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CADTH TECHNOLOGY REVIEW

Drugs for the Treatment and Prevention of Osteoporosis in Postmenopausal Women — Project Protocol

PROSPERO REGISTRATION NUMBER: CRD42019147448

Service Line:	Technology Review
Publication Date:	September 2019
Report Length:	43 Pages

CADTH

Cite As: *Drugs for the Treatment and Prevention of Osteoporosis in Postmenopausal Women — Project Protocol*. Ottawa: CADTH; 2019 Sep. (CADTH Technology Review).

ISSN: 2369-7835

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Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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Abbreviations

AACE/ACE	American Association of Clinical Endocrinologists and American College of Endocrinology
BMD	bone mineral density
CAROC	Canadian Association of Radiologists and Osteoporosis Canada fracture risk assessment tool
DXA	dual-energy X-ray absorptiometry
NMA	network meta-analysis
PBM	peak bone mass
SD	standard deviation
WHO	World Health Organization

Introduction and Rationale

Osteoporosis is a systemic skeletal disease where deterioration of the bone microarchitecture leads to increased loss of bone strength and risk of fractures. It affects two million Canadians, predominantly postmenopausal women due to decreased production of estrogen following menopause.[1] Fractures associated with osteoporosis, especially fractures of the hip, lead to significant morbidity and increase the risk of one-year mortality by nearly 25%.[2] Health care costs associated with osteoporotic fractures are estimated to account for more than 50% of the economic burden in acute care.[3]

The diagnosis of osteoporosis is defined on the basis of an assessment of bone mineral density (BMB). The World Health Organization (WHO) criteria definition is based on femoral-neck bone mass density measured by dual-energy X-ray absorptiometry (DXA), 2.5 standard deviations (SDs) or more below the peak bone mass (PBM).[4] The PBM refers to the maximum bone density attained during adulthood, typically compared to a 30-year-old adult.[5] BMD can be converted into a T score, which directly expresses the number of SDs that a BMD value is below the PBM. WHO recognizes three diagnostic categories of T scores. Values of –1 or higher are considered normal bone density (i.e., the BMD is within 1 SD of the PBM), values of –1 to –2.5 are considered osteopenia (i.e., the BMD is 1 to 2.5 SDs lower than the PBM), and T scores lower than –2.5 are indicative of osteoporosis (i.e., the BMD is more than 2.5 SDs below the PBM).

However, BMD is only one determinant of bone strength and accounts for bone quantity rather than bone quality.[6] It does not consider structural or material bone properties, and post-hoc studies assessing whether increases in BMD reliably predict reductions in fracture incidence are inconsistent across interventions.[7,8] The FDA therefore requires fracture as the primary end point in the registration of new drug and biologic products for the treatment of osteoporosis, and guidelines indicate that fracture prevention is the most clinically important outcome.[9,10] The International Osteoporosis Foundation recommends treatment failure in osteoporosis to be defined in the context of fractures that occur or are prevented in participants during the course of treatment; for example, within one year of starting treatment, as opposed to a singular decrease in BMD.[11]

Organizations such as the Canadian Association of Radiologists recommend using an individual's 10-year risk of fracture as the threshold for intervention.[12] The *2010 Clinical Practice Guidelines for the Diagnosis and Management of Osteoporosis in Canada* recommend the Fracture Risk Assessment Tool, or FRAX, and the Canadian Association of Radiologists and Osteoporosis Canada fracture risk assessment tool (CAROC) to evaluate an individual's absolute 10-year fracture risk, accounting for risk factors such as age, history of fracture, and glucocorticoid use.[9]

The 2010 clinical practice guidelines by Osteoporosis Canada do not recommend pharmacotherapy in those assessed as having a low risk of fracture (i.e., 10-year fracture risk lower than 10%).[9] However, patients with a prior spine or hip fracture, multiple fragility fractures, or with a 10-year risk of fracture greater than 10% are considered for pharmacotherapy. Drug therapy strategies are divided into the prevention and treatment of fractures based on the patient's baseline level of fracture risk. Those who have a moderate risk of fracture (i.e., a 10-year fracture risk of 10% to 20%) and those at high risk of fracture (i.e., a 10-year fracture risk greater than 20%; a prior fragility fracture of hip or spine; and greater than 1 fragility fracture) are recommended to be considered for medications. The 2010 Canadian clinical practice guidelines recommend the bisphosphonates alendronate

and risedronate as first-line treatments, with high-quality evidence supporting efficacy in the prevention of hip, non-vertebral, and vertebral fractures. Alternative first-line medications include denosumab, zoledronic acid, and raloxifene. Teriparatide is also listed; however, the high cost for therapy and the need for daily injections restrict access to the medication. Raloxifene is only recommended for the prevention of vertebral fractures. Evidence supporting the efficacy of cyclic etidronate with calcium supplementation and calcitonin is of lower quality. For patients at high risk of fractures residing in long-term care, raloxifene and cyclic etidronate with calcium supplementation are not recommended.

Recommendations in the *Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis — 2016* by the American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) differ for patients with moderate risk (i.e., no prior fragility fractures or 10-year major osteoporotic fracture risk of less than 20%) and high risk (i.e., prior fragility fracture, 10-year major osteoporotic fracture risk of greater than or equal to 20%, hip fracture risk of greater than or equal to 3%, or with high risk factors).[13] These guidelines recommend alendronate, denosumab, risedronate and zoledronic acid for those at moderate risk. Alternatively, ibandronate (not available in Canada) and raloxifene are reserved for those intolerant to first-line medications such as oral bisphosphonates (e.g., patients with esophageal disorders, a history of bariatric surgery, chronic kidney disease, or with an inability to stay upright for at least 30 minutes). Patients at high risk of fracture are recommended to take denosumab, teriparatide, or zoledronic acid, while alendronate and risedronate are for use in those intolerant to the aforementioned drugs.

In Canada, different classes of drugs are indicated for osteoporosis, including four bisphosphonates (alendronate, risedronate, etidronate, and zoledronic acid), various dosage forms of hormone replacement therapy, a selective estrogen receptor modulator (raloxifene), calcitonin, a biologic (denosumab), and a parathyroid hormone analogue (teriparatide).

