group standard of care?	Funding	Relevance?
Reid IR et al., 2006[62] Calcium Australia/NZ	Yes	Source: Unclear; Role: NR	Yes
Ringe JD et al., 2006[63] Risedronate Germany	Yes	Source: Not reported	Yes
Rosen CJ et al., 2005[64] Alendronate, Resindronate US FOSAMAX ACTONEL COMPARISON TRI	Yes	Source: Industry; Role: NR	Yes
Sato S et al., 2003[65] Etidronate Japan	Yes	Source: Not reported	Yes
Sato Y et al., 2004[66] Etidronate Japan	No	Source: Not reported	Limited
Sato Y et al., 2005[67] Risedronate Japan	No	Source: Not reported	Yes
Sato Y et al., 2005[68] Risedronate Japan	Yes	Source: Not reported	Yes
Sato Y et al., 2005[69] Vitamin D Japan	No	Source: Not reported	Yes
Sato Y et al., 2005[70] Risedronate Japan	No	Source: Not reported	Yes

Author, Year, Drug, Country, Trial name	Control group standard of care?	Funding	Relevance?
Sato Y et al., 2005[71] Calcium, Vitamin D Japan	No	Source: Not reported	Yes
Sato Y et al., 2006[72] Alendronate Japan	No	Source: Not reported	Yes
Sato Y et al., 2006[73] Etidronate Japan	Yes	Source: Not reported	Yes
Sorensen OH et al., 2003[74] Risedronate UK, Western Europe, Eastern Europe, Australia/NZ VERT	Yes	Source: Industry; Role: NR	Yes
Tauchmanova L et al., 2006[75] Estrogen, Resindronate, Zoledronic acid Italy	Yes	Source: Government; Role: NR	Yes
Torres A et al., 2004[76] Calcium, Vitamin D Spain	Yes	Source: Government; Role: NR	Yes
Toth E et al., 2005[77] Calcitonin Eastern Europe	No	Source: Not reported	Yes
Trovas GP et al., 2002[78] Calcitonin Greece	No	Source: Industry; Role: NR	Yes
Uchida S et al., 2005[79] Alendronate Japan	Yes	Source: Not reported	Yes

Author, Year, Drug, Country, Trial name	Control group standard of care?	Funding	Relevance?
Ushiroyama T et al., 2001[80] Calcitonin Japan	No	Source: Not reported	Yes
Vogel VG et al., 2006[81] Raloxifine, Tamoxifen US, Canada STAR P-2	Yes	Source: Government & Industry; Role: described	Yes
Wimalawansa SJ, 1998[82] Estrogen, Etidronate UK	Yes	Source: Not reported	Yes
Zein CO et al., 2005[83] Alendronate US	Yes	Source: Industry; Role: NR	Yes

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once daily in Japanese patients with osteoporosis: a double-blind, randomized study. J Bone Miner Metab 2005;23(5):382-8.

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Author, Year	(1) Aims	(2) Time period covered
Torgerson, 2001[1]	Determine if HRT reduced vertebral fractures	All trials until end of August 2001
Crannery, 2001[2]	Review the effect of etidronate on bone density & fractures in post menopausal women.	1966-1998
Wells, 2002[3]	Review the effects of HRT on bone density and fractures in postmenopausal women.	1966-1999
Cranney, 2002[4]	Review the effects of risedronate on bone density & #'s in post menopausal women	1966 to the end of 2000
Cranney, 2002[5]	Review the effect of alendronate on bone density and fractures in post menopausal women.	1980-1999
Cranney, 2002[6]	Review the effect of calcitonin on bone density and fractures in postmenopausal women	1966-2000
Karpf, 1997[7]	To evaluate the effect of treatment with alendronate sodium, on the incidence of nonvertebral fractures in postmenopausal women with osteoporosis	All completed prospective, randomized, placebo-controlled alendronate trails of at least two years duration
Papapoulos, 2004[8]	Assess consistency of the effect of alendronate in reducing the risk of hip fractures among different studies & populations.	All randomized clinical trials w/ alendronate
Cranney, 2000[9]	Review the efficacy of calcitonin (subcutaneous or nasal) for the treatment & prevention of corticosteroid induced osteoporosis	Up to May 1998
Cranney, 2003[10]	Review efficiency of risedronate on bone density and fracture reduction in postmenopausal women.	1990-2001
Cranney, 2001[11]	Review the efficacy of etidronate therapy in the prevention and treatment of postmenopausal osteoporosis	1966-1998
Farquhar, 2005[12]	To assess the effect of long-term hormone therapy on mortality, heart disease, venous thromboembolism, stroke, transient ischemic attacks, breast cancer, colorectal cancer, ovarian cancer, endometrial cancer, gallbladder disease, cognitive function, dementia, fractures, and quality of life	Up to 2004
Stevenson, 2005[13]	To establish the clinical effectiveness and cost-effectiveness of alendronate, etidronate, risedronate, raloxifine, or teriparatide for the prevention and treatment of osteoporosis and the prevention of osteoporotic fractures in postmenopausal women.	Up to 2002
Boonen, 2005[14]	To compare the effects of alendronate, risedronate, raloxifene, strontium, ibandronate, and calcitonin on the risk of nonvertebral fractures in intention-to-treat studies of at least 3 years duration	1966 to March 2004
Nguyen, 2006[15]	To quantitatively assess the effects of bisphosphonates on hip fracture	1966 to March 2004
Sawka, 2005[16]	To assess the efficacy of alendronate for fracture prevention in men with osteoporosis	Up to May 2004
Miller, 2005[17]	To assess the safety and efficacy of risedronate in patients with reduced renal function	Trials conducted 1993-1998

Author, Year	(1) Aims	(2) Time period covered
Palmer, 2006[18]	To assess the efficacy of agents for prevention of bone disease in kidney transplant patients	1966 to August 2004
Seeman, 2006[19]	To assess the efficacy of raloxifene for prevention of vertebral fractures among postmenopausal women	1966 to February 2005
Richy, 2004[20]	To assess the efficacy of two different vitamin D analogs in preserving bone mineral density and decreasing fracture rate in patients with primary or GC-induced osteoporosis	Jan 1985-July 2002
Richy, 2005[21]	To assess the efficacy of vitamin D analogs and native vitamin D for prevention of bone loss and fractures in patients with osteoporosis	1985-2003
de Nijs, 2004[22]	To assess the effect of active vitamin D analogs on prevention and treatment of GC-induced osteoporosis and to compare with bisphosphonates	1966-2003
Blair 2000[23]	To review the use of bisphosphonates in the prevention and treatment of GC-induced OP	Not specified
Wallach 2000[24]	To examine the effects of risedronate treatment on GC-induced OP by combining the results of two RCTs	Not specified or relevant
Watts, 2003[25]	To assess the efficacy of risedronate in preventing new vertebral fractures in high-risk postmenopausal women	Not specified or relevant
Torgerson, 2001[26]	To determine if HRT reduced nonvertebral fractures.	RCTs. 1997-2000 plus older systematic reviews.

Author, Year	(3) Eligibility criteria	(4) Number of patients	(5) Characteristics of identified articles: Study designs
Torgerson, 2001[1]	(1) RCT of HRT where women had been randomized to at least 12 mon. of HRT or to no HRT.	6,723	13 RCTs
Crannery, 2001[2]	(1) RCTs of at least 1yr duration comparing etidronate therapy with placebo or with calcium and/or vitamin D, 2)outcomes included fracture incidence or bone density and 3)participants were postmenopausal women	1,267	13 RCTs; all published and unpublished RCTs
Wells, 2002[3]	(1) RCT in postmenopausal women that compared an HRT intervention (estrogen used alone or estrogen opposed by progestin) with a placebo (2)HRT could be given in conjunction with a calcium and vitamin D, provided the other group received the same (3)results had to be reported with a follow up of at least one year on one or more of the outcomes of interest (4) both prevention and rx trials were accepted (rx referring to studies that included women w/ prevalent #'s at baseline)	9,958	57 RCTs
Cranney, 2002[4]	(1) Randomized, placebo-controlled trials of risedronate for osteoporosis in postmenopausal women defined as greater than 6 months postmenopausal); 2)follow up of at least one year; and 3)fracture incidence or bone mineral density data available	14,832	8 RCTs
Cranney, 2002[5]	(1) RCTs comparing postmenopausal women receiving alendronate to those not receiving alendronate with follow up of at least 1 year; and 2)fracture incidence, or bmd data	12,855	11 RCTs
Cranney, 2002[6]	(1) RCTs of at least 1-yr duration, comparing calcitonin therapy vs. placebo or calcium and/or vitamin D; 2)outcomes included bmd or fracture incidence; and 3)participants were postmenopausal women	3,993	30 RCTs
Karpf, 1997[7]	All postmenopausal women randomized to treatment with placebo or alendronate at a dose higher than 1mg per day for at least 2 year that evaluated the efficacy of treatment	1,602	5 RCTs
Papapoulos, 2004[8]	Aimed to included all RCT with alendronate in postmenopausal women with a t-score of 2.0 or less, or w/ a vertebral # in which there were sufficient data to evaluate the relative risk; specifically there was at least one patient in each treatment group that experienced a hip fracture	9,023	6 RCTs; one study listed as active-control, rest were placebo control
Cranney, 2000[9]	RCT that used calcitonin for the prevention or treatment of steroid induced osteoporosis; men or women over age 18 with any underlying disease requiring therapy with steroids; randomized allocation of patients into treatment groups; adequate description of the intervention medications in terms of dosage scheduling and administration	441	9 RCTs
Cranney, 2003[10]	Randomized women to risedronate or an alternative (placebo or calcium and/or vit d. D) and measured bmd for at least 1yr)	14,500	8 RCTs
Cranney, 2001[11]	Trials that randomized postmenopausal women to etidronate or an alternative (placebo or calcium and /or vitamin D) and measured bone density for at least 1 year	1,010	13 RCTs

Author, Year	(3) Eligibility criteria	(4) Number of patients	(5) Characteristics of identified articles: Study designs
Farquhar, 2005[12]	Randomized double blind trials of hormone therapy (estrogens with or without progestogens) versus placebo, taken for at least one year by perimenopausal or postmenopausal women	35,089	15 RCTs
Stevenson, 2005[13]	Interventions- bisphosphonates: alendronate, etidronate and risedronate- serms: raloxifene- teriparatide [recombinant human pth (1-34)]• comparators- vitamin D- calcitriol (a vitamin 1 alph-hydroxylated derivative)- pharmacological doses of calcium- estrogens (opposed and unopposed)- exercise- placebo-no treatment• Outcome measures: vertebral or non-vertebral fracture, associated effects, quality of life related to the study intervention, continuance and compliance.• Study design: RCTs; trials were accepted as RCTs if the allocation of subjects to treatment groups was described by the authors as either randomized or double-blind.	Not tabulated	90 RCTs
Boonen, 2005[14]	Phase III RCTs of osteoporosis treatments of at least 3 years duration that measured radiographically confirmed nonvertebral fractures in intention to treat populations measuring incidence of new fractures by individual patient; Interventions: Bisphosphonates: alendronate, risedronate, ibandronate; SERM: raloxifene; Other: strontium, calcitonin, placebo; Outcome measure: radiographically verified nonvertebral fracture; Meta-analysis performed only on alendronate and risedronate trials	35,984	11 RCTs, 3 each for alendronate and risedronate
Nguyen, 2006[15]	RCTs of the following interventions: Alendronate, etidronate, risedronate, clodronate, placebo; Outcomes measured: BMD change, hip fracture incidence	18,667	12 RCTs: 6 for alendronate, 2 etidronate, 3 risedronate, 1 clodronate
Sawka, 2005[16]	RCTs and CCTs comparing alendronate to calcium and/or vitamin D or no treatment and enrolling at least 50% men	375	2 RCTs
Miller, 2005[17]	Phase III RCTs comparing daily administration of risedronate to placebo for the treatment of patients with osteoporosis, excluding one trial that administered estrogen with risedronate and one that focused on Pagets	8,996	9 RCTs
Palmer, 2006[18]	RCTs and quasi-RCTs with predictable treatment allocation method assessing options for bone disease treatment (actually prevention) following kidney transplantation	1,209	23 trials (2 for calcitonin)
Seeman, 2006[19]	RCTs at least 1 year in duration, with radiographically verifiable vertebral fracture data at baseline and subsequently	8,282	5 trials
Richy, 2004[20]	RCTs of alphacalcidol or calcitriol with at least 6 months follow-up	1,918	13 RCTs
Richy, 2005[21]	RCTs of at least 6 months duration	13,102	21 RCTs

Author, Year	(3) Eligibility criteria	(4) Number of patients	(5) Characteristics of identified articles: Study designs
de Nijs, 2004[22]	RCTs, randomized open-label studies, 1 non-randomized open label study		1 RCT, 3 open-label randomized trials, 1 open-label non-randomized trial
Blair 2000[23]	RCTs of adults using bisphosphonates in which central DEXA used to measure BMD	1,711	13 RCTs
Wallach 2000[24]	Two RCTs of adults 18-85 yrs, receiving moderate to high doses of GC therapy, and expecting to be on GC for at least a year		2 RCTs
Watts, 2003[25]	Two parallel RCTs of postmenopausal osteoporotic women treated with risedronate: VERT MN and VERT NA		2 RCTs
Torgerson, 2001[26]	RCT of HRT ≥ 12 months, including unblinded trials.	8,774	22 RCTs

Author, Year	(6) Characteristics of identified articles: Populations	(7) Characteristics of identified articles: Interventions
Torgerson, 2001[1]	Postmenopausal women	Estrogens (transdermal estradiol-.1mg,50ug; oral estradiol-1mg,2mg; oral conjugated estrogens-.625mg,.3mg)
Crannery, 2001[2]	Postmenopausal women	Intermittent cyclical method of administration of etidronate at 400mg per day for 14-20 days followed by 56-91 days of calcium and/or vitamin D; duration 1-3 years
Wells, 2002[3]	Postmenopausal women	HRT preparations (estrogen-progestin preparation were diverse) ;1-5 years duration
Cranney, 2002[4]	Postmenopausal women (defined as greater than 6 mon. post menopausal)	Risedronate 2.5mg; risedronate 5.0mg; duration 1-3 years
Cranney, 2002[5]	Postmenopausal women	Alendronate 1mg-40mg; duration 1-4yrs
Cranney, 2002[6]	Postmenopausal women	Calcitonin 40iu-400iu; salmon calcitonin; esl calcitonin; duration 1-5yrs; 1m, intranasal, suppository
Karpf, 1997[7]	Women with osteoporosis between ages of 42 & 85 years, postmenopausal at least four years, with lumbar spine bone mineral density at least 2.0 sd below the mean for young adult woman; all received 500mg of ca and were screened for vit d deficiency	Alendronate dose higher than 1mg per day for at least 2yrs;alendronate; 1mg, 2.5mg, 5mg, 10mg, 20/0mg, 20/5 mg, 40/0mg, 40/2.5mg; all received calcium 500mg and were screened for vitamin D deficiency
Papapoulos, 2004[8]	Postmenopausal women w/a t score of less than equal to 2.0, or w/a vertebral #	Alendronate 5-20mg/day; duration of studies 1-4.5years
Cranney, 2000[9]	Men or woman over age of 18, with any underlying disease that requires therapy with systematic steroids	Calcitonin; intranasal 100iu, 200iu, 400iu, 50iu, 100iu; control groups received placebo or were untreated; ca+vitd were accepted in control group if they were also given in equal doses to the treated group
Cranney, 2003[10]	Postmenopausal women - 2 major groups of women included were those with mild bone less (prevention) or those with more severe bone less as defined by a t score <-2.0 sd or prevalent vertebral facture (treatment)	Risedronate dosages included 2.5mg cyclical, 2.5 mg/d, 5mg cyclical, & 5mg/d for durations of at least one year
Cranney, 2001[11]	Postmenopausal women	Intermittent cyclic method of administration of etidronate at 400mg per day for 14-20 days followed by calcium and/or vitamin D