Bisphosphonates are the most widely used anti-osteoporosis treatments in Canada.[14] Among these, alendronate and risedronate accounted for more than 72% of all dispensed oral osteoporosis medications in 2012.[15] However, bisphosphonates are associated with reduced compliance due to gastrointestinal adverse events[16,17] and are investigated for potential association with rare and serious adverse events, including atrial fibrillation, osteonecrosis of the jaw, and atypical femoral fracture.[18] New regimens for bisphosphonates have been developed to facilitate adherence, including weekly and monthly administrations, as well as additional routes of administration such as injectable bisphosphonates. A systematic review of women's values and preferences indicated that the convenience of taking an osteoporosis drug treatment is important: less frequent dosing and oral administration is preferred, and an injectable is preferred over oral medication if given less frequently.[19]

New anti-osteoporosis treatments include romosozumab, a biologic approved by the US FDA in April 2019[20] and by Health Canada in June 2019.[21] The introduction of new drugs offers patients access to additional treatment options.

Based on stakeholder feedback received on the proposed project scope, the technology review will focus on the comparative effectiveness of anti-resorptive drugs, including oral bisphosphonates, zoledronic acid, and denosumab. Raloxifene, teriparatide, and romosozumab are not included in the project scope. Teriparatide is not currently reimbursed by most jurisdictional drug plans. Similarly, romosozumab recently received market approval and is not yet considered for reimbursement. Based on clinical expert opinions, raloxifene is also excluded given its limited use and side effect profile. Consideration will be given to include the bone-forming drugs (teriparatide, romosozumab and other emerging drugs) in a subsequent technology review.

Project Scope and Protocol Development

To inform the final scope of the Technology Review and protocol development, a proposed scope was developed with the assistance of clinical experts. In addition, stakeholder feedback was solicited and considered in the development of the protocol. This protocol will be followed throughout the review process.

Objective

The aim of this Technology Review report is to inform the policy questions by addressing the benefits and harms of the bisphosphonate drugs and denosumab for the treatment or prevention of osteoporosis in postmenopausal women. The focus will be treatments available in Canada. Other comparators may include interventions used in international clinical practice for osteoporosis.

Deliverable

The following deliverable is planned:

- a Technology Review report that will include a systematic review and a network meta-analysis comparing the benefits and harms of bisphosphonate drugs and denosumab used in the prevention or treatment of osteoporosis in postmenopausal women.

Policy Questions

The policy questions were revised based on stakeholder feedback received on the proposed scoping plan.

1. Within the bisphosphonates, which is the best pharmacologic treatment option?
2. How do the bisphosphonates compare against denosumab in fracture prevention?
3. Are zoledronic acid or denosumab effective alternatives in case of a contraindication to an oral bisphosphonate?

Research Questions

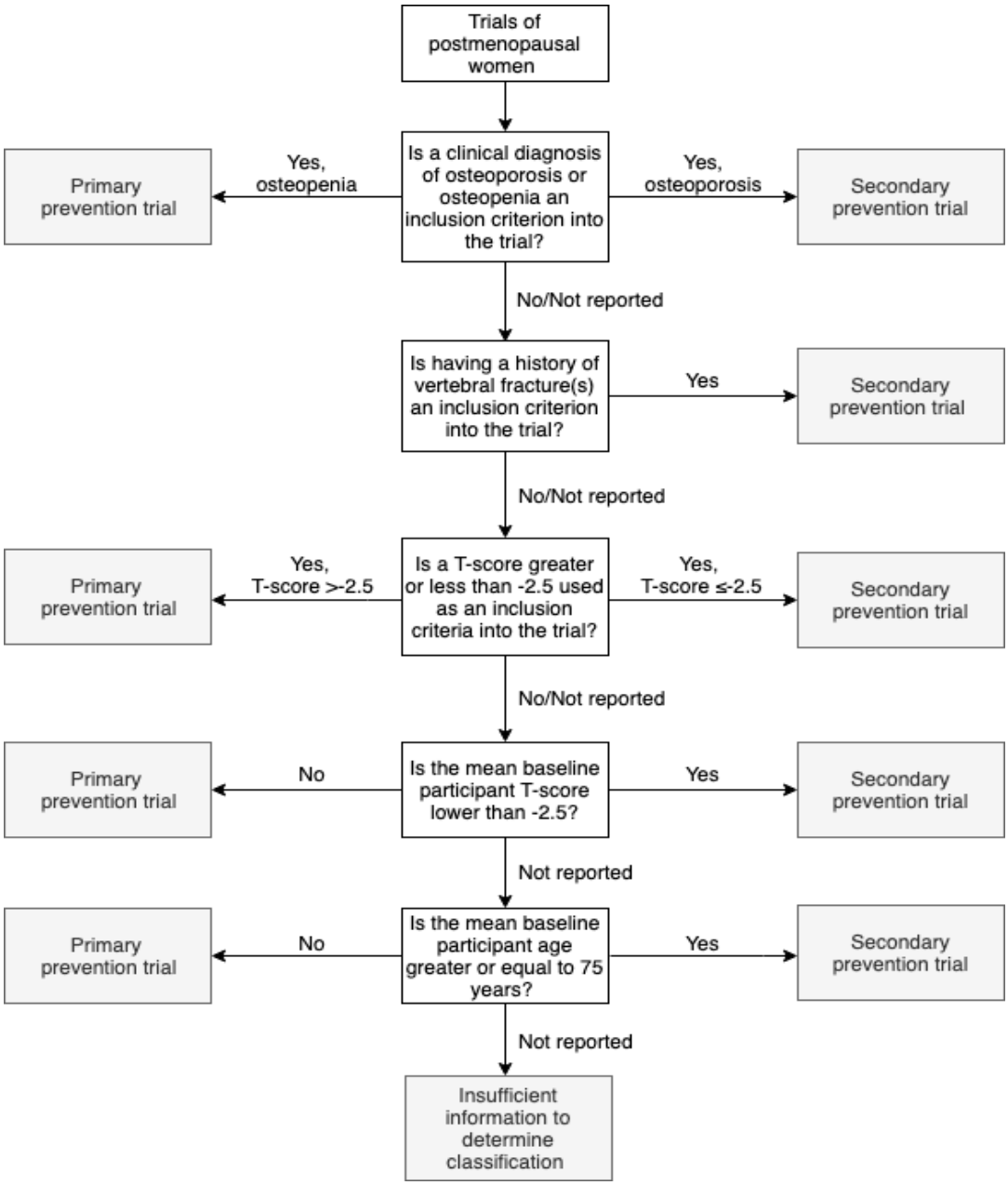
The project will address the following research questions.

1. What are the comparative benefits and harms of bisphosphonate drugs and denosumab in the primary prevention of fractures in postmenopausal women?
2. What are the comparative benefits and harms of bisphosphonate drugs and denosumab in the secondary prevention of fractures in postmenopausal women?

Because of the complexity of the clinical care for postmenopausal women and the diversity in osteoporosis trials, we aim to extract and synthesize evidence for different treatment purposes. Secondary prevention studies include women at a high risk of fracture (e.g., diagnosed with osteoporosis; with low bone mineral density, prior fracture or older age) recommended for pharmacotherapy, while primary prevention studies include women at a lower risk of fracture (e.g., osteopenic bone mineral density, no prior fracture or younger age) who qualify for pharmacotherapy. All eligible studies will be categorized into primary prevention of fractures or secondary prevention of fractures using a hierarchical classification based on the availability of participant information (Figure 1).

All trials that meet the eligibility criteria will be classified at the data extraction stage as a primary or secondary prevention study using the following criteria. Inclusion and exclusion criteria of studies will be examined, followed by baseline characteristics. Studies that include osteoporosis participants, those with a history of vertebral fracture, a BMD t score lower than –2.5, or a mean age older than 75 years will be classified as secondary fracture prevention. As the population of interest is postmenopausal women, studies with participants that do not meet these criteria will be classified as primary prevention. Where there is insufficient information, the following criteria will be examined. Where there are insufficient data for all criteria, the study will be separately described.

Figure 1: Hierarchical Classification of Primary and Secondary Prevention Trials



Methods

Clinical Review

Literature Search Methods

The literature search will be performed by an information specialist using a peer-reviewed search strategy. Published literature will be identified by searching the following bibliographic databases: MEDLINE (1946–) with In-Process records and daily updates via Ovid; Embase (1974–) via Ovid; Cochrane Central Register of Controlled Trials via Ovid; and PubMed. The search strategy (Appendix 1) will consist of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts are alendronate, risedronate, etidronate, zoledronic acid, and denosumab for postmenopausal women.

Retrieval will be limited to the human population and randomized controlled trials but will not be limited by date or language of publication. Conference abstracts will be included.

Grey literature (literature that is not commercially published) will be included by searching publicly available regulatory documents from Canada, the US, and Europe. Additionally, records of clinical trials from the registry databases Clinicaltrials.gov and the *WHO International Clinical Trials Registry Platform* will be screened for inclusion. These searches will be supplemented by reviewing the included studies of systematic reviews published in the last ten years since 2009.

Eligibility Criteria

Study Selection

Two reviewers will independently screen titles and abstracts for relevance to the clinical research questions. Full texts of potentially relevant articles will be retrieved and independently assessed for possible inclusion based on the predetermined selection criteria (Table 1). The two reviewers will then compare their chosen included and excluded studies; disagreements will be discussed until consensus is reached. The study selection process will be presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses, or PRISMA, flow chart.[22]

Drug regimens eligible for inclusion in the review are those that have been approved by Health Canada or are considered of clinical relevance based on expert advice or international clinical practice guidelines. Drug products which are of interest to this review are shown in Table 1.

Inclusion and Exclusion Criteria

Table 1: Selection Criteria

Population	Inclusion: • Postmenopausal women with natural or surgically induced menopause Exclusion: • Premenopausal women • Patients with comorbid conditions or taking medications associated with secondary osteoporosis (e.g., breast cancer, rheumatoid arthritis; tamoxifen, glucocorticoids) • Men (≥ 5% of study participants)
Interventions	• Oral bisphosphonates (alendronate, risedronate, etidronate) • Zoledronic acid • Denosumab
Comparators	• Placebo (no treatment, placebo or background supplementation[a] of calcium and/or vitamin D) • Head-to-head comparisons between interventions of interest
Outcomes	**Efficacy:** • Radiographic vertebral fractures • Clinical vertebral fractures • Non-vertebral fractures (including hip and wrist) • Hip fractures • Wrist fractures • Health-related quality of life **Safety:** • Withdrawal due to adverse events • Serious adverse events • Gastrointestinal adverse events • Osteonecrosis of the jaw • Atypical femoral fracture • Atrial fibrillation
Study Design	**Inclusion:** • Randomized controlled trials with at least one year of treatment **Exclusion:** • Non-randomized studies (e.g., single-arm extensions, narrative reviews, case series, observational cohort studies, qualitative studies) • Duplicate publications

[a] Supplementation of calcium (< 1,200 mg/day) and vitamin D (< 1000 IU/day) equally administered to all participants in a trial will be considered background therapy, based on recommendations from the 2010 clinical practice guidelines by Osteoporosis Canada.[21]

Data Extraction and Critical Appraisal

Study and participant characteristic data will be extracted by one reviewer and verified by a second reviewer using a data extraction form developed a priori, which will be piloted and modified as necessary. Abstraction will cover the following items:

- study characteristics, inclusion and exclusion criteria, and definitions where required
- baseline patient characteristics, including fracture history, T score, BMD, demographics, and prior bisphosphonate experience
- interventions evaluated, including dose, duration, route of administration, and additional calcium and/or vitamin D supplementation
- type of analysis (intention-to-treat or safety population)

Study-specific outcomes data will be extracted independently by two reviewers. Any disagreements will be resolved through discussion and consensus with a third reviewer, if necessary.

Quality Assessment

Quality assessment of comparative randomized studies will be performed independently by two reviewers using the Cochrane Risk of Bias (ROB) tool.[23]

Data Analysis and Synthesis

Prior to the quantitative pooling of study-specific outcomes, a qualitative feasibility assessment will be undertaken to assess clinical and methodological heterogeneity in the available data. Trials included in the same evidence network will be compared to identify any potential heterogeneity based on differences in baseline characteristics or study design. If substantial heterogeneity exists in certain comparisons or subsets of studies, narrative summaries of findings will be reported. Where appropriate, network meta-analyses (NMA) incorporating direct and indirect treatment comparisons will be performed. However, if data for outcomes are limited, meta-analyses of direct comparisons and narrative descriptions will be provided.