Author, Year	(6) Characteristics of identified articles: Populations	(7) Characteristics of identified articles: Interventions
Farquhar, 2005[12]	Perimenopausal (women with spontaneous menopause who had menstruated irregularly within the last 12 months) and postmenopausal (surgical menopause or women with spontaneous menopause and amenorrhea for more than 12 months) women recruited from any health	All estrogens with or without progestins, administered by oral, transdermal, subcutaneous, or intranasal routes; trials lasted 1 to 10 years
Stevenson, 2005[13]	Women with primary osteoporosis who were at least 6 months postmenopausal	Dosages: 1. alendronate-1-40 mg per day 2. etidronate- 200 and 400 mg per day 3. risedronate-2.5 and 5 mg per day 4. raloxifine-60 and 120 mg 5. teriparatide-20,25 and 40 ug per day duration: maximum total length of treatment with teriparatide should be 18 months; the length of treatment with the other interventions is not specified
Boonen, 2005[14]	Gender not specified, average age 69 yrs	Not described
Nguyen, 2006[15]	Women with postmenopausal osteoporosis or low BMD	Dosages: 1. Cycles of Etidronate 400 mg/dx2 wks, no drug x13 wks x 10 cycles; 2. Etidronate 400mg/d x 14d, Ca only for 74 d; 3. Alendronate: 5, 10, 20 mg/dx2 years or 20mg/d followed by 5 mg/d; 4, 5. Alendronate 5 mg/dx2years followed by 10 mg/d; 6. Alend
Sawka, 2005[16]	Men with LBD or with a history of prevalent fractures due to hypogonadism, as defined by T-score	Dosages: 1. Alendronate 10 mg +500 mg Ca+400-450 IU Vitamin D vs. Ca + Vit D x 2 yrs; 2. Alendronate 10 mg+ 500 mg Ca vs. Ca + 1 mcg alfacalcidiol x 3 yrs
Miller, 2005[17]	Patients with postmenopausal or glucocorticoid-induced osteoporosis and renal impairment (91%)	Dosage: 5 mg/d risedronate
Palmer, 2006[18]	Kidney transplant recipients	1. Calcitonin intranasal 100 IU bd + Ca x 14 days followed by 75 days w/out treatment; 2. calcitonin 200 IU/d x 12 mos; remaining trials tested various bisphosphonates and Vitamin D but none included in a meta-analysis
Seeman, 2006[19]	Postmenopausal women with or at risk for osteoporosis	1 and 2. 60 or 120 mg/d raloxifene x 3 yrs; 3. 60 or 150 mg/d x 3 years; 4 and 5. 60 or 120 mg/d x 1 yr
Richy, 2004[20]	Men or women with primary osteoporosis or individuals with glucocorticoid-induced osteoporosis	Calcitriol: 0.5-1 mcg/d + 0-1g Ca/d; Alphacalcidol: 0.5-1.0 mcg/d + 0-1 g Ca/d; Duration: 6-36 mos
Richy, 2005[21]	Pre- or postmenopausal women or men age 50 and over or patients with a condition requiring GC at a dose equivalent of greater than 10 mEq prednisone/d	Native vitamin D: 300-7142 IU/d; alfacalcidol: 0.5-1.0 mcg/d; 0.25-0.62 mcg calcitriol/d; Duration: 6-36 mos.

Author, Year	(6) Characteristics of identified articles: Populations	(7) Characteristics of identified articles: Interventions
de Nijs, 2004[22]	Adults taking glucocorticoids	Alfacalcidol 1mcg/d vs. etidronate 400mg/d; calcitriol 0.25-0.5 mcg/d vs. pamidronate IV 0.5 mg/kg every 3 mos.; calcitriol 0.5 mcg/d vs. etidronate 400 mg/d; alfacalcidol 1 mcg/d vs. Ibandronate IV 2 mg every 3rd mo.; calcitriol 0.5-0.75mcg/d vs. alendro
Blair 2000[23]	Adults using bisphosphonates	Alendronate: 5-10 mg/d with 500-1000 mg Ca and 250-500 mcg/d vit D, 1 year; Clondronate: 800, 1600, 2400 mg/d x 1 yr; Etidronate: cyclical 400mg/dx2 weeks then 500 mg Ca/d or 97 mg Ca + 400 mcg/d vit D x11-13 weeks x 1-2yr Risedronate: 2.5-5 mg/d alone or
Wallach 2000[24]	Adults 18-85 yrs, receiving moderate to high doses of GC therapy for a variety of conditions; in North America, participants had to have been on GC 3 months or less; in Europe, participants had to have been on GC for at least 6 mos.	2.5-5 mg/d risedronate x 12 months or placebo. Prevention study: all pts received 500 mg Ca/d; in the Treatment study, all patients received 1000mg Ca/d and 400 IU vitamin D/d.
Watts, 2003[25]	Postmenopausal women (at least 5 years PM) 85 yrs or younger, with two or more radiographically confirmed vertebral fractures or one vertebral fracture ad low lumbar spine BMD or BMD of =0.94 g/cm2 (T score=-2)	2.5-5 mg/d risedronate or placebo; all patients received 1000mg Ca/d and up to 500 IU vitamin D/d if baseline serum vitamin D<40 nmol/l.
Torgerson, 2001[26]	Women--post menopausal or hysterectomy.	Estrogens (transdermal estradiol-.1mg,50ug; oral estradiol-1mg,2mg; oral conjugated estrogens-.625mg,.3mg)

Author, Year	(8) Main results	(9) Subgroups
Torgerson, 2001[1]	HRT use is associated with reduction in vertebral fractures, particularly among osteoporotic women.	None
Crannery, 2001[2]	Beneficial effect of etidronate on reducing vertebral fractures with an associated increase in lumbar spine bone density; data suggested a reduction in vertebral fractures with a pooled relative risk of 0.63 (95% CI 0.44 to 0.92); there was no effect on nonvertebral fractures (relative risk 0.99 (95% CI 0.69 to 1.42).	None
Wells, 2002[3]	Data shows a nonsignificant trend toward a reduced incidence in vertebral and nonvertebral fractures; HRT has a consistent, favorable and large effect on bone density at all sites.	
Cranney, 2002[4]	The 5mg daily dose of risedronate tended to show a larger impact on bone density than did the 2.5mg dose or cyclic administration ; longer duration of therapy produced larger effects; risedronate produces a substantial reduction of vertebral and nonvertebral fractures; the pooled relative risk for vertebral fractures in women given 2.5mg or more was 0.64 (95% CI 0.54 to 0.77); the pooled rr of nonvertebral fractures in patients given 2.5mg or more was 0.73 (95% CI 0.61 to 0.87)	
Cranney, 2002[5]	Alendronate increases bone density in both early post menopausal and those with established osteoporosis while reducing the rate of vertebral fracture over 2-3 years of treatment; the pooled relative risk for vertebral fractures in patients given 5mg or more of alendronate was 0.52 (95%ci,0.43-0.65); the rr of nonvertebral fractures in patients given 10 mg or more was 0.51 (95% CI 0.38-0.69)	
Cranney, 2002[6]	Calcitonin likely increases bone density in postmenopausal women predominantly at the lumbar spine and forearm for weekly doses greater than 250 iu, although the true effect may be smaller than the pooled estimate would suggest; calcitonin likely reduces the risk of vertebral fractures; its effect on nonvertebral fractures remains uncertain	
Karpf, 1997[7]	In postmenopausal women with osteoporosis, treatment with alendronate reduces the risk of nonvertebral fractures over at least 3 years; the estimated cumulative of nonvertebral fractures after 3 years was 12.6%in the placebo group and 9.0% in the alendronate group; the relative risk for nonvertebral fractures estimated using cox model was 0.71(95% CI, 0.502-0.997)(p=.048)	

Author, Year	(8) Main results	(9) Subgroups
Papapoulos, 2004[8]	Therapy with alendronate is associated with significant and clinically important reductions in the incidence of hip fractures in women with postmenopausal osteoporosis.	In patients with a t-score of less than or equal to -2.0, or with a vertebral fracture, the effect of hip fracture risk consistently favored patients receiving alendronate therapy, with an overall reduction in risk of hip fracture of 45% (95% CI 16% to 64%, p=0.007); for patients who met the criteria of osteoporosis as defined by the who, the overall risk reduction was 55% (95% CI 29% to 72%, p=0.0008).
Cranney, 2000[9]	Calcitonin has not yet demonstrated effectiveness at preventing fractures with steroid induced osteoporosis; calcitonin appears to prevent bone loss at the lumbar spine by about 3% in the first year; effect on bone density is greater in patients taking corticosteroids for more than 3 months; no consistent effect of different dosages; subcutaneous calcitonin showed greater prevention of bone loss (may be due to greater bioavailability of drug)	
Cranney, 2003[10]	There is good evidence for the efficacy of risedronate in the reduction of both vertebral and non vertebral fractures; risedronate is able to achieve this without increasing risk for overall withdrawals due to adverse effects.	Vertebral fractures: 1.prevention population - the relative risk was 2.43 (95% CI 0.12-49.43) 2. treatment population-estimate of rr using random effects model was 0.63 (95% CI 0.52-0.77);p<0.01. nonvertebral fracture: 1.prevention population-rr was 0.48 (95% CI 0.10-2.26) 2.treatment population -pooled estimate of rr was 0.73(95% CI 0.61-0.88);p<0.01
Cranney, 2001[11]	Data suggested a reduction in vertebral fractures with a pooled relative risk of 0.60% (95% CI 0.41-0.88); there was no effect on nonvertebral fractures; etidronate increases bone density at the lumbar spine and the femoral neck ; effects were larger at 4 years, though the numbers of patients followed was much smaller.	The treatment effect of etidronate was consistent across subgroups: prevention(rr:0.61) vs. treatment(rr:0.59)
Farquhar, 2005[12]	Hormone therapy offered the benefit of a significant reduction in the risk of fracture (no greater in women at high risk of fractures) but only after 4 or 5 years of treatment.	

Author, Year	(8) Main results	(9) Subgroups
Stevenson, 2005[13]	Of the five interventions, only raloxifene appeared to reduce the risk of vertebral fracture in postmenopausal women unselected for low bone mineral density (bmd). However, as the full data have not been made public, there is some uncertainty regarding this result. None of the five interventions has been shown to reduce the risk of non-vertebral fracture in women unselected for low bmd. All of the proposed interventions provided gains in qalys compared with no treatment in women with sufficient calcium and vitamin D intakes. The size of the qaly gain for each intervention was strongly related to the age of the patient. the estimated costs varied widely for the interventions. these net costs were markedly different by age, with some interventions becoming cost-saving at higher age ranges in patients with a prior fracture.	
Boonen, 2005[14]	Significant reductions in NVF found in only three trials: two of risedronate and one of strontium. However analysis of the pooled data for alendronate and risedronate showed significant reductions in the RR for NVF for both	
Nguyen, 2006[15]	Only two trials showed significant treatment effect: one for alendronate and 1 for risedronate; no pooled trials for a single drug showed significant effect; pooling of all studies showed significant effect. Alendronate appeared most effective of the 4 drugs.	
Sawka, 2005[16]	Significant reductions in risk (OR) for vertebral fractures but data insufficient to determine effect on nonvertebral fractures.	
Miller, 2005[17]	Incidence of adverse events was similar within and between treatment groups. Most common urinary- and renal-function related event was urinary tract infection. Mean serum creatine did not differ from placebo. Changes in serum Ca and P were not considered clinically meaningful. Mean % increase in LS, femoral neck, and trochanter BMD greater in risedronate group. Incidence of new vertebral fractures was significantly lower in the risedronate group.	Mild (48%), moderate (45%), severe renal impairment (7%): No between-subgroup differences were seen except incidence of new fractures in the placebo group increased with severity of renal impairment
Palmer, 2006[18]	Calcitonin had no significant effect on fracture risk; calcitonin significantly improved LS BMD but not FN BMD (via DXA).	
Seeman, 2006[19]	Raloxifene at all 3 doses consistently reduced the risk of vertebral fracture.	Raloxifene at 120 or 150 mg/d resulted in a slightly greater reduction in risk than raloxifene at 60 mg/d.

Author, Year	(8) Main results	(9) Subgroups
Richy, 2004[20]	Both analogs reduced the risk of overall fracture rate, vertebral fracture rate, and nonvertebral fracture rate. Calcitriol had similar efficacy to alphacalcidol but no study tested them head to head.	CS-induced vs. primary osteoporosis: Prevention of fracture in patients with GC-induced osteoporosis did not reach significance; high vs low quality studies showed similar decreases in risk; non vertebral fractures showed a similar decrease in risk to vertebral fractures; women and men showed similar decreases in risk
Richy, 2005[21]	Findings were expressed as fracture rate difference (RD); In patients with primary osteoporosis, native vitamin D and both analogs showed a significant RD compared with placebo at 24 and 36 mos. RD for analogues was significantly greater than for native vitamin D but there were no head-to-head comparisons.	In patients with GC-induced osteoporosis, no significant fracture prevention was seen with native vitamin D or analogs; however, a single head-to-head comparison of alfacalcidol and native vitamin D showed a significant RD in favor of alfacalcidol
de Nijs, 2004[22]	Active vitamin D metabolites were less effective in reducing risk for vertebral fractures than bisphosphonates.	
Blair 2000[23]	10 of 13 studies showed increased lumbar spine BMD but few studies showed positive effects on the femoral neck or femoral trochanter. 9 studies addressed fracture risk; only 1 study found a significant improvement in vertebral fracture risk	Six studies addressed possible differences in effects based on sex and menopausal status: Postmenopausal women seemed to derive greater benefit from treatment.

Author, Year	(8) Main results	(9) Subgroups
Wallach 2000[24]	Outcomes included DXA-assessed lumbar spine, femoral neck, femoral trochanter, distal radius, and midshaft radius BMD (baseline, 6, and 12 mos.); serum bone-specific alkaline phosphatase and bone resorption adjusted for creatine excretion; radiographic evidence of vertebral fracture. Risedronate 5mg/d increased mean LS BMD from baseline (placebo group decreased from baseline) and either increased or maintained BMD at all other sites (compared with a decrease in placebo groups). Difference in BMD between treated and placebo group was significant at all sites. 5 mg risedronate also reduced vertebral fracture by a significant 70% cf. placebo.	Risedronate was efficacious in both men and women, irrespective of underlying disease or duration of CS therapy.
Watts, 2003[25]	Risk of new vertebral fractures in the 5mg/d group decreased 62% at 1 year in the pooled cohorts (RR 0.38; 95% CI 0.25, 0.56); 61% in VERT-MN and 65% in VERT-NA; risedronate also reduced incidence of multiple new vertebral fractures (3.1% in controls vs. 0.3% in 5 mg treated;90% decrease in risk; rr, 0.10, 95% CI, 0.04, 0.26)	Similar decreases in new fracture risk were seen in women under 70 (7% vs. 2.6%, or 64% reduction (rr, 0.36, 95% CI 0.19, 0.68) and women over 70 (10.8% vs. 4.4%, or 62% reduction (rr, 0.38, 95% CI 0.23, 0.64). Risedronate also decreased the fracture risk in women with at least two existing fractures at baseline (12% vs. 4.1%, or 68% reduction; rr, 0.32; 95%CI, 0.20, 0.49) and in women with low BMD in the femoral neck (12.8% vs. 5.6% or 60% reduction; rr, 0.40, 95% CI, 0.23, 0.67) and women with low lumbar spine BMD (6.9% vs. 3.7% or 48% reduction, rr, 0.52, 95% CI, 0.29, 0.93).
Torgerson, 2001[26]	HRT associated with reduction in all nonvertebral fractures (RR 0.73, 95% CI 0.56-0.94)	HRT was more effective in trials of women under age 60 (RR 0.67, 95% CI 0.46-0.98) than in trials of women age 60 and above (RR 0.88, 95% CI 0.71-1.08)

Author, Year	(10) Adverse events	(11) Comments
Torgerson, 2001[1]	Not reported	
Crannery, 2001[2]	Not reported	
Wells, 2002[3]	Not reported	
Cranney, 2002[4]	Treatment had little or no impact on the risk of discontinuing medication (rr 0.94; 95% CI 0.80, 1.10); for discontinuation due to gastrointestinal side effects, the pooled rr was 0.97 (95% CI 0.90, 1.04);the pooled rr for dyspepsia and abdominal pain were similar; for esophagitis, the pooled rr from 5 trials was 0.91(95% CI 0.70,1.18)	The serious methodological limitation of these studies is the consistently very high loss to follow up
Cranney, 2002[5]	The relative risk for discontinuing alendronate (5mg or greater) due to adverse effects was 1.15 (95% CI 0.93-1.42); the pooled rr for discontinuing medication due to gastrointestinal side effects for 5mg or grater was 1.03(0.81-1.30, p=0.83) and the pooled rr for gastrointestinal adverse effects with continuation of medication was 1.03 (0.98-1.07) p=0.23	The major methodological limitation was the loss to follow up; another limitation is the length of follow up, 4years or less in all studies to date
Cranney, 2002[6]	According to the authors in general the trials were poor in their reporting of adverse events	Large loss to follow up, particularly in the proof trials
Karpf, 1997[7]	Not reported	A limitation was that nonvertebral fractures were self reported ; however, all fractures were confirmed by radiography or by physician examination, and self report has been shown to be accurate for most nonvertebral fracture; another possible criticism in the individual studies is that nonvertebral fractures were captured as safety end points, as opposed to efficacy end points
Papapoulos, 2004[8]	Not reported	Limitations: 1.primarily Caucasian women only 2.not all studies can be classified as fracture studies and thus the question arises whether all the trials should be weighted equally
Cranney, 2000[9]	Flushing rashes & nausea- these were increased in calcitonin group relative to control group	All trials had small sample sizes (less than 40 per group);
Cranney, 2003[10]		
Cranney, 2001[11]	The pooled estimate showed no statistical difference between placebo and etidronate for the risk of withdrawal overall (rr:0.89, 95% ci:0.71-1.13), with consistency across studies; drop out due to side effects (rr:1.51(0.69 to 3.32), consistent across studies	

Author, Year	(10) Adverse events	(11) Comments
Farquhar, 2005[12]	Studies included a range of adverse effects doubling or tripling of the risk of thromboembolic events, a large increase in endometrial cancer risk in women taking estrogen without progestogen, an increased incidence of gallbladder disease and a possible link between hormone therapy and breast cancer, significantly increased incidence of stroke; significantly increased risk of coronary events and venous thromboembolism, with the increased risk becoming evident during the first year of use	The authors state that hormone therapy should only be considered for the prevention of fractures if other treatments are contraindicated and if the cardiovascular risks are low (the benefits of hormone therapy will generally be outweighed by the ongoing and cumulative risk of cardiovascular disease or breast cancer)
Stevenson, 2005[13]	Alendronate : one third of alendronate users reported gastrointestinal adverse events etidronate : has been associated with gastrointestinal adverse events risedronate : overall distribution of adverse events and of adverse upper gastrointestinal events, was comparable in the intervention and placebo groups raloxifene : three fold increase risk of venous thromboembolism ; higher incidence of hot flashes; arthalgia, dizziness, leg cramps, influenza like syndrome, endometrial cavity fluid, peripheral edema, and worsening of diabetes are more common teriparatide : nausea, headache mild discomfort at injection site	
Boonen, 2005[14]	Not examined	Excluded studies shorter than 3 years or that did not carry out ITT analysis, stating that such studies were not valid
Nguyen, 2006[15]	Not examined	Study examined fracture cases as per 1000 patients at risk rather than as patient years at risk
Sawka, 2005[16]	Not examined	Results of the male trials were pooled using Bayesian random effx models incorporating prior information of antifracture efficacy from meta-analyses of women; Pooled results reported as Odds Ratios.
Miller, 2005[17]	Primary purpose of analysis was to evaluate safety, as defined by incidence of overall, urinary-, and renal-function-related, specific renal-function related adverse events, and change from baseline in serum creatinine, calcium, and phosphorus. No differences were seen in safety between placebo and risedronate; no subgroup differences.	Renal impairment defined as estimated creatinine clearance less than 80 ml/min
Palmer, 2006[18]	Calcitonin did not increase risk for all-cause mortality or graft loss and did not affect plasma creatinine	

Author, Year	(10) Adverse events	(11) Comments
Seeman, 2006[19]	Not examined	Intent to treat analysis; Ettinger distinguished women with prior vertebral fractures from those without, finding a slightly greater effect of raloxifene in the women without prior fractures at 60 mg but not at 120 mg. Authors had access to all original patient data so did not need to rely on summary statistics.
Richy, 2004[20]	Not examined	
Richy, 2005[21]	Not examined	
de Nijs, 2004[22]	Not reported	Remainder of studies analyzed compared vitamin D metabolites to combination of placebo, active vitamin D, and no treatment
Blair 2000[23]	20% of dropouts due to adverse events of which 78% deemed unrelated to study medication; no significant difference between treatment and placebo; only 1 study found a trend toward increased GI complaint with increasing alendronate dose	
Wallach 2000[24]	Safety profile was favorable. Upper GI adverse event rates were similar for treated and placebo groups.	
Watts, 2003[25]	Not reported here.	
Torgerson, 2001[26]	Not reported.	

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15. Nguyen ND, Eisman JA, Nguyen TV. Anti-hip fracture efficacy of biophosphonates: a Bayesian analysis of clinical trials. J Bone Miner Res 2006;21(2):340-9.

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18. Palmer S, McGregor DO, Strippoli GF. Interventions for preventing bone disease in kidney transplant recipients. Cochrane Database Syst Rev 2005;(2):CD005015 .

19. Seeman E, Crans GG, Diez-Perez A, et al. Anti-vertebral fracture efficacy of raloxifene: a meta-analysis. Osteoporos Int 2006;17(2):313-6.

20. Richy F, Ethgen O, Bruyere O, et al. Efficacy of alphacalcidol and calcitriol in primary and corticosteroid-induced osteoporosis: a meta-analysis of their effects on bone mineral density and fracture rate. Osteoporos Int 2004;15(4):301-10.

21. Richy F, Schacht E, Bruyere O, et al. Vitamin D analogs versus native vitamin D in preventing bone loss and osteoporosis-related fractures: a comparative meta-analysis. Calcif Tissue Int 2005;76(3):176-86.

22. de Nijs RN, Jacobs JW, Algra A, et al. Prevention and treatment of glucocorticoid-induced osteoporosis with active vitamin D3 analogues: a review with meta-analysis of randomized controlled trials including organ transplantation studies. Osteoporos Int 2004;15(8):589-602.

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25. Watts NB, Josse RG, Hamdy RC, et al. Risedronate prevents new vertebral fractures in postmenopausal women at high risk. J Clin Endocrinol Metab 2003;88(2):542-9.

26. Torgerson DJ , Bell-Syer SE. Hormone replacement therapy and prevention of nonvertebral fractures: a meta-analysis of randomized trials. JAMA 2001;285(22):2891-7.

Author, Year	Comprehensive sources?	Literature search strategy specified?	Important studies missing?	Explicit eligibility criteria?	Adequate detail about primary studies?	Standard method of appraisal of studies?
Torgerson, 2001[1]	Yes	Yes	No	Yes	Yes	Yes
Cranney, 2001[2]	Yes	Yes	No	Yes	Yes	Yes
Wells, 2002[3]	Yes	Yes	No	Yes	Yes	Yes
Cranney, 2002[4]	Yes	Yes	No	Yes	Yes	Yes
Cranney, 2002[5]	Yes	Yes	No	Yes	Yes	Yes
Cranney, 2002[6]	Yes	Yes	No	Yes	Yes	Yes
Karpf, 1997[7]	Not reported	No	No	Yes	Yes	No
Papapoulos, 2004[8]	Yes	Yes	No	Yes	Yes	Yes
Cranney, 2000[9]	Yes	Yes	No	Yes	Yes	Yes
Cranney, 2003[10]	Yes	Yes	No	Yes	Yes	Yes
Cranney, 2001[11]	Yes	Yes	No	Yes	Yes	Yes
Farquhar, 2005[12]	Yes	Yes	No	Yes	Yes	Yes
Stevenson, 2005[13]	Yes	Yes	No	Yes	Yes	Yes
Boonen, 2005[14]	Yes	Yes	No	Yes	No dose information	Yes
Nguyen, 2006[15]	Only English; only peer-reviewed	Yes	No	Yes	Yes	Yes
Sawka, 2005[16]	Yes	Yes	No	YES	Yes	Yes
Miller, 2005[17]	Yes	No	No	Yes	Yes	No
Palmer, 2006[18]	Yes	Yes	No	Yes	Yes	Yes
Seeman, 2006[19]	Yes	Yes	No	Yes	Yes	Yes
Richy, 2004[20]	Yes	Yes	No	Yes	Yes	Yes
Richy, 2005[21]	Yes	Yes	No	Yes	Yes	Yes
de Nijs, 2004[22]	Yes	Yes	No	Yes	Yes	Yes
Blair, 2000[23]	Yes	Yes	No	Yes	Yes	Yes

Appendix C5. Systematic Reviews Quality Assessment Evidence Table - Internal Validity

Author, Year	Comprehensive sources?	Literature search strategy specified?	Important studies missing?	Explicit eligibility criteria?	Adequate detail about primary studies?	Standard method of appraisal of studies?
Wallach, 2000[24]	No	Not applicable	N/A	Yes	Yes	N/A
Watts, 2003[25]	No	Not applicable	N/A	Yes	Yes	N/A
Torgerson, 2001[26]	Yes	Yes	No	Yes	Yes	Yes

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3. Wells G, Tugwell P, Shea B, et al. Meta-analyses of therapies for postmenopausal osteoporosis. V. Meta-analysis of the efficacy of hormone replacement therapy in treating and preventing osteoporosis in postmenopausal women. Endocr Rev 2002;23(4):529-39.

4. Cranney A, Tugwell P, Adachi J, et al. Meta-analyses of therapies for postmenopausal osteoporosis. III. Meta-analysis of risedronate for the treatment of postmenopausal osteoporosis. Endocr Rev 2002;23(4):517-23.

5. Cranney A, Wells G, Willan A, et al. Meta-analyses of therapies for postmenopausal osteoporosis. II. Meta-analysis of alendronate for the treatment of postmenopausal women. Endocr Rev 2002;23(4):508-16.

6. Cranney A, Tugwell P, Zytaruk N, et al. Meta-analyses of therapies for postmenopausal osteoporosis. VI. Meta-analysis of calcitonin for the treatment of postmenopausal osteoporosis. Endocr Rev 2002;23(4):540-51.

7. Karpf DB, Shapiro DR, Seeman E, et al. Prevention of nonvertebral fractures by alendronate. A meta-analysis. Alendronate Osteoporosis Treatment Study Groups. JAMA 1997;277(14):1159-64.

8. Papapoulos SE , Quandt SA, Liberman UA, et al. Meta-analysis of the efficacy of alendronate for the prevention of hip fractures in postmenopausal women. Osteoporos Int 2005;16(5):468-74.

9. Cranney A, Adachi JD, Homik JJEH, et al. Calcitonin for preventing and treating corticosteroid-induced osteoporosis. Cochrane Database of Systematic Reviews 2005;(3)

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11. Cranney A, Welch V, Adachi JD, et al. Etidronate for treating and preventing postmenopausal osteoporosis. Cochrane Database of Systematic Reviews 2005;(3)

12. Farquhar CM, Marjoribanks J, Lethaby A, et al. Long term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database of Systematic Reviews 2005;(3)

13. Stevenson M, Lloyd Jones M, De Nigris E, et al. A systematic review and economic evaluation of alendronate, etidronate, risedronate, raloxifene and teriparatide for the prevention and treatment of postmenopausal osteoporosis. Health Technol Assess 2005;9(22):1-160.

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24. Wallach S, Cohen S, Reid DM, et al. Effects of risedronate treatment on bone density and vertebral fracture in patients on corticosteroid therapy. Calcif Tissue Int 2000;67(4):277-85.

25. Watts NB, Josse RG, Hamdy RC, et al. Risedronate prevents new vertebral fractures in postmenopausal women at high risk. J Clin Endocrinol Metab 2003;88(2):542-9.

26. Torgerson DJ , Bell-Syer SE. Hormone replacement therapy and prevention of nonvertebral fractures: a meta-analysis of randomized trials. JAMA 2001;285(22):2891-7.

Author, Year	Study results synthesized?	(1) Exclusion criteria: All trials except:	(2) Relevant to a key question?
Cranney, 2000[1]	Yes	RCT that used calcitonin for the prevention or treatment of steroid induced osteoporosis; men or women over age 18 with any underlying disease requiring therapy with steroids; randomized allocation of patients into treatment groups; adequate description of the intervention medications in terms of dosage scheduling and administration	Yes
Cranney, 2001[2]	Yes	See Wells, 2002 for eligibility criteria; additional exclusion criteria: * didn't include data from the HRT arm or combined HRT/etibronate arm of Wimalawansa 1995 & 1998.	Yes
Cranney, 2001[3]	Yes	INCLUDED Trials that randomized postmenopausal women to etidronate or an alternative (placebo or calcium and /or vitamin D) and measured bone density for at least 1 year	Yes
Cranney, 2002[4]	Yes	INCLUDED (1) Randomized, placebo-controlled trials of risedronate for osteoporosis in postmenopausal women defined as greater than 6 months postmenopausal); 2)follow up of at least one year; and 3)fracture incidence or bone mineral density data available	Yes
Cranney, 2002[5]	Yes	INCLUDED (1) RCTs comparing postmenopausal women receiving alendronate to those not receiving alendronate with follow up of at least 1 year; and 2)fracture incidence, or BMD data	Yes
Cranney, 2002[6]	Yes	INCLUDED (1) RCTs of at least 1-yr duration, comparing calcitonin therapy vs. placebo or calcium and/or vitamin D; 2) outcomes included BMD or fracture incidence; and 3) participants were postmenopausal women	Yes
Cranney, 2003[7]	Yes	INCLUDED Studies which randomized women to risedronate or an alternative (placebo or calcium and/or vit. D) and measured BMD for at least 1yr	Yes
Farquahr, 2005[8]	Yes	Randomized double blind trials of hormone therapy (estrogens with or without progestogens) versus placebo, taken for at least one year by perimenopausal or postmenopausal women additional exclusion criteria: *studies with co interventions that might effect the outcomes being measured or which used topical vaginal hormone therapy creams, topical hormone therapy tablets, or hormone therapy rings	Yes
Karpf, 1997[9]	Yes	INCLUDED all postmenopausal women randomized to treatment with placebo or alendronate at a dose higher than 1mg per day for at least 2 year that evaluated the efficacy of treatment	Yes
Papapoulos, 2004[10]	Yes	Aimed to include all RCT with alendronate in postmenopausal women with a t-score of 2.0 or less, or w/ a vertebral # in which there were sufficient data to evaluate the relative risk; specifically there was at least one patient in each treatment group that experienced a hip fracture	Yes