Table 2 details the planned NMA for the base case, subgroup, and sensitivity analyses.

The base-case analysis will include studies that meet the eligibility criteria, assess one of the four bisphosphonates of interest, and report at least one outcome of interest. The analysis will be separated for primary prevention or secondary prevention trials.

Subgroup analyses will be conducted for fracture outcomes (i.e., radiographic vertebral, clinical vertebral, non-vertebral, hip, and wrist fractures), where appropriate; these will include patient treatment experience with bisphosphonates (i.e., bisphosphonate-naive and bisphosphonate-experienced) and treatment durations by year. We will also include an analysis of denosumab with the bisphosphonates in a network meta-analysis to compare the efficacy of fracture prevention. Where data are available, a subgroup analysis will include trials that enrol only participants with contraindications to oral bisphosphonates. In this meta-analysis, we will assess the intervention drugs denosumab and zoledronic acid.

Sensitivity analyses will be conducted for the fracture outcomes, where appropriate; this will include a sensitivity analysis of studies with high methodological quality to evaluate the robustness of findings. We will also include a sensitivity analysis to assess the robustness of the age criterion for primary and secondary prevention by removing studies that have been included as primary or secondary prevention due to age, and to examine the effect of their exclusion on each fracture outcome. We also plan to include a sensitivity analysis comparing the correlation of the hierarchical criteria used in the base-case analysis with the fracture risk calculator CAROC,[24] where data are available. If a trial reports baseline T score and the mean age of participants, we will determine the category of a 10-year fracture risk according to the CAROC system and provide a comparison with the primary or secondary prevention category of classification.

Bayesian NMAs will be conducted for the outcomes specified in Tables 1 and 2, and for the subgroups of interest, where appropriate. The choice of outcomes for the NMA will be based on the sufficiency of the data available to derive robust and consistent network models. WinBUGS software version 1.4.3 (MRC Biostatistics Unit, University of Cambridge, UK) will be used to conduct NMA considering models such as a binomial likelihood model (dichotomous) or a normal likelihood model (continuous), which allows for the use of multi-arm trials.[25,26] A random-effects model will be considered to capture anticipated clinical and methodological heterogeneity. Both vague and informative priors will be considered for the between-study variance for random-effects meta-analyses.[27] Trace plots and the Brooks-Gelman-Rubin statistic will be used to assess convergence, and assumptions for network meta-analysis (i.e., exchangeability, homogeneity, consistency) will be assessed.[28] Three chains will be fit in WinBUGS for each analysis, with at least 20,000 iterations and a burn-in of at least 10,000 iterations.

Data Availability

The primary source of data is in the public domain. All stakeholders will be given the option of identifying and providing additional data.

Table 2: Base Case, Subgroup, and Sensitivity Analyses

Outcomes		Base Case	Subgroup Analyses									Sensitivity Analyses		
			#1	#2 Treatment Durations					#3 Treatment Experience		#4	#1	#2	#3
		BIS	BIS, DEN	1 Yr	2 Yr	3 Yr	4 Yr	5 Yr	BIS-naive	BIS-experienced	Oral BIS-intolerant	Studies with high methodological quality	Excluding studies classified by age	Studies defined by CAROC as primary/secondary
Primary Prevention	RVF	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
	NVF	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
	HF	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
	WF	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
	CVF	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
	HRQoL	✔												
	WDAE	✔												
	SAE	✔												
	GI AE	✔												
	ONJ	✔												
	AFF	✔												
	AF	✔												
Secondary Prevention	RVF	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
	NVF	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
	HF	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
	WF	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
	CVF	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
	HRQoL	✔												
	WDAE	✔												
	SAE	✔												
	GI AE	✔												
	ONJ	✔												
	AFF	✔												
	AF	✔												

AF = atrial fibrillation; AFF = atypical femoral fracture; BIS = bisphosphonates (alendronate, risedronate, etidronate, zoledronic acid); CAROC = Canadian Association of Radiologists and Osteoporosis Canada fracture risk assessment tool; CVF = clinical vertebral fracture; DEN = denosumab; GI AE = gastrointestinal adverse event; HF = hip fracture; HRQoL = health-related quality of life; NVF = non-vertebral fractures; ONJ = osteonecrosis of the jaw; RVF = radiographic/morphometric vertebral fractures; SAE = serious adverse event; WDAE = withdrawal due to adverse event; WF = wrist fracture.

Opportunities for Stakeholder Feedback

Stakeholders have been previously given the opportunity to comment on the proposed project scope that informed this protocol. Stakeholders will be given the opportunity to provide feedback on the draft included studies list and the draft report.

Areas for Potential Amendments

If amendments are required at any time during the study, reasons for changes will be recorded in a study file and subsequently reported within the final study report. If necessary, a rescreening of the previous literature search or an updated literature search will be performed to capture additional data according to the amendments.

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Appendix 1: Literature Search Strategy

Denosumab and Teriparatide

Database: Embase Classic+Embase <1947 to 2019 June 04>, Ovid MEDLINE(R) ALL <1946 to June 04, 2019>, EBM Reviews - Cochrane Central Register of Controlled Trials <April 2019>

Search Strategy:

1 Osteoporosis, Postmenopausal/ (19645)

2 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).tw,kf. (23325)

3 (bone loss* adj5 (postmenopaus* or post-menopaus*)).tw,kf. (4324)

4 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).tw,kf. (173)

5 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).tw,kf. (206)

6 (osteoporo* adj5 "after" adj5 menopaus*).tw,kf. (626)

7 (osteoporo* adj5 menopaus*).tw,kf. (4793)

8 (bone loss* adj5 menopaus*).tw,kf. (1640)

9 (bone loss* adj5 "after" adj5 menopaus*).tw,kf. (475)

10 (osteoporo* adj5 age-related).tw,kf. (1218)

11 (bone loss* adj5 age-related).tw,kf. (1711)

12 (osteoporo* adj5 senil*).tw,kf. (1844)

13 (bone loss* adj5 senil*).tw,kf. (54)

14 or/1-13 (43978)

15 Osteoporosis/ (158815)

16 osteoporo*.tw,kf. (193185)

17 Bone Density/ (142862)

18 (bone? adj3 densit*).tw,kf. (135213)

19 bmd.tw,kf. (78560)

20 bone loss*.tw,kf. (66857)

21 or/15-20 (376379)

22 Menopause/ (77798)

23 Postmenopause/ (91320)

24 (postmenopaus* or post-menopaus*).tw,kf. (163754)

25 or/22-24 (232730)

26 21 and 25 (58667)

27 14 or 26 [POST-MENOPAUSAL OSTEOPOROSIS] (70715)

28 Denosumab/ (9306)

29 (denosumab or "amg 162" or amg162 or prolia or xgeva).tw,kf. (8323)

30 Teriparatide/ (9093)

31 (teriparatide or "chs 13340" or chs13340 or forsteo or forteo or "ly 333334" or ly333334 or movymia or parathar or "parathormone 1 34" or "sun e3001" or sune3001 or terrosa).tw,kf. (5797)

32 ((parathyroid hormone or pth) adj2 "1-34").tw,kf. (4692)

33 or/28-32 [BISPHOSPHONATES OF INTEREST] (22616)

34 27 and 33 [POST-MENOPAUSAL OSTEOPOROSIS - BISPHOSHONATES OF INTEREST] (4975)

35 (controlled clinical trial or randomized controlled trial or pragmatic clinical trial).pt. (1128994)

36 clinical trials as topic/ (292386)

37 exp Randomized Controlled Trials as Topic/ (295398)

38 (randomi#ed or randomi#ation* or randomly or RCT? or placebo*).tw,kf. (3102220)

39 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kf. (642661)

40 trial.ti. (755130)

41 or/35-40 (3968626)

42 34 and 41 [Post-menopausal Osteoporosis - Bisphosphonates of Interest - RCTs] (2165)

43 Male/ not (Female/ and Male/) (5515219)

44 42 not 43 [MALE-ONLY REMOVED] (2146)

45 exp Animals/ not Humans/ (18276792)

46 44 not 45 [ANIMAL-ONLY REMOVED] (1445)

47 (comment or editorial or interview or news or newspaper article).pt. (1954050)

48 (letter not (letter and randomized controlled trial)).pt. (2094952)

49 46 not (47 or 48) [OPINION PIECES REMOVED] (1433)

50 49 use medall [MEDLINE RECORDS] (486)

51 postmenopause osteoporosis/ (13835)

52 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (24380)

53 (bone loss* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (4353)

54 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (207)

55 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (209)

56 (osteoporo* adj5 "after" adj5 menopaus*).tw,kw. (627)

57 (osteoporo* adj5 menopaus*).tw,kw. (5583)

58 (bone loss* adj5 menopaus*).tw,kw. (1654)

59 (bone loss* adj5 "after" adj5 menopaus*).tw,kw. (475)

60 (osteoporo* adj5 age-related).tw,kw. (1221)

61 (bone loss* adj5 age-related).tw,kw. (1727)

62 (osteoporo* adj5 senil*).tw,kw. (1864)

63 (bone loss* adj5 senil*).tw,kw. (55)

64 or/51-63 (40670)

65 osteoporosis/ (158815)

66 osteoporo*.tw,kw. (200650)

67 bone density/ (142862)

68 (bone? adj3 densit*).tw,kw. (137288)

69 bmd.tw,kw. (78820)

70 bone loss*.tw,kw. (67392)

71 or/65-70 (379669)

72 menopause/ (77798)

73 postmenopause/ (91320)

74 (postmenopaus* or post-menopaus*).tw,kw. (164951)

75 or/72-74 (233689)

76 71 and 75 (59403)

77 64 or 76 [POST-MENOPAUSAL OSTEOPOROSIS] (68733)

78 denosumab/ (9306)

79 (denosumab or "amg 162" or amg162 or prolia or xgeva).tw,kw. (8492)

80 teriparatide/ (9093)

81 (teriparatide or "chs 13340" or chs13340 or forsteo or forteo or "ly 333334" or ly333334 or movymia or parathar or "parathormone 1 34" or "sun e3001" or sune3001 or terrosa).tw,kw. (5914)

82 ((parathyroid hormone or pth) adj2 "1-34").tw,kw. (4704)

83 or/78-82 [BISPHOSPHONATES OF INTEREST] (22686)

84 77 and 83 [POST-MENOPAUSAL OSTEOPOROSIS - BISPHOSHONATES OF INTEREST] (5360)

85 randomized controlled trial/ (1037431)

86 controlled clinical study/ (463094)

87 exp "clinical trial (topic)"/ (294922)

88 (randomi#ed or randomi#ation* or randomly or RCT? or placebo*).tw,kw. (3155455)

89 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (665659)

90 trial.ti. (755130)

91 or/85-90 (3926497)

92 84 and 91 [Bisphosphonates of Interest - RCTs] (2316)

93 male/ not (female/ and male/) (5515219)

94 92 not 93 [MALE-ONLY REMOVED] (2294)

95 exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (49778412)

96 exp human/ or exp human experimentation/ or exp human experiment/ (39370483)

97 95 not 96 (10409650)

98 94 not 97 [ANIMAL-ONLY REMOVED] (2273)

99 editorial.pt. (1096605)

100 letter.pt. not (letter.pt. and randomized controlled trial/) (2094824)

101 98 not (99 or 100) [OPINION PIECES REMOVED] (2249)

102 101 use emczd [EMBASE RECORDS] (1307)

103 Osteoporosis, Postmenopausal/ (19645)

104 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).ti,ab,kw. (24380)

105 (bone loss* adj5 (postmenopaus* or post-menopaus*)).ti,ab,kw. (4353)

106 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).ti,ab,kw. (207)

107 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).ti,ab,kw. (209)

108 (osteoporo* adj5 "after" adj5 menopaus*).ti,ab,kw. (627)

109 (osteoporo* adj5 menopaus*).ti,ab,kw. (5583)

110 (bone loss* adj5 menopaus*).ti,ab,kw. (1654)

111 (bone loss* adj5 "after" adj5 menopaus*).ti,ab,kw. (475)