Author, Year	Study results synthesized?	(1) Exclusion criteria: All trials except:	(2) Relevant to a key question?
Stevenson, 2005[11]	Yes	Studies were excluded if they included participants with secondary osteoporosis (e.g. related to therapy with corticosteroids), or drew their participants exclusively from patients with specific diseases known to effect fracture rates (e.g. parkinson's disease) - only published studies (including those only available in abstract form) were included - it was possible only to include studies published in English, French, German, Italian, or Spanish. This led to an exclusion of one possibly relevant study published only in Japanese	Yes
Torgerson, 2001[12]	Yes	INCLUDED RCT of HRT where women had been randomized to at least 12 mon. of HRT or to no HRT.	Yes
Wells, 2002[13]	Yes	INCLUDED 1) RCT in postmenopausal women that compared an HRT intervention (estrogen used alone or estrogen opposed by progestin) with a placebo (2)HRT could be given in conjunction with a calcium and vitamin D, provided the other group received the same (3)results had to be reported with a follow up of at least one year on one or more of the outcomes of interest (4) both prevention and rx trials were accepted (rx referring to studies that included women w/ prevalent #'s at baseline)	Yes
Boonen, 2005[14]	Yes	Sstudies, including RCTs, of less than three years duration; studies that did not use radiographic verification	Yes
Nguyen, 2006[15]	Yes	Duration of follow up less than 12 months; papers in languages other than English; papers not published in peer reviewed journals	Yes
Sawka, 2005[16]	Yes	Trials with fewer than 50% men; trials that included patients with bone or mineral disorders other than primary osteoporosis, with the exception of osteoporosis secondary to hypogonadism; trials in which controls received active anti-osteoporotic therapy; Duration of followup less than 1 year	Yes
Miller, 2005[17]	Yes	One trial in which participants received risedronate + estrogen; one trial that focused on Paget's Disease	Yes
Seeman, 2006[18]	Yes	Trials of less than one year, trials without radiographic verification of fracture and baseline measures	Yes
Richy, 2004[19]	Yes	Trials of less than 6 months	Yes
Richy, 2005[20]	Yes	Trials of less than 6 months; trials reported only in abstracts if authors failed to provide complete report after being contacted	Yes
de Nijs, 2004[21]	Yes	Trials of nonadult patients	Yes

Author, Year	Study results synthesized?	(1) Exclusion criteria: All trials except:	(2) Relevant to a key question?
Blair, 2000[22]	Yes	Trials of nonadult patients or patients not taking GCs; trials that did not use central DEXA to assess BMD	Yes
Wallach, 2000[23]	Yes? Pooled results of two studies	All studies except two parallel RCTs of risedronate treatment of postmenopausal women of at least 5 years duration, 85 yoa or less at high risk of fracture who had not received drugs known to affect bone metabolism and did not have conditions that would affect evaluation of spinal bone loss	Yes
Watts, 2003[24]	Yes? Pooled results of two studies	All studies except two parallel RCTs of risedronate treatment of adults on GC therapy for less than 3 or more than 6 months; other exclusion criteria for trials included evidence of metabolic bone disease other than GC-induced osteoporosis, recent use of	Yes
Torgerson, 2001[25]	Yes	INCLUDED: RCTs of HRT where women had been randomized to at least 12 months of HRT and no HRT.	Yes

Author, Year	(3) Funding source and role of funder
Cranney, 2000[1]	External sources of support-no courses of support supplied; Internal sources of support-Loeb Research Institute, Clinical Epidemiology Unit Canada.
Cranney, 2001[2]	Not reported
Cranney, 2001[3]	Merck provided an unrestricted educational grant Canada ; Proctor & Gamble contributed a small unrestricted educational grant Canada; Ottawa Health Research Institute- Clinical Epidemiology Unit, Ottawa Hospital, Ottawa, Ontario Canada; University of Ottawa- Institute of Population Health Canada
Cranney, 2002[4]	Merck provided partial funding.
Cranney, 2002[5]	Work was supported in part through educational grants from Merck, Inc.
Cranney, 2002[6]	Not reported
Cranney, 2003[7]	A. Cranney was supported by a Arthritis Society Junior Research Scholar and A. Papaioannou is a Ministry of Health Clinician Scientist Canada; Ottawa Health Research Institute, Clinical Epidemiology Canada; Queen's University, Department of Medicine Canada
Farquahr, 2005[8]	External sources of support - no sources of support supplied; internal sources of support - University of Aukland New Zealand
Karpf, 1997[9]	Published data & data on file at Merck Research Laboratories; this study was supported in part by Merck Research Laboratories
Papapoulos, 2004[10]	Not reported
Stevenson, 2005[11]	Commissioned and funded by health technology assessment program on behalf of NICE (National Institute for Health and Clinical Excellence), United Kingdom
Torgerson, 2001[12]	Review partly funded from an unrestricted educational grant from Wyeth Pharmaceuticals
Wells, 2002[13]	Not reported
Boonen, 2005[14]	Fund for Scientific Research, Flanders Belgium, Grant # G.0171.03N
Nguyen, 2006[15]	Not Reported
Sawka, 2005[16]	Not Reported
Miller, 2005[17]	Proctor and Gamble Pharmaceuticals and sanofi-aventis
Seeman, 2006[18]	Eli Lilly
Richy, 2004[19]	TEVA Pharmaceutical Industries
Richy, 2005[20]	Not Reported

Author, Year	(3) Funding source and role of funder
de Nijs, 2004[21]	Dutch Health Insurance Fund Council
Blair, 2000[22]	Not reported
Wallach, 2000[23]	Proctor and Gamble Pharmaceuticals and Aventis Pharma
Watts, 2003[24]	Proctor and Gamble Pharmaceuticals and Aventis Pharma
Torgerson, 2003[25]	Not reported.

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5. Cranney A, Wells G, Willan A, et al. Meta-analyses of therapies for postmenopausal osteoporosis. II. Meta-analysis of alendronate for the treatment of postmenopausal women. Endocr Rev 2002;23(4):508-16.

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9. Karpf DB, Shapiro DR, Seeman E, et al. Prevention of nonvertebral fractures by alendronate. A meta-analysis. Alendronate Osteoporosis Treatment Study Groups. JAMA 1997;277(14):1159-64.

10. Papapoulos SE, Quandt SA, Liberman UA, et al. Meta-analysis of the efficacy of alendronate for the prevention of hip fractures in postmenopausal women. Osteoporos Int 2005;16(5):468-74.

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12. Torgerson DJ, Bell-Syer SE. Hormone replacement therapy and prevention of vertebral fractures: a meta-analysis of randomised trials. BMC Musculoskelet Disord 2001;2(1):7.

13. Wells G, Tugwell P, Shea B, et al. Meta-analyses of therapies for postmenopausal osteoporosis. V. Meta-analysis of the efficacy of hormone replacement therapy in treating and preventing osteoporosis in postmenopausal women. Endocr Rev 2002;23(4):529-39.

14. Boonen S, Laan RF, Barton IP, et al. Effect of osteoporosis treatments on risk of non-vertebral fractures: review and meta-analysis of intention-to-treat studies. Osteoporos Int 2005;16(10):1291-8.

15. Nguyen ND, Eisman JA, Nguyen TV. Anti-hip fracture efficacy of biophosphonates: a Bayesian analysis of clinical trials. J Bone Miner Res 2006;21(2):340-9.

16. Sawka AM, Papaioannou A, Adachi JD, et al. Does alendronate reduce the risk of fracture in men? A meta-analysis incorporating prior knowledge of anti-fracture efficacy in women. BMC Musculoskelet Disord 2005;6:39.

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18. Seeman E, Crans GG, Diez-Perez A, et al. Anti-vertebral fracture efficacy of raloxifene: a meta-analysis. Osteoporos Int 2006;17(2):313-6.

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24. Watts NB, Josse RG, Hamdy RC, et al. Risedronate prevents new vertebral fractures in postmenopausal women at high risk. J Clin Endocrinol Metab 2003;88(2):542-9.

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Appendix D. Excluded Studies

REJECTED: Abstract review

1. Alendronate reduced days of bed rest and limited activity in postmenopausal women with osteoporosis and existing fractures. ACP Journal Club. 2000 Jul-2000 Aug 31; 133(1):14.
   Rec #: 1207

2. Alendronate safely reduced fractures in postmenopausal women with low bone mass density. ACP Journal Club. 1997 May-1997 Jun 30; 126:73.
   Rec #: 1236

3. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ Tech Rep Ser. 1994; 843:1-129.
   Rec #: 2981

4. Design of the Women's Health Initiative clinical trial and observational study. The Women's Health Initiative Study Group. Control Clin Trials. 1998 Feb; 19(1):61-109.
   Rec #: 2882

5. Drugs for prevention and treatment of postmenopausal osteoporosis. Med Lett Drugs Ther. 2000 Oct 16; 42(1090):97-100.
   Rec #: 2479

6. Effects of estrogen or estrogen/progestin regimens on heart disease risk factors in postmenopausal women. The Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. The Writing Group for the PEPI Trial. JAMA. 1995 Jan 18; 273(3):199-208.
   Rec #: 3560

7. Effects of hormone therapy on bone mineral density: results from the postmenopausal estrogen/progestin interventions (PEPI) trial. The Writing Group for the PEPI. JAMA. 1996 Nov 6; 276(17):1389-96.
   Rec #: 2885

8. Etidronate for postmenopausal osteoporosis. Med Lett Drugs Ther. 1990 Dec 14; 32(833):111-2.
   Rec #: 2574

9. Meta-analysis: Bone mineral density measurement predicts risk for fractures in women. ACP Journal Club. 1996 Sep-1996 Oct 31; 125:48.
   Rec #: 1241

10. Raloxifene for postmenopausal osteoporosis. Med Lett Drugs Ther. 1998 Mar 13; 40(1022):29-30.
    Rec #: 2622

11. Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. American College of Rheumatology Task Force on Osteoporosis Guidelines. Arthritis Rheum. 1996 Nov; 39(11):1791-801.
    Rec #: 2927

12. Review: Etidronate decreases vertebral but not nonvertebral fractures in postmenopausal women. ACP Journal Club. 2002 May-2002 Jun 30; 136(3):98.
    Rec #: 1191

13. Risedronate. Drugs-Aging. 1998; 13(1):83-91; discussion 92.
    Rec #: 1525

14. Synthetic calcitonin for postmenopausal osteoporosis. Med Lett Drugs Ther. 1985 Jun 21; 27(690):53-4.
Rec #: 2714

15. Vitamin D analogs appear superior to native form in preventing bone loss, fractures. Geriatrics and Aging. 2005; 8(3): 9.
Rec #: 3469

16. Adachi, J. D.; Adarni, S.; Miller, P. D., and et al. Tolerability of risedronate in alendronate-intolerant postmenopausal women [abstract]. 2000; 43, (Suppl): S202 Abstract 815_.
Rec #: 2965

17. Adachi, J. D. and Rostom, A. Metabolic bone disease in adults with inflammatory bowel disease. Inflamm Bowel Dis. 1999 Aug; 5(3):200-11.
Rec #: 2932

18. Adam, M.; Spacek, P.; Hulejova, H.; Galianova, A., and Blahos, J. [Postmenopausal osteoporosis. Treatment with calcitonin and a diet rich in collagen proteins]. Casopis Lekaru Ceskych. 1996; 135(3):74-8.
Rec #: 1725

19. Adami, S.; Delmas, P., and Felsenberg, D. Three-monthly 2 mg intravenous ibandronate bolus injections significantly increase bone mineral density in women with postmenopausl osteoporosis. Osteoporos. Int. 2002; 13:S14.
Rec #: 3117

20. Adami, S.; Orranell, S.; Lombardi, P.; Campagnoli, C.; Ferrari, A.; Marchesoni, D., and Balena, R. Prevention of early postmenopausal bone loss with cyclical etidronate: a double-blind, placebo-controlled study. IBMS Second Meeting; San Francisco, CA.
Rec #: 3136

21. Agnusdei, D. ; Azria, M., and et al. Acute metabolic and analgesic effect of salmon calcitonin infusion in patients with metastatic bone disease.
Rec #: 1812

22. Agnusdei, D. ; Civitelli, R.; Camporeale, A., and Gennari, C. Calcitonin and estrogens. Journal of Endocrinological Investigation. 1990; 13(8):625-30.
Rec #: 1908

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REJECTED: No condition of interest

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2. Kaji, H. and Sugimoto, T. [Treatment of osteoporosis with parathyroid hormone: evidence and perspective]. Clin Calcium. 2005 Apr; 15(4):611-5.
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Appendix E. Adverse Events Analyses

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Cardiac (mild)	Alendr	placebo	7	61	541	53	429	0.96(0.62, 1.47)
Cardiac (mild)	Ibandr	placebo	4	515	2613	254	1189	0.98(0.82, 1.17)
Cardiac (mild)	Risedr	placebo	2	0	187	3	85	0(0, 1.14)
Cardiac (mild)	Calcit	placebo	2	1	166	2	103	0.3(0, 6.06)
Cardiac (mild)	Estrog	placebo	2	25	157	32	157	0.73(0.38, 1.37)
Cardiac (mild)	Ralox	placebo	6	86	1658	39	1028	1.53(1.01, 2.35)*
Cardiac (mild)	PTH	placebo	1	1	8	0	8	Inf+(0.03, Inf+)
Cardiac (mild)	Alendr	Calcit	1	3	118	0	123	Inf+(0.43, Inf+)
Cardiac (mild)	Alendr	Estrog	1	25	93	23	93	1.12(0.55, 2.28)
Cardiac (mild)	Alendr	Ralox	2	20	799	14	789	1.44(0.68, 3.16)
Cardiac (mild)	Alendr	vitd	1	0	60	1	57	0(0, 37.1)
Cardiac (mild)	Calcit	PTH	2	5	86	0	81	Inf+(1.05, Inf+)*
Cardiac (mild)	Ralox	Estrog	1	21	123	2	64	6.34(1.47, 57.6)*
Cardiac (serious)	Alendr	placebo	7	231	4626	151	3999	1.2(0.96, 1.49)
Cardiac (serious)	Etidro	placebo	2	2	34	0	38	Inf+(0.21, Inf+)
Cardiac (serious)	Ibandr	placebo	2	131	2062	68	980	0.95(0.69, 1.3)
Cardiac (serious)	Pamidr	placebo	1	0	31	1	30	0(0, 37.7)
Cardiac (serious)	Risedr	placebo	3	2	90	2	76	0.8(0.06, 11.3)
Cardiac (serious)	Zoledr	placebo	1	221	3889	171	3876	1.31(1.06, 1.61)*
Cardiac (serious)	Calcit	placebo	3	2	128	2	124	0.98(0.07, 13.7)
Cardiac (serious)	Estrog	placebo	6	358	6815	393	7489	0.92(0.79, 1.08)
Cardiac (serious)	Estrog-proges	placebo	3	1213	9996	1209	9987	1.04(0.93, 1.15)
Cardiac (serious)	Ralox	placebo	6	320	8569	129	4318	1.2(0.97, 1.5)
Cardiac (serious)	Tamox	placebo	1	115	6681	97	6707	1.19(0.9, 1.58)