112 (osteoporo* adj5 age-related).ti,ab,kw. (1221)

113 (bone loss* adj5 age-related).ti,ab,kw. (1727)

114 (osteoporo* adj5 senil*).ti,ab,kw. (1864)

115 (bone loss* adj5 senil*).ti,ab,kw. (55)

116 or/103-115 (45303)

117 Osteoporosis/ (158815)

118 osteoporo*.ti,ab,kw. (200650)

119 Bone Density/ (142862)

120 (bone? adj3 densit*).ti,ab,kw. (137287)

121 bmd.ti,ab,kw. (78807)

122 bone loss*.ti,ab,kw. (67392)

123 or/117-122 (379658)

124 Menopause/ (77798)

125 Postmenopause/ (91320)

126 (postmenopaus* or post-menopaus*).ti,ab,kw. (164951)

127 or/124-126 (233689)

128 123 and 127 (59403)

129 116 or 128 [POST-MENOPAUSAL OSTEOPOROSIS] (71504)

130 Denosumab/ (9306)

131 (denosumab or "amg 162" or amg162 or prolia or xgeva).ti,ab,kw. (8088)

132 Teriparatide/ (9093)

133 (teriparatide or "chs 13340" or chs13340 or forsteo or forteo or "ly 333334" or ly333334 or movymia or parathar or "parathormone 1 34" or "sun e3001" or sune3001 or terrosa).ti,ab,kw. (5470)

134 ((parathyroid hormone or pth) adj2 "1-34").ti,ab,kw. (4703)

135 or/130-134 [BISPHOSPHONATES OF INTEREST] (22676)

136 129 and 135 [POST-MENOPAUSAL OSTEOPOROSIS - BISPHOSHONATES OF INTEREST] (5016)

137 Male/ not (Female/ and Male/) (5515219)

138 136 not 137 [MALE-ONLY REMOVED] (4932)

139 138 use cctr [CENTRAL RECORDS] (674)

140 50 or 102 or 139 [ALL DATABASES] (2467)

141 remove duplicates from 140 (1668)

142 141 use medall [MEDLINE UNIQUE RECORDS] (486)

143 141 use emczd [EMBASE UNIQUE RECORDS] (903)

144 141 use cctr [CENTRAL UNIQUE RECORDS] (279)

Alendronate

Database: Embase Classic+Embase <1947 to 2019 June 04>, Ovid MEDLINE(R) ALL <1946 to June 04, 2019>, EBM Reviews - Cochrane Central Register of Controlled Trials <April 2019>

Search Strategy:

1 Osteoporosis, Postmenopausal/ (19645)

2 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (24380)

3 (bone loss* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (4353)

4 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (207)

5 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (209)

6 (osteoporo* adj5 "after" adj5 menopaus*).tw,kw. (627)

7 (osteoporo* adj5 menopaus*).tw,kw. (5583)

8 (bone loss* adj5 menopaus*).tw,kw. (1654)

9 (bone loss* adj5 "after" adj5 menopaus*).tw,kw. (475)

10 (osteoporo* adj5 age-related).tw,kw. (1221)

11 (bone loss* adj5 age-related).tw,kw. (1727)

12 (osteoporo* adj5 senil*).tw,kw. (1864)

13 (bone loss* adj5 senil*).tw,kw. (55)

14 or/1-13 (45303)

15 Osteoporosis/ (158815)

16 osteoporo*.tw,kw. (200650)

17 Bone Density/ (142862)

18 (bone? adj3 densit*).tw,kw. (137288)

19 bmd.tw,kw. (78820)

20 bone loss*.tw,kw. (67392)

21 or/15-20 (379669)

22 Menopause/ (77798)

23 Postmenopause/ (91320)

24 (postmenopaus* or post-menopaus*).tw,kw. (164951)

25 or/22-24 (233689)

26 21 and 25 (59403)

27 14 or 26 [POST-MENOPAUSAL OSTEOPOROSIS] (71504)

28 Alendronate/ (19107)

29 (aminohydroxybutane bisphosphonate or actimax or adelan or adronat or adrovance or aldren or aldrion or aldromax or aldronac or aldrox or alefos or alehelm or alenat* or alendi* or alendo or alendra* or alendris or alendro* or alenic or alenato or alend or alenvir or alenwin or aleostito or alexonal or aliot or alovell or alxis or ampine or andante or arendal or arthroplus or aurodren).tw,kw,rn. (22987)

30 (berlex or bestalen or bifemelan or bifoal seminal or bifosa* or blindafe or binosto or blocan or bonacton or bonal?n or bonapex or bonemax or bonendro* or boniran or brek or calbion or calcisedron-d or caldronate or caltera or cleveron or dargol or debenal or defixal or delfoza or deparex or difonate or discozal or doryx or drofaz or dronadil or dronal or dronatex or dronatifer or elandur or eldinir or endronax or en-por or epolar or eucalen).tw,kw,rn. (2932)

31 (filxine or findeclin or fixopan or flamisul or forosa or fortimax or fosal?n or fosamax or fosandron or fosavance or fosazom or fosfacid or fosmin or fosteo* or fostolin or fosval or genalen or gendron or glamor or holadren or jamax-s or lafedam or landrolen or ledronin or lefosan or lendral or lendronal or leodrin or lindron or lozostun or marvil or massidron or maxibone or maxtral or "minusorb mk 0217" or mk 217 or mk0217 or mk217 or morale or mosmass or nafadren or neobon or nichospor or nofrattil or nozat).tw,kw,rn. (8997)

32 (oncalst or onclast or osalen or osaston or osdr?n or osdronat or oseotenk or oseum or osficar or oslene or ossmax or osso* or ostadil or ostaham or ostalert or ostalon or ostemax or ostenan or ostenil or osteobon or osteodur or osteof* or osteomax or osteomel or osteonate or osteonorm or osteopor or osteoral or osteosan or osteotrat or osteovan or osticalcin or ostolek or ostomax).tw,kw,rn. (2459)

33 (pasodron or phostarac or porocalm or porodron or porosal or promax or ralenost or randronate or realen or regenesis or rekostin or reyoin or ridon or riledron or romax or sedron or semandrol or silidral or sinfract or siranin or strongos or synostep or teiroc or terost or tevabone or tevanate or tibolene or tilios or tivarun or tonadron or trabecan or vegabon or voroste).tw,kw,rn. (1103)

34 or/28-33 [ALENDRONATE] (36532)

35 27 and 34 [ALENDRONATE IN POSTMENOPAUSAL OSTEOPOROSIS] (6599)

36 (controlled clinical trial or randomized controlled trial or pragmatic clinical trial).pt. (1128994)

37 clinical trials as topic.sh. (220409)

38 exp Randomized Controlled Trials as Topic/ (295398)

39 (randomi#ed or randomi#ation* or randomly or RCT? or placebo*).tw,kw. (3155455)

40 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (665659)

41 trial.ti. (755130)

42 or/36-41 (3965361)

43 35 and 42 [RCTs - ALENDRONATE IN POSTMENOPAUSAL OSTEOPOROSIS] (2722)

44 Male/ not (Female/ and Male/) (5515219)

45 43 not 44 [MALE-ONLY REMOVED] (2688)

46 exp Animals/ not (exp Animals/ and Humans/) (18276792)

47 45 not 46 [ANIMAL-ONLY REMOVED] (2117)

48 (comment or editorial or interview or news or newspaper article).pt. (1954050)

49 (letter not (letter and randomized controlled trial)).pt. (2094952)

50 47 not (48 or 49) [OPINION PIECES REMOVED] (2095)

51 (2017082* or 201709* or 201710* or 201711* or 201712* or 2018* or 2019*).dt. (2308886)

52 50 and 51 (25)

53 52 use medall [MEDLINE RECORDS] (25)

54 postmenopause osteoporosis/ (13835)

55 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (24380)

56 (bone loss* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (4353)

57 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (207)

58 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (209)

59 (osteoporo* adj5 "after" adj5 menopaus*).tw,kw. (627)

60 (osteoporo* adj5 menopaus*).tw,kw. (5583)

61 (bone loss* adj5 menopaus*).tw,kw. (1654)

62 (bone loss* adj5 "after" adj5 menopaus*).tw,kw. (475)

63 (osteoporo* adj5 age-related).tw,kw. (1221)

64 (bone loss* adj5 age-related).tw,kw. (1727)

65 (osteoporo* adj5 senil*).tw,kw. (1864)

66 (bone loss* adj5 senil*).tw,kw. (55)

67 or/54-66 (40670)

68 osteoporosis/ (158815)

69 osteoporo*.tw,kw. (200650)

70 bone density/ (142862)

71 (bone? adj3 densit*).tw,kw. (137288)

72 bmd.tw,kw. (78820)

73 bone loss*.tw,kw. (67392)

74 or/68-73 (379669)

75 menopause/ (77798)

76 postmenopause/ (91320)

77 (postmenopaus* or post-menopaus*).tw,kw. (164951)

78 or/75-77 (233689)

79 74 and 78 (59403)

80 67 or 79 [POST-MENOPAUSAL OSTEOPOROSIS] (68733)

81 alendronic acid/ (15633)

82 (aminohydroxybutane bisphosphonate or actimax or adelan or adronat or adrovance or aldren or aldrion or aldromax or aldronac or aldrox or alefos or alehelm or alenat* or alendi* or alendo or alendra* or alendris or alendro* or alenic or alenato or alend or alenvir or alenwin or aleostito or alexonal or aliot or alovell or alxis or ampine or andante or arendal or arthroplus or aurodren).tw,kw,rn. (22987)

83 (berlex or bestalen or bifemelan or bifoal seminal or bifosa* or blindafe or binosto or blocan or bonacton or bonal?n or bonapex or bonemax or bonendro* or boniran or brek or calbion or calcisedron-d or caldronate or caltera or cleveron or dargol or debenal or defixal or delfoza or deparex or difonate or discozal or doryx or drofaz or dronadil or dronal or dronatex or dronatifer or elandur or eldinir or endronax or en-por or epolar or eucalen).tw,kw,rn. (2932)

84 (filxine or findeclin or fixopan or flamisul or forosa or fortimax or fosal?n or fosamax or fosandron or fosavance or fosazom or fosfacid or fosmin or fosteo* or fostolin or fosval or genalen or gendron or glamor or holadren or jamax-s or lafedam or landrolen or ledronin or lefosan or lendral or lendronal or leodrin or lindron or lozostun or marvil or massidron or maxibone or maxtral or "minusorb mk 0217" or mk 217 or mk0217 or mk217 or morale or mosmass or nafadren or neobon or nichospor or nofrattil or nozat).tw,kw,rn. (8997)

85 (oncalst or onclast or osalen or osaston or osdr?n or osdronat or oseotenk or oseum or osficar or oslene or ossmax or osso* or ostadil or ostaham or ostalert or ostalon or ostemax or ostenan or ostenil or osteobon or osteodur or osteof* or osteomax or osteomel or osteonate or osteonorm or osteopor or osteoral or osteosan or osteotrat or osteovan or osticalcin or ostolek or ostomax).tw,kw,rn. (2459)

86 (pasodron or phostarac or porocalm or porodron or porosal or promax or ralenost or randronate or realen or regenesis or rekostin or reyoin or ridon or riledron or romax or sedron or semandrol or silidral or sinfract or siranin or strongos or synostep or teiroc or terost or tevabone or tevanate or tibolene or tilios or tivarun or tonadron or trabecan or vegabon or voroste).tw,kw,rn. (1103)

87 or/81-86 [ALENDRONATE] (36503)

88 80 and 87 [ALENDRONATE - POST-MENOPAUSAL OSTEOPOROSIS] (6770)

89 randomized controlled trial/ (1037431)

90 controlled clinical study/ (463094)

91 exp "clinical trial (topic)"/ (294922)

92 (randomi#ed or randomi#ation* or randomly or RCT? or placebo*).tw,kw. (3155455)

93 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (665659)

94 trial.ti. (755130)

95 or/89-94 (3926497)

96 88 and 95 [ALENDRONATE - POST-MENOPAUSAL OSTEOPOROSIS - RCTs] (2838)

97 male/ not (female/ and male/) (5515219)

98 96 not 97 [MALE-ONLY REMOVED] (2801)