Appendix E. Adverse Events Analyses

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Cardiac (serious)	Alendr	Calcit	1	0	140	1	75	0(0, 20.9)
Cardiac (serious)	Alendr	Estrog	2	3	123	1	123	3.03(0.24, 161)
Cardiac (serious)	Alendr	Estrog-proges	1	99	997	15	110	0.7(0.38, 1.35)
Cardiac (serious)	Etidro	Estrog	1	1	17	0	18	Inf+(0.03, Inf+)
Cardiac (serious)	Calcit	PTH	1	1	57	1	47	0.82(0.01, 65.9)
Cardiac (serious)	Ralox	Estrog	1	2	309	1	158	1.02(0.05, 60.7)
Acute Coronary Syndrome	Alendr	placebo	4	4	373	1	254	3.59(0.35, 180)
Acute Coronary Syndrome	Etidro	placebo	2	2	34	0	38	Inf+(0.21, Inf+)
Acute Coronary Syndrome	Ibandr	placebo	1	1	150	0	30	Inf+(0.01, Inf+)
Acute Coronary Syndrome	Pamidr	placebo	1	0	31	1	30	0(0, 37.7)
Acute Coronary Syndrome	Risedr	placebo	2	1	55	2	45	0.38(0.01, 7.62)
Acute Coronary Syndrome	Zoledr	placebo	1	77	3889	78	3876	0.98(0.71, 1.37)
Acute Coronary Syndrome	Calcit	placebo	3	2	128	2	124	0.98(0.07, 13.7)
Acute Coronary Syndrome	Estrog	placebo	5	177	6092	187	6196	0.94(0.76, 1.18)
Acute Coronary Syndrome	Estrog-proges	placebo	2	809	9886	819	9485	0.96(0.86, 1.09)
Acute Coronary Syndrome	Ralox	placebo	3	180	8163	70	4014	1.23(0.92, 1.66)
Acute Coronary Syndrome	Tamox	placebo	1	115	6681	97	6707	1.19(0.9, 1.58)
Acute Coronary Syndrome	Alendr	Calcit	1	0	140	1	75	0(0, 20.9)
Acute Coronary Syndrome	Alendr	Estrog	2	3	123	0	123	Inf+(0.41, Inf+)
Acute Coronary Syndrome	Etidro	Estrog	1	1	17	0	18	Inf+(0.03, Inf+)
Acute Coronary Syndrome	Calcit	PTH	1	0	57	1	47	0(0, 32.2)
Acute Coronary Syndrome	Ralox	Estrog	1	2	309	1	158	1.02(0.05, 60.7)
Cardiac Death	Alendr	placebo	2	2	140	0	90	Inf+(0.13, Inf+)
Cardiac Death	Etidro	placebo	1	1	17	0	20	Inf+(0.03, Inf+)
Cardiac Death	Pamidr	placebo	1	0	31	1	30	0(0, 37.7)
Cardiac Death	Risedr	placebo	1	1	31	0	29	Inf+(0.02, Inf+)

Appendix E. Adverse Events Analyses

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Cardiac Death	Zoledr	placebo	1	39	3889	33	3876	1.18(0.72, 1.94)
Cardiac Death	Calcit	placebo	1	0	16	1	15	0(0, 36.6)
Cardiac Death	Estrog	placebo	2	114	5823	125	5933	0.92(0.71, 1.2)
Cardiac Death	Estrog-proges	placebo	2	136	9886	113	9485	1.18(0.91, 1.54)
Cardiac Death	Ralox	placebo	2	29	7854	11	3862	1.25(0.6, 2.78)
Cardiac Death	Tamox	placebo	1	44	6681	35	6707	1.26(0.79, 2.03)
Atrial fibrillation	Alendr	placebo	1	128	3236	102	3223	1.26(0.96, 1.66)
Atrial fibrillation	Risedr	placebo	1	1	35	0	31	Inf+(0.02, Inf+)
Atrial fibrillation	Zoledr	placebo	1	144	3889	93	3876	1.56(1.19, 2.06)*
GI (mild)	Alendr	placebo	54	3893	11265	3411	9525	1.05(0.99, 1.13)
GI (mild)	Etidro	placebo	18	880	8842	1248	16814	1.33(1.21, 1.46)*
GI (mild)	Ibandr	placebo	10	1793	5773	803	2559	1.02(0.92, 1.13)
GI (mild)	Pamidr	placebo	7	125	340	44	253	3.14(1.93, 5.21)*
GI (mild)	Risedr	placebo	22	2123	9601	1334	5654	1.03(0.95, 1.13)
GI (mild)	Zoledr	placebo	3	35	362	11	125	1.34(0.6, 3.21)
GI (mild)	Calcit	placebo	15	92	799	65	620	0.96(0.63, 1.48)
GI (mild)	Estrog	placebo	6	78	1201	70	1672	1(0.65, 1.52)
GI (mild)	Estrog-proges	placebo	2	84	1395	62	1398	1.38(0.97, 1.97)
GI (mild)	Ralox	placebo	8	281	7199	135	3816	0.97(0.78, 1.21)
GI (mild)	Tamox	placebo	1	1	23	1	23	1(0.01, 82)
GI (mild)	PTH	placebo	2	133	1383	49	691	1.39(0.98, 2)
GI (mild)	calcium	placebo	2	12	237	15	243	0.79(0.33, 1.87)
GI (mild)	vitd	placebo	3	3	141	10	141	0.27(0.04, 1.11)
GI (mild)	Alendr	Etidro	3	18	132	3	105	5.89(1.61, 32.7)*
GI (mild)	Alendr	Pamidr	1	2	21	0	19	Inf+(0.17, Inf+)
GI (mild)	Alendr	Risedr	4	340	2013	249	1692	1.06(0.88, 1.28)

Appendix E. Adverse Events Analyses

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
GI (mild)	Risedr	Zoledr	1	3	15	0	15	Inf+(0.43, Inf+)
GI (mild)	Alendr	Calcit	4	56	413	13	288	3.42(1.79, 7)*
GI (mild)	Alendr	Estrog	4	78	255	68	306	1.57(1, 2.46)
GI (mild)	Alendr	Ralox	5	252	1301	198	1296	1.33(1.08, 1.64)*
GI (mild)	Alendr	vitd	10	164	766	136	701	1.21(0.91, 1.6)
GI (mild)	Etidro	Calcit	1	1	66	0	66	Inf+(0.03, Inf+)
GI (mild)	Etidro	Estrog	3	10	97	0	99	Inf+(2.85, Inf+)*
GI (mild)	Etidro	calcium	7	58	251	50	271	1.57(0.96, 2.59)
GI (mild)	Etidro	vitd	2	1	102	1	100	0.97(0.01, 76.3)
GI (mild)	Ibandr	vitd	2	31	110	35	109	0.83(0.44, 1.54)
GI (mild)	Risder	Estrog-proges	1	3	15	0	15	Inf+(0.43, Inf+)
GI (mild)	Calcit	PTH	2	23	86	10	81	2.48(1.04, 6.33)*
GI (mild)	Ralox	Estrog	2	16	804	16	671	0.89(0.41, 1.93)
GI (mild)	Ralox	Estrog-proges	1	10	495	22	513	0.46(0.19, 1.03)
GI (mild)	calcium	vitd	1	1	29	6	34	0.17(0, 1.55)
Upper GI	Alendr	placebo	46	3111	12177	2602	9908	1.04(0.97, 1.11)
Upper GI	Etidro	placebo	15	198	8668	214	16633	1.53(1.25, 1.88)*
Upper GI	Ibandr	placebo	5	754	4624	331	2204	1.06(0.91, 1.24)
Upper GI	Pamidr	placebo	5	89	262	18	183	4.31(2.4, 8.06)*
Upper GI	Risedr	placebo	20	1293	9474	833	5568	1.07(0.96, 1.19)
Upper GI	Zoledr	placebo	2	26	307	3	74	1.82(0.53, 9.73)
Upper GI	Calcit	placebo	8	54	403	33	300	0.83(0.43, 1.57)
Upper GI	Estrog	placebo	3	43	254	43	161	0.73(0.42, 1.26)
Upper GI	Estrog-proges	placebo	2	17	125	125	517	0.55(0.3, 0.98)*
Upper GI	Ralox	placebo	3	72	1375	28	804	1.1(0.68, 1.81)
Upper GI	PTH	placebo	2	133	1383	49	691	1.39(0.98, 2)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Upper GI	calcium	placebo	2	12	237	15	243	0.79(0.33, 1.87)
Upper GI	vitd	placebo	2	3	75	10	75	0.27(0.04, 1.11)
Upper GI	Alendr	Etidro	3	8	132	1	105	8.13(1.04, 371)*
Upper GI	Alendr	Pamidr	1	2	21	0	19	Inf+(0.17, Inf+)
Upper GI	Alendr	Risedr	3	164	1259	157	1288	1.08(0.85, 1.39)
Upper GI	Risedr	Zoledr	1	3	15	0	15	Inf+(0.43, Inf+)
Upper GI	Alendr	Calcit	4	46	413	9	288	3.65(1.72, 8.66)*
Upper GI	Alendr	Estrog	4	61	255	45	306	1.82(1.12, 2.99)*
Upper GI	Alendr	Estrog-proges	1	256	997	17	110	1.89(1.09, 3.45)*
Upper GI	Alendr	Ralox	4	209	1218	176	1214	1.22(0.97, 1.53)
Upper GI	Alendr	vitd	7	63	411	53	364	1.22(0.78, 1.91)
Upper GI	Etidro	Estrog	2	9	31	0	33	Inf+(2.55, Inf+)*
Upper GI	Etidro	calcium	5	33	222	17	230	2.14(1.11, 4.27)*
Upper GI	Ibandr	vitd	2	24	110	26	109	0.89(0.45, 1.76)
Upper GI	Risder	Estrog-proges	1	3	15	0	15	Inf+(0.43, Inf+)
Upper GI	Calcit	PTH	2	20	86	10	81	2.02(0.82, 5.26)
Reflux and Esophageal	Alendr	placebo	27	850	10400	719	8719	1.11(0.99, 1.23)
Reflux and Esophageal	Ibandr	placebo	2	36	2445	12	1137	1.35(0.68, 2.88)
Reflux and Esophageal	Pamidr	placebo	3	7	211	3	133	1.49(0.33, 9.24)
Reflux and Esophageal	Risedr	placebo	13	159	8991	107	5310	0.9(0.69, 1.17)
Reflux and Esophageal	Calcit	placebo	1	0	123	4	58	0(0, 0.69)*
Reflux and Esophageal	Estrog	placebo	2	34	236	40	143	0.68(0.37, 1.24)
Reflux and Esophageal	Estrog-proges	placebo	1	0	110	22	502	0(0, 0.81)*
Reflux and Esophageal	Alendr	Etidro	1	1	70	0	36	Inf+(0.01, Inf+)
Reflux and Esophageal	Alendr	Risedr	3	19	1259	20	1288	0.97(0.49, 1.93)
Reflux and Esophageal	Alendr	Calcit	1	3	118	0	123	Inf+(0.43, Inf+)

Appendix E. Adverse Events Analyses

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Reflux and Esophageal	Alendr	Estrog	2	51	185	34	236	2.03(1.15, 3.64)*
Reflux and Esophageal	Alendr	Estrog-proges	1	47	997	0	110	Inf+(1.39, Inf+)*
Reflux and Esophageal	Alendr	Ralox	1	6	223	5	233	1.26(0.32, 5.3)
Reflux and Esophageal	Alendr	vitd	2	6	144	12	109	0.45(0.13, 1.38)
Diarrhea	Alendr	placebo	8	17	442	15	407	1.03(0.46, 2.35)
Diarrhea	Etidro	placebo	4	4	138	13	142	0.3(0.07, 1)
Diarrhea	Ibandr	placebo	2	41	309	3	111	4.87(1.48, 25.3)*
Diarrhea	Pamidr	placebo	2	9	126	5	95	0.97(0.27, 3.94)
Diarrhea	Risedr	placebo	5	38	538	34	352	0.94(0.53, 1.67)
Diarrhea	Calcit	placebo	2	1	45	0	49	Inf+(0.03, Inf+)
Diarrhea	Ralox	placebo	1	1	102	6	102	0.16(0, 1.35)
Diarrhea	Alendr	Etidro	1	1	46	0	53	Inf+(0.03, Inf+)
Diarrhea	Alendr	Ralox	1	27	716	11	707	2.48(1.18, 5.58)*
Diarrhea	Alendr	vitd	1	4	68	3	66	1.31(0.21, 9.3)
Diarrhea	Etidro	calcium	3	20	127	16	128	1.29(0.59, 2.85)
Diarrhea	Ibandr	vitd	2	6	110	4	109	1.51(0.35, 7.46)
Elevated Transaminase	Alendr	placebo	4	4	424	0	231	Inf+(0.51, Inf+)
Elevated Transaminase	Pamidr	placebo	1	1	51	2	50	0.48(0.01, 9.57)
Elevated Transaminase	Calcit	placebo	1	1	75	0	71	Inf+(0.02, Inf+)
Elevated Transaminase	Alendr	Calcit	1	1	140	1	75	0.53(0.01, 42.4)
Elevated Transaminase	Calcit	PTH	1	1	29	0	34	Inf+(0.03, Inf+)
Hepatobiliary	Alendr	placebo	1	0	140	1	71	0(0, 19.8)
Hepatobiliary	Pamidr	placebo	1	0	51	1	50	0(0, 38.2)
Hepatobiliary	Calcit	placebo	2	2	243	1	154	1.25(0.06, 76.3)
Hepatobiliary	Estrog	placebo	1	11	723	12	1293	1.65(0.66, 4.11)
Hepatobiliary	Estrog-proges	placebo	1	84	1380	62	1383	1.38(0.97, 1.97)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Hepatobiliary	Ralox	placebo	1	130	5129	66	2576	0.99(0.73, 1.36)
GI (serious)	Alendr	placebo	20	290	8656	202	7566	1.01(0.83, 1.24)
GI (serious)	Etidro	placebo	7	254	8226	383	16249	1.32(1.12, 1.55)*
GI (serious)	Ibandr	placebo	3	96	4357	61	2087	0.77(0.55, 1.08)
GI (serious)	Pamidr	placebo	4	14	135	3	116	3.63(0.94, 20.6)
GI (serious)	Risedr	placebo	12	169	8508	153	4721	0.93(0.72, 1.19)
GI (serious)	Ralox	placebo	1	1	202	1	100	0.49(0.01, 39.1)
GI (serious)	Alendr	Etidro	2	1	86	1	52	0.72(0.01, 59.4)
GI (serious)	Alendr	Pamidr	1	5	21	2	19	2.59(0.36, 30.9)
GI (serious)	Alendr	Risedr	2	1	739	3	755	0.34(0.01, 4.23)
GI (serious)	Alendr	Ralox	1	1	223	0	233	Inf+(0.03, Inf+)
GI (serious)	Alendr	vitd	3	4	249	1	214	3.61(0.35, 182)
Upper GI Perforations, Ulcers or Bleeds (excl	Alendr	placebo	12	170	5388	102	4543	0.88(0.66, 1.18)
Upper GI Perforations, Ulcers or Bleeds (excl	Etidro	placebo	3	123	8066	186	16083	1.32(1.04, 1.67)*
Upper GI Perforations, Ulcers or Bleeds (excl	Ibandr	placebo	2	12	2445	17	1137	0.33(0.14, 0.74)*
Upper GI Perforations, Ulcers or Bleeds (excl	Pamidr	placebo	3	5	102	3	100	1.67(0.31, 11.2)
Upper GI Perforations, Ulcers or Bleeds (excl	Risedr	placebo	7	14	2011	12	1406	0.64(0.27, 1.53)
Upper GI Perforations, Ulcers or Bleeds (excl	Alendr	Pamidr	1	5	21	2	19	2.59(0.36, 30.9)
Upper GI Perforations, Ulcers or Bleeds (excl	Alendr	Risedr	2	1	739	3	755	0.34(0.01, 4.23)
Upper GI Perforations, Ulcers or Bleeds (excl	Alendr	vitd	2	3	179	1	180	3.06(0.24, 162)
Death due to PUBs	Alendr	Risedr	1	0	520	1	533	0(0, 40)
Upper GI (serious)	Alendr	placebo	2	1	449	2	454	0.5(0.01, 9.67)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Upper GI (serious)	Etidro	placebo	3	5	133	7	139	0.75(0.18, 2.84)
Upper GI (serious)	Risedr	placebo	2	122	844	119	844	1.02(0.77, 1.37)
Upper GI (serious)	Alendr	Ralox	1	1	223	0	233	Inf+(0.03, Inf+)
Esophogeal (serious)	Alendr	placebo	8	49	6735	33	6433	1.42(0.89, 2.29)
Esophogeal (serious)	Etidro	placebo	1	126	7977	190	15954	1.33(1.05, 1.68)*
Esophogeal (serious)	Ibandr	placebo	1	5	1954	2	975	1.25(0.2, 13.1)
Esophogeal (serious)	Pamidr	placebo	1	9	33	0	16	Inf+(1.11, Inf+)*
Esophogeal (serious)	Risedr	placebo	6	26	7242	19	3653	0.69(0.37, 1.32)
Esophogeal (serious)	Alendr	Etidro	1	1	70	0	36	Inf+(0.01, Inf+)
Esophogeal (serious)	Alendr	vitd	1	1	70	0	34	Inf+(0.01, Inf+)
Hepatobiliary (serious)	Alendr	Etidro	1	0	16	1	16	0(0, 39)
Death due to Hepatobiliary	Alendr	Etidro	1	0	16	1	16	0(0, 39)
Musculoskeletal	Alendr	placebo	13	764	1975	396	1186	1.05(0.88, 1.27)
Musculoskeletal	Etidro	placebo	6	42	245	36	243	1.24(0.72, 2.14)
Musculoskeletal	Ibandr	placebo	5	1304	2969	578	1328	1.16(1, 1.34)
Musculoskeletal	Pamidr	placebo	4	37	191	19	117	1.24(0.6, 2.64)
Musculoskeletal	Risedr	placebo	9	224	992	243	673	0.4(0.29, 0.54)*
Musculoskeletal	Zoledr	placebo	3	722	4236	166	3986	4.52(3.78, 5.43)*
Musculoskeletal	Calcit	placebo	2	1	48	2	46	0.48(0.01, 9.28)
Musculoskeletal	Estrog	placebo	6	93	1249	92	1631	0.84(0.6, 1.19)
Musculoskeletal	Estrog-proges	placebo	1	62	110	299	502	0.88(0.57, 1.36)
Musculoskeletal	Ralox	placebo	9	128	2398	52	1467	1.66(1.18, 2.38)*
Musculoskeletal	PTH	placebo	1	16	1093	5	544	1.6(0.56, 5.62)
Musculoskeletal	Alendr	Estrog	1	2	30	0	30	Inf+(0.19, Inf+)
Musculoskeletal	Alendr	Estrog-proges	1	627	997	62	110	1.31(0.86, 1.99)
Musculoskeletal	Alendr	Ralox	1	2	33	3	33	0.65(0.05, 6.09)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Musculoskeletal	Alendr	PTH	2	98	174	56	175	3.84(2.22, 6.8)*
Musculoskeletal	Alendr	vitd	1	5	68	4	66	1.23(0.25, 6.49)
Musculoskeletal	Etidro	calcium	1	2	15	0	11	Inf+(0.14, Inf+)
Musculoskeletal	Ibandr	vitd	2	14	110	8	109	1.83(0.68, 5.26)
Musculoskeletal	Calcit	PTH	1	5	57	2	47	2.15(0.33, 23.6)
Musculoskeletal	Ralox	Estrog	3	45	927	13	735	2.44(1.27, 5.02)*
Arthritis and Arthralgias	Alendr	placebo	3	5	165	11	160	0.41(0.1, 1.38)
Arthritis and Arthralgias	Etidro	placebo	1	12	75	10	77	1.27(0.47, 3.55)
Arthritis and Arthralgias	Risedr	placebo	6	30	526	34	384	0.51(0.29, 0.92)*
Arthritis and Arthralgias	Zoledr	placebo	3	303	4236	92	3986	2.98(2.33, 3.84)*
Arthritis and Arthralgias	Calcit	placebo	2	1	48	1	46	0.95(0.01, 74.8)
Arthritis and Arthralgias	Estrog	placebo	3	58	1001	67	1391	0.92(0.61, 1.39)
Arthritis and Arthralgias	Etidro	calcium	1	1	15	0	11	Inf+(0.02, Inf+)
Arthritis and Arthralgias	Ibandr	vitd	1	8	58	4	57	2.11(0.52, 10.2)
Myalgias, Cramps and Limb Pain	Alendr	placebo	3	5	97	3	97	1.7(0.32, 11.2)
Myalgias, Cramps and Limb Pain	Ibandr	placebo	2	191	2383	39	1106	2.25(1.57, 3.29)*
Myalgias, Cramps and Limb Pain	Pamidr	placebo	1	0	79	1	42	0(0, 20.7)
Myalgias, Cramps and Limb Pain	Risedr	placebo	1	3	17	2	17	1.58(0.16, 21.7)
Myalgias, Cramps and Limb Pain	Zoledr	placebo	3	413	4236	71	3986	5.79(4.47, 7.6)*
Myalgias, Cramps and Limb Pain	Estrog	placebo	1	10	268	4	87	0.8(0.22, 3.61)
Myalgias, Cramps and Limb Pain	Ralox	placebo	2	12	135	5	135	2.52(0.8, 9.39)
Myalgias, Cramps and Limb Pain	Alendr	Estrog	1	2	30	0	30	Inf+(0.19, Inf+)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Myalgias, Cramps and Limb Pain	Alendr	Ralox	1	0	33	3	33	0(0, 2.38)
Myalgias, Cramps and Limb Pain	Alendr	PTH	1	12	101	4	102	3.29(0.95, 14.5)
Myalgias, Cramps and Limb Pain	Alendr	vitd	1	3	68	3	66	0.97(0.13, 7.51)
Myalgias, Cramps and Limb Pain	Ibandr	vitd	1	6	52	4	52	1.56(0.34, 8.01)
Myalgias, Cramps and Limb Pain	Calcit	PTH	1	5	57	1	47	4.37(0.46, 214)
Dermatologic	Alendr	placebo	6	357	1464	188	718	0.97(0.78, 1.21)
Dermatologic	Etidro	placebo	1	1	51	0	51	Inf+(0.03, Inf+)
Dermatologic	Ibandr	placebo	3	465	2463	242	1159	0.91(0.76, 1.09)
Dermatologic	Pamidr	placebo	4	2	207	1	131	1.29(0.07, 78.9)
Dermatologic	Risedr	placebo	2	5	187	2	85	2.08(0.31, 23.8)
Dermatologic	Calcit	placebo	8	56	305	9	276	6.13(2.81, 14.9)*
Dermatologic	Estrog	placebo	2	164	294	63	111	0.82(0.5, 1.33)
Dermatologic	Estrog-proges	placebo	2	35	146	170	541	0.82(0.51, 1.28)
Dermatologic	Ralox	placebo	1	2	102	0	102	Inf+(0.19, Inf+)
Dermatologic	Tamox	placebo	1	1	23	1	23	1(0.01, 82)
Dermatologic	Testos	placebo	2	36	50	15	52	8.64(2.94, 29.7)*
Dermatologic	PTH	placebo	1	5	10	1	13	10.6(0.88, 613)
Dermatologic	Alendr	Estrog-proges	1	321	997	31	110	1.21(0.77, 1.94)
Dermatologic	Alendr	vitd	1	2	68	2	66	0.97(0.07, 13.8)
Dermatologic	Etidro	calcium	1	1	15	0	11	Inf+(0.02, Inf+)
Dermatologic	Calcit	PTH	2	4	86	4	81	0.85(0.15, 4.81)
Dermatologic	calcium	vitd	1	1	29	2	34	0.58(0.01, 11.6)
Injection/Application Site Reactions	Ibandr	placebo	1	46	1912	1	950	23.4(3.98, 945)*

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Injection/Application Site Reactions	Calcit	placebo	1	3	24	0	21	Inf+(0.37, Inf+)
Injection/Application Site Reactions	Estrog	placebo	1	147	268	51	87	0.86(0.51, 1.44)
Injection/Application Site Reactions	PTH	placebo	1	5	10	1	13	10.6(0.88, 613)
Respiratory	Alendr	placebo	3	810	1183	435	637	0.86(0.68, 1.09)
Respiratory	Ibandr	placebo	3	1191	2463	577	1159	0.98(0.85, 1.14)
Respiratory	Estrog	placebo	1	14	723	29	1293	0.86(0.42, 1.7)
Respiratory	Estrog-proges	placebo	1	78	110	387	502	0.72(0.45, 1.19)
Respiratory	Testos	placebo	2	2	78	1	78	2.01(0.1, 119)
Respiratory	PTH	placebo	1	0	8	1	8	0(0, 39)
Respiratory	Alendr	Estrog-proges	1	744	997	78	110	1.21(0.75, 1.89)
Respiratory	Calcit	PTH	2	5	86	3	81	1.47(0.27, 9.84)
Renal	Etidro	placebo	2	1	108	0	115	Inf+(0.03, Inf+)
Renal	Zoledr	placebo	2	205	3921	167	3906	1.24(1, 1.53)
Renal	PTH	placebo	1	16	1093	8	544	1(0.4, 2.7)
Renal	Ralox	Tamox	1	13	9875	9	9872	1.44(0.57, 3.83)
Renal	Alendr	vitd	1	21	74	30	75	0.6(0.28, 1.24)
Serious Renal	Zoledr	placebo	1	1	32	0	30	Inf+(0.02, Inf+)
Serious Renal	Alendr	vitd	1	4	74	7	75	0.56(0.11, 2.31)
Neurologic (mild)	Alendr	placebo	10	133	944	92	655	1.24(0.89, 1.73)
Neurologic (mild)	Etidro	placebo	3	4	295	1	308	4.28(0.42, 211)
Neurologic (mild)	Ibandr	placebo	3	582	2463	290	1159	0.95(0.81, 1.13)
Neurologic (mild)	Pamidr	placebo	1	18	81	5	41	2.05(0.66, 7.66)
Neurologic (mild)	Risedr	placebo	5	67	402	50	290	1.42(0.89, 2.27)
Neurologic (mild)	Zoledr	placebo	3	280	3959	90	3942	3.26(2.55, 4.19)*

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Neurologic (mild)	Calcit	placebo	5	53	1059	24	430	0.96(0.56, 1.68)
Neurologic (mild)	Estrog	placebo	3	67	371	54	191	0.89(0.54, 1.45)
Neurologic (mild)	Estrog-proges	placebo	1	5	15	0	15	Inf+(1.07, Inf+)*
Neurologic (mild)	Ralox	placebo	2	9	516	14	518	0.64(0.24, 1.6)
Neurologic (mild)	PTH	placebo	2	122	1383	77	691	0.76(0.56, 1.05)
Neurologic (mild)	calcium	placebo	1	1	173	2	176	0.49(0.01, 9.48)
Neurologic (mild)	Ralox	Tamox	1	7	9875	6	9872	1.17(0.34, 4.2)
Neurologic (mild)	Alendr	Estrog	1	52	93	44	93	1.41(0.76, 2.62)
Neurologic (mild)	Alendr	Ralox	1	0	33	1	33	0(0, 39)
Neurologic (mild)	Etidro	calcium	2	2	100	2	102	1.01(0.07, 14.1)
Neurologic (mild)	Risder	Estrog-proges	1	0	15	5	15	0(0, 0.93)*
Neurologic (mild)	Zoledr	Estrog-proges	1	0	15	5	15	0(0, 0.93)*
Neurologic (mild)	Calcit	Estrog-proges	1	0	25	1	25	0(0, 39)
Neurologic (mild)	Calcit	PTH	2	23	86	8	81	3.15(1.23, 8.86)*
Neurologic (mild)	Ralox	Estrog	1	10	495	18	513	0.57(0.23, 1.31)
Neurologic (mild)	calcium	vitd	1	0	29	1	34	0(0, 45.7)
Headaches	Alendr	placebo	6	37	641	24	403	1.01(0.57, 1.81)
Headaches	Etidro	placebo	3	4	295	1	308	4.28(0.42, 211)
Headaches	Pamidr	placebo	1	18	81	5	41	2.05(0.66, 7.66)
Headaches	Risedr	placebo	4	31	245	23	236	1.36(0.73, 2.56)
Headaches	Zoledr	placebo	2	273	3904	90	3891	3.18(2.48, 4.09)*
Headaches	Calcit	placebo	3	45	1023	23	395	0.74(0.43, 1.31)
Headaches	Estrog	placebo	2	23	278	12	98	0.62(0.28, 1.43)
Headaches	Estrog-proges	placebo	1	5	15	0	15	Inf+(1.07, Inf+)*
Headaches	Ralox	placebo	1	1	33	0	33	Inf+(0.03, Inf+)
Headaches	PTH	placebo	2	73	1383	44	691	0.81(0.54, 1.23)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Headaches	calcium	placebo	1	1	173	2	176	0.49(0.01, 9.48)
Headaches	Alendr	Ralox	1	0	33	1	33	0(0, 39)
Headaches	Etidro	calcium	2	2	100	2	102	1.01(0.07, 14.1)
Headaches	Risder	Estrog-proges	1	0	15	5	15	0(0, 0.93)*
Headaches	Zoledr	Estrog-proges	1	0	15	5	15	0(0, 0.93)*
Headaches	Calcit	PTH	1	5	57	0	47	Inf+(0.78, Inf+)
Headaches	Ralox	Estrog	1	10	495	18	513	0.57(0.23, 1.31)
Headaches	calcium	vitd	1	0	29	1	34	0(0, 45.7)
Cerebrovascular Events	Calcit	Estrog-proges	1	0	25	1	25	0(0, 39)
Neurologic (serious)	Alendr	placebo	3	1	83	1	82	0.98(0.01, 77.3)
Neurologic (serious)	Ibandr	placebo	2	31	2062	23	980	0.65(0.37, 1.18)
Neurologic (serious)	Pamidr	placebo	1	2	81	0	41	Inf+(0.09, Inf+)
Neurologic (serious)	Zoledr	placebo	1	107	3889	99	3876	1.08(0.81, 1.44)
Neurologic (serious)	Calcit	placebo	1	2	37	2	38	1.03(0.07, 14.9)
Neurologic (serious)	Estrog	placebo	3	185	6546	144	7226	1.34(1.07, 1.68)*
Neurologic (serious)	Estrog-proges	placebo	2	235	9886	181	9485	1.28(1.05, 1.57)*
Neurologic (serious)	Ralox	placebo	4	154	3131	62	1590	1.2(0.88, 1.65)
Neurologic (serious)	Tamox	placebo	1	64	6681	57	6707	1.13(0.78, 1.64)
Neurologic (serious)	Testos	placebo	1	1	24	0	24	Inf+(0.03, Inf+)
Neurologic (serious)	Etidro	calcium	1	0	14	1	14	0(0, 39)
Neurologic (serious)	Calcit	PTH	1	1	57	1	47	0.82(0.01, 65.9)
Neurologic (serious)	Estrog	calcium	1	0	15	1	14	0(0, 36.4)
Neurological Death	Zoledr	placebo	1	20	3889	11	3876	1.82(0.83, 4.2)
Neurological Death	Tamox	placebo	1	4	6681	3	6707	1.34(0.23, 9.14)
Cerebrovascular Events (serious)	Ibandr	placebo	2	1	2062	1	980	0.32(0, 27.3)
Cerebrovascular Events (serious)	Pamidr	placebo	1	2	81	0	41	Inf+(0.09, Inf+)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Cerebrovascular Events (serious)	Zoledr	placebo	1	87	3889	88	3876	0.98(0.72, 1.34)
Cerebrovascular Events (serious)	Calcit	placebo	1	2	37	2	38	1.03(0.07, 14.9)
Cerebrovascular Events (serious)	Estrog	placebo	3	185	6546	144	7226	1.34(1.07, 1.68)*
Cerebrovascular Events (serious)	Estrog-proges	placebo	2	235	9886	181	9485	1.28(1.05, 1.57)*
Cerebrovascular Events (serious)	Ralox	placebo	3	154	2929	61	1490	1.22(0.89, 1.68)
Cerebrovascular Events (serious)	Tamox	placebo	1	60	6681	52	6707	1.16(0.79, 1.72)
Cerebrovascular Events (serious)	Testos	placebo	1	1	24	0	24	Inf+(0.03, Inf+)
Cerebrovascular Events (serious)	Etidro	calcium	1	0	14	1	14	0(0, 39)
Cerebrovascular Events (serious)	Calcit	PTH	1	1	57	1	47	0.82(0.01, 65.9)
Cerebrovascular Events (serious)	Estrog	calcium	1	0	15	1	14	0(0, 36.4)
Cerebrovascular Death	Ralox	placebo	1	6	2725	1	1286	2.84(0.34, 131)
Cerebrovascular Death	Tamox	placebo	1	3	6681	3	6707	1(0.13, 7.5)
Metabolic	Alendr	placebo	3	10	347	0	253	Inf+(1.86, Inf+)*
Metabolic	Etidro	placebo	1	0	169	1	180	0(0, 37.7)
Metabolic	Ibandr	placebo	3	340	2463	154	1159	1.1(0.89, 1.36)
Metabolic	Pamidr	placebo	4	2	82	0	82	Inf+(0.19, Inf+)
Metabolic	Risedr	placebo	1	22	157	10	54	0.72(0.3, 1.84)
Metabolic	Zoledr	placebo	1	13	32	3	30	5.98(1.38, 37.2)*
Metabolic	Calcit	placebo	3	10	144	8	151	1.6(0.49, 5.4)
Metabolic	PTH	placebo	2	294	1103	14	557	14(8.09, 26.2)*
Metabolic	calcium	placebo	2	4	237	5	243	0.84(0.16, 4.04)
Metabolic	vitd	placebo	3	14	476	14	473	0.99(0.43, 2.28)
Metabolic	Alendr	Etidro	1	0	46	1	53	0(0, 44.9)
Metabolic	Alendr	Calcit	1	3	15	2	15	1.6(0.15, 22.3)
Metabolic	Alendr	PTH	1	0	101	3	102	0(0, 2.43)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Metabolic	Alendr	vitd	6	30	379	71	366	0.33(0.2, 0.54)*
Metabolic	Etidro	Estrog	1	3	14	0	15	Inf+(0.47, Inf+)
Metabolic	Etidro	calcium	3	3	114	3	116	0.97(0.12, 7.6)
Metabolic	Ibandr	vitd	2	2	110	9	109	0.21(0.02, 1.04)
Metabolic	Pamidr	calcium	1	1	14	1	13	0.93(0.01, 78.4)
Metabolic	Calcit	PTH	1	3	29	6	34	0.54(0.08, 2.87)
Metabolic	Calcit	vitd	2	2	64	0	65	Inf+(0.19, Inf+)
Metabolic	calcium	vitd	1	1	29	8	34	0.12(0, 0.99)*
Hypercalcemia	Etidro	placebo	2	4	179	5	190	0.71(0.1, 4.78)
Hypercalcemia	Calcit	placebo	3	13	139	12	146	1.3(0.45, 3.76)
Hypercalcemia	PTH	placebo	2	294	1103	14	557	14(8.09, 26.2)*
Hypercalcemia	calcium	placebo	2	4	237	5	243	0.84(0.16, 4.04)
Hypercalcemia	Alendr	PTH	1	0	101	3	102	0(0, 2.43)
Hypercalcemia	Alendr	vitd	2	1	138	9	139	0.11(0, 0.79)*
Hypercalcemia	Etidro	Calcit	1	4	10	5	10	0.68(0.08, 5.36)
Hypercalcemia	Etidro	calcium	2	0	100	3	102	0(0, 2.25)
Hypercalcemia	Calcit	PTH	1	0	29	2	34	0(0, 6.23)
Hypercalcemia	calcium	vitd	1	1	29	8	34	0.12(0, 0.99)*
Hypercalciuria	Etidro	placebo	1	9	10	10	10	0(0, 39)
Hypercalciuria	Calcit	placebo	1	7	10	10	10	0(0, 2.26)
Hypercalciuria	vitd	placebo	1	14	360	14	357	0.99(0.43, 2.28)
Hypercalciuria	Alendr	vitd	3	11	210	38	207	0.25(0.11, 0.51)*
Hypercalciuria	Etidro	Calcit	1	9	10	7	10	3.61(0.23, 225)
Hypercalciuria	Ibandr	vitd	1	1	58	5	57	0.18(0, 1.73)
Hypercalciuria	Pamidr	calcium	1	1	14	1	13	0.93(0.01, 78.4)
Hypocalcemia	Alendr	placebo	2	9	301	0	207	Inf+(1.6, Inf+)*

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Hypocalcemia	Pamidr	placebo	3	1	62	0	62	Inf+(0.03, Inf+)
Hypocalcemia	Zoledr	placebo	1	13	32	3	30	5.98(1.38, 37.2)*
Hypocalcemia	Calcit	placebo	1	2	15	0	15	Inf+(0.19, Inf+)
Hypocalcemia	Alendr	Calcit	1	3	15	2	15	1.6(0.15, 22.3)
Hypocalcemia	Alendr	vitd	1	3	15	0	15	Inf+(0.43, Inf+)
Hypocalcemia	Calcit	vitd	1	2	15	0	15	Inf+(0.19, Inf+)
Genitourinary	Alendr	placebo	3	371	1167	184	621	1.05(0.85, 1.32)
Genitourinary	Etidro	placebo	1	0	10	1	10	0(0, 39)
Genitourinary	Ibandr	placebo	3	405	2463	186	1159	1.06(0.87, 1.29)
Genitourinary	Pamidr	placebo	1	11	21	11	19	0.8(0.19, 3.31)
Genitourinary	Risedr	placebo	1	1	35	0	31	Inf+(0.02, Inf+)
Genitourinary	Zoledr	placebo	1	36	55	30	51	1.32(0.56, 3.14)
Genitourinary	Calcit	placebo	1	0	10	1	10	0(0, 39)
Genitourinary	Estrog	placebo	1	11	158	2	152	5.59(1.19, 52.7)*
Genitourinary	Estrog-proges	placebo	1	99	110	168	502	17.8(9.21, 37.9)*
Genitourinary	Ralox	placebo	4	10	638	6	379	1.39(0.43, 4.98)
Genitourinary	Testos	placebo	2	23	88	13	87	2.04(0.9, 4.8)
Genitourinary	Alendr	Estrog-proges	1	345	997	99	110	0.06(0.03, 0.11)*
Genitourinary	Alendr	vitd	2	2	136	6	132	0.32(0.03, 1.8)
Genitourinary	Ralox	Estrog	2	3	804	186	671	0.01(0, 0.03)*
Genitourinary	Ralox	Estrog-proges	1	6	495	45	513	0.13(0.04, 0.3)*
Prostate	Ralox	placebo	1	2	25	3	25	0.64(0.05, 6.19)
Prostate	Testos	placebo	2	21	88	12	87	1.97(0.85, 4.77)
Nephrolithiasis	Alendr	placebo	1	1	24	0	24	Inf+(0.03, Inf+)
Nephrolithiasis	Etidro	placebo	1	0	10	1	10	0(0, 39)
Nephrolithiasis	Calcit	placebo	1	0	10	1	10	0(0, 39)

Appendix E. Adverse Events Analyses

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Nephrolithiasis	Alendr	vitd	2	2	136	6	132	0.32(0.03, 1.8)
Infection	Alendr	placebo	3	79	394	34	235	1.44(0.91, 2.33)
Infection	Etidro	placebo	4	43	154	39	150	1.15(0.66, 2.01)
Infection	Ibandr	placebo	1	2	150	1	30	0.39(0.02, 23.9)
Infection	Pamidr	placebo	1	0	81	1	41	0(0, 19.7)
Infection	Risedr	placebo	3	2	211	1	101	1.49(0.07, 93.4)
Infection	Zoledr	placebo	3	329	4213	66	3965	4.92(3.75, 6.54)*
Infection	Estrog	placebo	1	92	268	32	87	0.9(0.53, 1.54)
Infection	Ralox	placebo	1	6	102	6	102	1(0.26, 3.89)
Infection	Testos	placebo	1	0	54	1	54	0(0, 39)
Infection	Alendr	vitd	1	24	74	19	75	1.41(0.65, 3.08)
Infection	Pamidr	calcium	1	0	14	1	13	0(0, 36.2)
Infection	Calcit	PTH	1	4	57	5	47	0.64(0.12, 3.16)
Infection	Ralox	Estrog	1	26	495	22	513	1.24(0.66, 2.32)
Death due to Infection	Zoledr	placebo	1	1	32	0	30	Inf+(0.02, Inf+)
Death due to Infection	Pamidr	calcium	1	0	14	1	13	0(0, 36.2)
Hematologic	Alendr	placebo	5	4	336	2	336	2.01(0.29, 22.5)
Hematologic	Ibandr	placebo	3	154	2463	66	1159	1.13(0.84, 1.55)
Hematologic	Pamidr	placebo	2	1	97	1	59	0.5(0.01, 40.2)
Hematologic	Risedr	placebo	3	4	588	0	514	Inf+(0.57, Inf+)
Hematologic	Calcit	placebo	2	0	234	2	149	0(0, 2.62)
Hematologic	Estrog	placebo	5	110	6705	82	7385	1.38(1.02, 1.86)*
Hematologic	Estrog-proges	placebo	3	187	9950	79	9549	2.3(1.76, 3.04)*
Hematologic	Ralox	placebo	8	213	6902	46	3691	2.3(1.66, 3.25)*
Hematologic	Tamox	placebo	1	56	6681	28	6707	2.02(1.26, 3.3)*
Hematologic	Testos	placebo	2	6	74	1	73	6.3(0.73, 299)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Hematologic	Ralox	Tamox	1	28	9875	32	9872	0.87(0.51, 1.5)
Hematologic	Alendr	Estrog	1	1	93	2	93	0.5(0.01, 9.69)
Hematologic	Alendr	Ralox	2	0	256	2	266	0(0, 5.44)
Hematologic	Etidro	Estrog	1	0	66	2	66	0(0, 5.31)
Hematologic	Calcit	Estrog	1	0	66	2	66	0(0, 5.31)
Hematologic	Calcit	PTH	1	3	57	0	47	Inf+(0.34, Inf+)
Hematologic	Estrog	vitd	1	2	66	0	66	Inf+(0.19, Inf+)
Hematologic	Ralox	Estrog	1	0	495	5	513	0(0, 1.13)
Thromboembolic Events	Alendr	placebo	2	1	126	0	126	Inf+(0.03, Inf+)
Thromboembolic Events	Estrog	placebo	4	105	6639	79	7319	1.36(1.01, 1.86)*
Thromboembolic Events	Estrog-proges	placebo	3	176	9950	75	9549	2.27(1.72, 3.02)*
Thromboembolic Events	Ralox	placebo	7	167	6878	41	3667	2.08(1.47, 3.02)*
Thromboembolic Events	Tamox	placebo	1	35	6681	22	6707	1.6(0.91, 2.87)
Thromboembolic Events	Alendr	Estrog	1	1	93	2	93	0.5(0.01, 9.69)
Thromboembolic Events	Alendr	Ralox	2	0	256	2	266	0(0, 5.44)
Thromboembolic Events	Ralox	Estrog	1	0	495	5	513	0(0, 1.13)
Pulmonary Embolism	Risedr	placebo	1	1	151	0	77	Inf+(0.01, Inf+)
Pulmonary Embolism	Estrog	placebo	1	3	513	3	504	0.98(0.13, 7.37)
Pulmonary Embolism	Estrog-proges	placebo	1	11	1380	4	1383	2.77(0.82, 12)
Pulmonary Embolism	Ralox	placebo	2	24	5153	2	2600	6.26(1.55, 54.8)*
Pulmonary Embolism	Tamox	placebo	1	21	6681	6	6707	3.52(1.37, 10.7)*
Pulmonary Death	Risedr	placebo	1	1	151	0	77	Inf+(0.01, Inf+)
Pulmonary Death	Ralox	placebo	1	5	5129	0	2576	Inf+(0.46, Inf+)
Pulmonary Death	Tamox	placebo	1	3	6681	0	6707	Inf+(0.41, Inf+)
Psychiatric	Alendr	placebo	1	312	997	156	502	1.01(0.8, 1.28)
Psychiatric	Etidro	placebo	1	1	53	0	54	Inf+(0.03, Inf+)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Psychiatric	Zoledr	placebo	1	0	32	1	30	0(0, 36.6)
Psychiatric	Estrog-proges	placebo	1	36	110	156	502	1.08(0.67, 1.71)
Psychiatric	Tamox	placebo	2	6676	6751	6706	6777	0.43(0.07, 1.87)
Psychiatric	Alendr	Estrog-proges	1	312	997	36	110	0.94(0.61, 1.47)
Psychiatric	Ralox	Estrog	1	0	495	7	513	0(0, 0.71)*
Depression	Etidro	placebo	1	1	53	0	54	Inf+(0.03, Inf+)
Depression	Tamox	placebo	1	6674	6681	6706	6707	0.14(0, 1.11)
Psychiatric Death	Zoledr	placebo	1	0	32	1	30	0(0, 36.6)
Immunologic	Alendr	placebo	3	3	255	0	186	Inf+(0.33, Inf+)
Immunologic	Etidro	placebo	2	0	36	2	38	0(0, 5.62)
Immunologic	Zoledr	placebo	2	3	42	5	40	0.52(0.07, 3.29)
Immunologic	PTH	placebo	1	59	1093	1	544	31(5.31, 1247)*
Immunologic	Alendr	Calcit	1	1	140	0	75	Inf+(0.01, Inf+)
Immunologic	Alendr	Ralox	1	1	33	0	33	Inf+(0.03, Inf+)
Immunologic	Alendr	PTH	1	0	73	3	73	0(0, 2.4)
Immunologic	Alendr	vitd	2	15	134	13	132	1.2(0.49, 2.99)
Immunologic	Ralox	Estrog-proges	1	2	495	3	513	0.69(0.06, 6.05)
Anaphylaxis	Etidro	placebo	2	0	36	2	38	0(0, 5.62)
Graft Rejection	Zoledr	placebo	2	3	42	5	40	0.52(0.07, 3.29)
Graft Rejection	Alendr	vitd	2	15	134	13	132	1.2(0.49, 2.99)
Death due to Graft Rejection	Zoledr	placebo	1	0	32	2	30	0(0, 4.96)
Sweats/Fever/Hot Flashes	Alendr	placebo	8	19	444	24	396	0.69(0.35, 1.35)
Sweats/Fever/Hot Flashes	Etidro	placebo	1	0	17	1	20	0(0, 45.9)
Sweats/Fever/Hot Flashes	Ibandr	placebo	1	47	108	20	36	0.62(0.27, 1.41)
Sweats/Fever/Hot Flashes	Pamidr	placebo	5	8	194	0	149	Inf+(1.39, Inf+)*
Sweats/Fever/Hot Flashes	Risedr	placebo	4	6	104	5	93	1.25(0.29, 5.63)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Sweats/Fever/Hot Flashes	Zoledr	placebo	4	725	4251	125	4001	9.18(7.25, 11.8)*
Sweats/Fever/Hot Flashes	Calcit	placebo	7	6	157	1	169	5.91(0.71, 274)
Sweats/Fever/Hot Flashes	Estrog	placebo	2	25	251	49	245	0.43(0.25, 0.75)*
Sweats/Fever/Hot Flashes	Ralox	placebo	11	443	2628	171	1617	1.31(1.07, 1.61)*
Sweats/Fever/Hot Flashes	Tamox	placebo	3	65	168	7	111	10.5(4.38, 29.3)*
Sweats/Fever/Hot Flashes	Risedr	Zoledr	1	0	15	12	15	0(0, 0.13)*
Sweats/Fever/Hot Flashes	Alendr	Estrog	2	6	123	9	123	0.65(0.18, 2.13)
Sweats/Fever/Hot Flashes	Alendr	Ralox	3	30	552	57	556	0.5(0.31, 0.82)*
Sweats/Fever/Hot Flashes	Etidro	calcium	2	0	34	1	28	0(0, 28.6)
Sweats/Fever/Hot Flashes	Zoledr	Estrog-proges	1	12	15	0	15	Inf+(7.46, Inf+)*
Sweats/Fever/Hot Flashes	Calcit	PTH	1	9	57	2	47	4.17(0.8, 41.7)
Sweats/Fever/Hot Flashes	Ralox	Estrog	2	126	804	32	671	2.79(1.79, 4.45)*
Fever	Pamidr	placebo	3	5	140	0	114	Inf+(0.84, Inf+)
Fever	Zoledr	placebo	2	660	4181	81	3935	9(7.1, 11.5)*
Hot Flashes	Alendr	placebo	2	2	125	6	79	0.17(0.02, 1.01)
Hot Flashes	Calcit	placebo	1	0	24	1	21	0(0, 34.1)
Hot Flashes	Estrog	placebo	1	17	158	41	152	0.33(0.17, 0.63)*
Hot Flashes	Ralox	placebo	5	409	1747	153	779	1.27(1.02, 1.58)*
Hot Flashes	Tamox	placebo	2	6728	6801	6707	6770	Inf+(9.92, Inf+)*
Hot Flashes	Ralox	Estrog	1	121	309	17	158	5.32(3.02, 9.88)*
Flushing	Zoledr	placebo	1	32	55	26	51	1.33(0.58, 3.09)
Flushing	Calcit	placebo	3	5	85	0	86	Inf+(0.92, Inf+)
Flushing	Ralox	placebo	4	30	316	13	271	1.97(0.96, 4.27)
Flushing	Tamox	placebo	2	18	48	7	48	3.71(1.24, 12.4)*
Flushing	Calcit	PTH	1	6	57	0	47	Inf+(1.02, Inf+)*
Weight Gain	Alendr	placebo	1	6	93	8	93	0.73(0.2, 2.53)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Weight Gain	Pamidr	placebo	1	1	33	0	16	Inf+(0.01, Inf+)
Weight Gain	Estrog	placebo	1	8	93	8	93	1(0.31, 3.21)
Weight Gain	Alendr	Estrog	1	6	93	8	93	0.73(0.2, 2.53)
Weight Gain	Ralox	Estrog	1	4	495	13	513	0.31(0.07, 1.02)
Pain	Alendr	placebo	1	5	46	4	46	1.28(0.25, 6.91)
Pain	Calcit	PTH	1	3	57	2	47	1.25(0.14, 15.5)
Gynecologic	Alendr	placebo	2	11	123	12	123	0.91(0.35, 2.36)
Gynecologic	Etidro	placebo	1	0	38	1	39	0(0, 40)
Gynecologic	Estrog	placebo	7	301	1573	62	2045	7.18(5.31, 9.82)*
Gynecologic	Estrog-proges	placebo	3	34	244	1	151	58.1(9.03, 2452)*
Gynecologic	Ralox	placebo	8	129	6924	63	3446	1.07(0.77, 1.51)
Gynecologic	Tamox	placebo	3	3725	6801	2333	6793	2.33(2.17, 2.5)*
Gynecologic	Estrog	Estrog-proges	1	10	135	0	144	Inf+(2.51, Inf+)*
Gynecologic	Ralox	Tamox	1	20	9875	14	9872	1.43(0.69, 3.06)
Gynecologic	Alendr	Estrog	2	9	133	48	133	0.1(0.04, 0.24)*
Gynecologic	Etidro	Estrog	1	0	14			.(., .)
Gynecologic	Calcit	Estrog-proges	1	0	25	1	25	0(0, 39)
Gynecologic	Estrog	calcium	1			0	14	.(., .)
Gynecologic	Ralox	Estrog	2	85	618	345	577	0.11(0.08, 0.14)*
Gynecologic	Ralox	Estrog-proges	1	1	495	4	513	0.26(0.01, 2.62)
Upper Respiratory	Alendr	placebo	2	3	164	3	104	1(0.13, 7.89)
Upper Respiratory	Calcit	placebo	5	231	1367	48	584	1.95(1.38, 2.79)*
Upper Respiratory	Estrog	placebo	1	26	268	16	87	0.48(0.23, 1.01)
Upper Respiratory	vitd	placebo	1	9	101	7	101	1.28(0.38, 4.46)
Upper Respiratory	Alendr	Calcit	1	0	118	6	123	0(0, 0.87)*
Upper Respiratory	Calcit	vitd	2	9	73	0	68	Inf+(2.04, Inf+)*
Breast Abnormality (other than Cancer)	Alendr	placebo	4	25	335	18	212	1.34(0.65, 2.82)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Breast Abnormality (other than Cancer)	Estrog	placebo	7	205	730	55	545	3.79(2.64, 5.5)*
Breast Abnormality (other than Cancer)	Estrog-proges	placebo	3	75	115	29	118	7.42(3.79, 15.2)*
Breast Abnormality (other than Cancer)	Ralox	placebo	8	63	1971	38	869	0.74(0.48, 1.15)
Breast Abnormality (other than Cancer)	Alendr	Estrog	2	22	123	57	123	0.22(0.11, 0.42)*
Breast Abnormality (other than Cancer)	Alendr	Ralox	1	0	33	1	33	0(0, 39)
Breast Abnormality (other than Cancer)	Etidro	Estrog	2	0	80	11	81	0(0, 0.23)*
Breast Abnormality (other than Cancer)	Risder	Estrog-proges	1	0	15	6	15	0(0, 0.67)*
Breast Abnormality (other than Cancer)	Zoledr	Estrog-proges	1	0	15	6	15	0(0, 0.67)*
Breast Abnormality (other than Cancer)	Calcit	Estrog	1	0	66	1	66	0(0, 39)
Breast Abnormality (other than Cancer)	Calcit	Estrog-proges	1	0	25	2	25	0(0, 5.29)
Breast Abnormality (other than Cancer)	Estrog	calcium	1	10	15	0	14	Inf+(4, Inf+)*
Breast Abnormality (other than Cancer)	Estrog	vitd	1	1	66	0	66	Inf+(0.03, Inf+)
Breast Abnormality (other than Cancer)	Ralox	Estrog	4	42	1048	257	790	0.09(0.07, 0.13)*
Cancer	Alendr	placebo	2	1	81	0	81	Inf+(0.03, Inf+)
Cancer	Etidro	placebo	3	3	172	1	178	3.12(0.25, 165)
Cancer	Ibandr	placebo	3	3	676	0	205	Inf+(0.12, Inf+)
Cancer	Pamidr	placebo	2	4	132	0	91	Inf+(0.4, Inf+)
Cancer	Risedr	placebo	1	0	35	1	31	0(0, 34.5)
Cancer	Calcit	placebo	1	1	32	0	31	Inf+(0.02, Inf+)
Cancer	Estrog	placebo	5	415	12124	497	12742	0.86(0.75, 0.99)*
Cancer	Estrog-proges	placebo	5	520	18492	469	17690	1.07(0.94, 1.22)
Cancer	Ralox	placebo	5	20	6316	12	3088	0.86(0.4, 1.95)
Cancer	Tamox	placebo	5	409	6919	653	6888	0.6(0.53, 0.69)*
Cancer	Testos	placebo	2	3	78	1	78	3.1(0.24, 168)
Cancer	PTH	placebo	3	25	1559	25	794	0.49(0.27, 0.9)*
Cancer	Ralox	Tamox	1	97	9875	100	9872	0.97(0.72, 1.3)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Cancer	Alendr	vitd	1	0	60	2	57	0(0, 5.04)
Cancer	Etidro	calcium	1	0	14	1	14	0(0, 39)
Cancer	Estrog	calcium	1	0	15	1	14	0(0, 36.4)
Gyn Cancer	Etidro	placebo	1	1	75	0	77	Inf+(0.03, Inf+)
Gyn Cancer	Estrog-proges	placebo	4	87	18456	82	17651	1.01(0.74, 1.39)
Gyn Cancer	Ralox	placebo	2	2	5231	1	2678	1.28(0.06, 78.8)
Gyn Cancer	Tamox	placebo	1	53	6681	35	6707	1.52(0.97, 2.41)
Gyn Cancer	Etidro	calcium	1	0	14	1	14	0(0, 39)
Gyn Cancer	Estrog	calcium	1	0	15	1	14	0(0, 36.4)
Death due to GYN Cancer	Tamox	placebo	1	12	6681	13	6707	0.93(0.39, 2.2)
Breast Cancer	Etidro	placebo	1	1	38	0	39	Inf+(0.03, Inf+)
Breast Cancer	Ibandr	placebo	1	1	150	0	30	Inf+(0.01, Inf+)
Breast Cancer	Estrog	placebo	5	238	12124	312	12742	0.79(0.66, 0.93)*
Breast Cancer	Estrog-proges	placebo	3	202	9922	152	9524	1.28(1.03, 1.6)*
Breast Cancer	Ralox	placebo	2	4	5988	2	2862	0.71(0.1, 7.97)
Breast Cancer	Tamox	placebo	3	254	6776	501	6802	0.49(0.42, 0.57)*
Death due to Breast Cancer	Estrog	placebo	1	4	5310	8	5429	0.51(0.11, 1.91)
Death due to Breast Cancer	Estrog-proges	placebo	1	3	8506	2	8102	1.43(0.16, 17.1)
Bone	Ralox	Tamox	1	2	9875	3	9872	0.67(0.06, 5.82)
Lung	Etidro	placebo	1	0	59	1	62	0(0, 41)
Lung	Pamidr	placebo	1	1	81	0	41	Inf+(0.01, Inf+)
Lung	Ralox	placebo	2	1	5153	2	2600	0.39(0.01, 7.87)
Lung	Tamox	placebo	1	28	6681	28	6707	1(0.57, 1.76)
Lung	Ralox	Tamox	1	39	9875	28	9872	1.39(0.84, 2.35)
Death due to Lung Cancer	Ralox	placebo	1	1	5129	0	2576	Inf+(0.01, Inf+)
Death due to Lung Cancer	Tamox	placebo	1	8	6681	11	6707	0.73(0.25, 1.99)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Colon	Pamidr	placebo	1	1	51	0	50	Inf+(0.03, Inf+)
Colon	Estrog	placebo	1	61	5310	58	5429	1.08(0.74, 1.57)
Colon	Estrog-proges	placebo	1	45	8506	67	8102	0.64(0.43, 0.95)*
Colon	Tamox	placebo	1	16	6681	13	6707	1.24(0.56, 2.8)
Colon	Ralox	Tamox	1	30	9875	31	9872	0.97(0.57, 1.65)
Death due to Colon Cancer	Tamox	placebo	1	1	6681	1	6707	1(0.01, 78.8)
Esophageal Cancer	Ralox	placebo	1	0	202	1	100	0(0, 19.3)
Esophageal Cancer	Ralox	Tamox	1	0	9875	1	9872	0(0, 39)
Gastric	Risedr	placebo	1	0	35	1	31	0(0, 34.5)
Gastric	Ralox	placebo	1	1	202	0	100	Inf+(0.01, Inf+)
Gastric	Tamox	placebo	1	1	6681	2	6707	0.5(0.01, 9.64)
Gastric	Ralox	Tamox	1	1	9875	3	9872	0.33(0.01, 4.15)
Gastrointestinal NOS	Ibandr	placebo	1	2	491	0	162	Inf+(0.06, Inf+)
Gastrointestinal NOS	Ralox	placebo	1	2	5129	0	2576	Inf+(0.09, Inf+)
Death due to GI	Ralox	placebo	1	2	5129	0	2576	Inf+(0.09, Inf+)
Death due to Cancer	Estrog	placebo	1	110	5310	118	5429	0.95(0.73, 1.25)
Death due to Cancer	Estrog-proges	placebo	2	123	9886	110	9485	1.08(0.82, 1.41)
Death due to Cancer	Ralox	placebo	1	1	202	0	100	Inf+(0.01, Inf+)
Death due to Cancer	Tamox	placebo	1	8	6681	22	6707	0.36(0.14, 0.85)*
Special Senses	Alendr	placebo	3	0	311	2	304	0(0, 5)
Special Senses	Ibandr	placebo	3	320	2463	171	1159	0.9(0.73, 1.11)
Special Senses	Pamidr	placebo	1	0	31	1	30	0(0, 37.7)
Special Senses	Ralox	placebo	3	746	5364	407	2709	0.91(0.79, 1.04)
Special Senses	Tamox	placebo	1	574	6681	507	6707	1.15(1.01, 1.3)*
Special Senses	Ralox	Tamox	1	1	9875	0	9872	Inf+(0.03, Inf+)
Special Senses	Alendr	Ralox	1	0	33	1	33	0(0, 39)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Eye	Alendr	placebo	2	0	86	1	80	0(0, 34.6)
Eye	Ibandr	placebo	1	1	1912	0	950	Inf+(0.01, Inf+)
Eye	Pamidr	placebo	1	0	31	1	30	0(0, 37.7)
Eye	Ralox	placebo	3	746	5364	407	2709	0.91(0.79, 1.04)
Eye	Tamox	placebo	1	574	6681	507	6707	1.15(1.01, 1.3)*
Eye	Ralox	Tamox	1	1	9875	0	9872	Inf+(0.03, Inf+)
Eye	Alendr	Ralox	1	0	33	1	33	0(0, 39)
Cataract	Ibandr	placebo	1	1	1912	0	950	Inf+(0.01, Inf+)
Cataract	Ralox	placebo	1	745	5129	406	2576	0.91(0.8, 1.04)
Cataract	Tamox	placebo	1	574	6681	507	6707	1.15(1.01, 1.3)*
Ear	Alendr	placebo	1	0	225	1	224	0(0, 38.8)
Endocrine	Ibandr	placebo	1	2	159	1	81	1.02(0.05, 60.9)
Endocrine	Estrog	placebo	1	11	723	16	1293	1.23(0.51, 2.85)
Endocrine	Ralox	Tamox	1	18	9875	8	9872	2.25(0.93, 5.99)
ENT	Alendr	placebo	3	5	179	6	119	0.81(0.18, 3.49)
ENT	Calcit	placebo	9	35	499	14	349	2.31(1.13, 4.99)*
ENT	Ralox	placebo	1	17	102	20	102	0.82(0.37, 1.78)
ENT	Alendr	Calcit	2	0	133	14	138	0(0, 0.29)*
ENT	Calcit	vitd	1	2	15	0	15	Inf+(0.19, Inf+)
ENT	calcium	vitd	1	7	29	9	34	0.89(0.24, 3.2)
Hypertension	Alendr	placebo	3	9	248	3	175	3.11(0.76, 18.2)
Hypertension	Ibandr	placebo	1	0	1912	1	950	0(0, 19.4)
Hypertension	Estrog	placebo	2	18	361	6	180	1.63(0.58, 5.26)
Hypertension	Ralox	placebo	2	2	304	5	202	0.35(0.03, 2.22)
Hypertension	Alendr	Estrog	1	5	93	6	93	0.82(0.19, 3.38)
Acute Phase Reactions	Ibandr	placebo	1	9	100	0	26	Inf+(0.52, Inf+)

				Drug 1		Drug 2		
Event Category	**drug1**	**drug2**	**# studies**	**# events**	**sample size**	**#events**	**sample size**	**OR (95% CI)**
Acute Phase Reactions	Pamidr	placebo	1	5	9	6	8	0.44(0.03, 4.73)
Acute Phase Reactions	Ibandr	vitd	1	1	52	0	52	Inf+(0.03, Inf+)
Pulmonary	Alendr	placebo	1	1	157	0	31	Inf+(0.01, Inf+)
Pulmonary	Pamidr	placebo	1	1	15	1	16	1.07(0.01, 89.6)
Pulmonary Death	Alendr	placebo	1	1	157	0	31	Inf+(0.01, Inf+)
Pulmonary Death	Pamidr	placebo	1	1	15	1	16	1.07(0.01, 89.6)
Peripheral Vascular Disease	Etidro	placebo	1	1	18	0	19	Inf+(0.03, Inf+)
Peripheral Vascular Disease	Estrog-proges	placebo	1	66	8506	73	8102	0.86(0.61, 1.22)
Death due to PVD	Etidro	placebo	1	1	18	0	19	Inf+(0.03, Inf+)