99 exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (49778412)

100 exp human/ or exp human experimentation/ or exp human experiment/ (39370483)

101 99 not 100 (10409650)

102 98 not 101 [ANIMAL-ONLY REMOVED] (2756)

103 editorial.pt. (1096605)

104 letter.pt. not (letter.pt. and randomized controlled trial/) (2094824)

105 102 not (103 or 104) [OPINION PIECES REMOVED] (2729)

106 (2017082* or 201709* or 201710* or 201711* or 201712* or 2018* or 2019*).dc. (3221271)

107 105 and 106 (107)

108 107 use emczd [EMBASE RECORDS] (107)

109 Osteoporosis, Postmenopausal/ (19645)

110 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).ti,ab,kw. (24380)

111 (bone loss* adj5 (postmenopaus* or post-menopaus*)).ti,ab,kw. (4353)

112 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).ti,ab,kw. (207)

113 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).ti,ab,kw. (209)

114 (osteoporo* adj5 "after" adj5 menopaus*).tw,kw. (627)

115 (osteoporo* adj5 menopaus*).ti,ab,kw. (5583)

116 (bone loss* adj5 menopaus*).ti,ab,kw. (1654)

117 (bone loss* adj5 "after" adj5 menopaus*).tw,kw. (475)

118 (osteoporo* adj5 age-related).ti,ab,kw. (1221)

119 (bone loss* adj5 age-related).ti,ab,kw. (1727)

120 (osteoporo* adj5 senil*).ti,ab,kw. (1864)

121 (bone loss* adj5 senil*).ti,ab,kw. (55)

122 or/109-121 (45303)

123 Osteoporosis/ (158815)

124 osteoporo*.ti,ab,kw. (200650)

125 Bone Density/ (142862)

126 (bone? adj3 densit*).ti,ab,kw. (137287)

127 bmd.ti,ab,kw. (78807)

128 bone loss*.ti,ab,kw. (67392)

129 or/123-128 (379658)

130 Menopause/ (77798)

131 Postmenopause/ (91320)

132 (postmenopaus* or post-menopaus*).ti,ab,kw. (164951)

133 or/130-132 (233689)

134 129 and 133 (59403)

135 122 or 134 [POST-MENOPAUSAL OSTEOPOROSIS] (71504)

136 Alendronate/ (19107)

137 (aminohydroxybutane bisphosphonate or actimax or adelan or adronat or adrovance or aldren or aldrion or aldromax or aldronac or aldrox or alefos or alehelm or alenat* or alendi* or alendo or alendra* or alendris or alendro* or alenic or alenato or alend or alenvir or alenwin or aleostito or alexonal or aliot or alovell or alxis or ampine or andante or arendal or arthroplus or aurodren).ti,ab,kw. (13259)

138 (berlex or bestalen or bifemelan or bifoal seminal or bifosa* or blindafe or binosto or blocan or bonacton or bonal?n or bonapex or bonemax or bonendro* or boniran or brek or calbion or calcisedron-d or caldronate or caltera or cleveron or dargol or debenal or defixal or delfoza or deparex or difonate or discozal or doryx or drofaz or dronadil or dronal or dronatex or dronatifer or elandur or eldinir or endronax or en-por or epolar or eucalen).ti,ab,kw. (280)

139 (filxine or findeclin or fixopan or flamisul or forosa or fortimax or fosal?n or fosamax or fosandron or fosavance or fosazom or fosfacid or fosmin or fosteo* or fostolin or fosval or genalen or gendron or glamor or holadren or jamax-s or lafedam or landrolen or ledronin or lefosan or lendral or lendronal or leodrin or lindron or lozostun or marvil or massidron or maxibone or maxtral or "minusorb mk 0217" or mk 217 or mk0217 or mk217 or morale or mosmass or nafadren or neobon or nichospor or nofrattil or nozat).ti,ab,kw. (7554)

140 (oncalst or onclast or osalen or osaston or osdr?n or osdronat or oseotenk or oseum or osficar or oslene or ossmax or osso* or ostadil or ostaham or ostalert or ostalon or ostemax or ostenan or ostenil or osteobon or osteodur or osteof* or osteomax or osteomel or osteonate or osteonorm or osteopor or osteoral or osteosan or osteotrat or osteovan or osticalcin or ostolek or ostomax).ti,ab,kw. (2270)

141 (pasodron or phostarac or porocalm or porodron or porosal or promax or ralenost or randronate or realen or regenesis or rekostin or reyoin or ridon or riledron or romax or sedron or semandrol or silidral or sinfract or siranin or strongos or synostep or teiroc or terost or tevabone or tevanate or tibolene or tilios or tivarun or tonadron or trabecan or vegabon or voroste).ti,ab,kw. (1087)

142 or/136-141 [ALENDRONATE] (33315)

143 135 and 142 [ALENDRONATE IN POSTMENOPAUSAL OSTEOPOROSIS] (6503)

144 Male/ not (Female/ and Male/) (5515219)

145 143 not 144 [MALE-ONLY REMOVED] (6428)

146 ("201708" or "201709" or "201710" or "201711" or "201712" or 2018* or 2019*).up. (34609819)

147 145 and 146 (2699)

148 147 use cctr [CENTRAL RECORDS] (703)

149 53 or 108 or 148 [ALL DATABASES] (835)

150 remove duplicates from 149 (766) [TOTAL UNIQUE RECORDS]

151 150 use medall [MEDLINE UNIQUE RECORDS] (25)

152 150 use emczd [EMBASE UNIQUE RECORDS] (86)

153 150 use cctr [CENTRAL UNIQUE RECORDS] (655)

Etidronate

Database: Embase Classic+Embase <1947 to 2019 June 04>, Ovid MEDLINE(R) ALL <1946 to June 04, 2019>, EBM Reviews - Cochrane Central Register of Controlled Trials <April 2019>

Search Strategy:

1 Osteoporosis, Postmenopausal/ (19645)

2 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (24380)

3 (bone loss* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (4353)

4 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (207)

5 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (209)

6 (osteoporo* adj5 "after" adj5 menopaus*).tw,kw. (627)

7 (osteoporo* adj5 menopaus*).tw,kw. (5583)

8 (bone loss* adj5 menopaus*).tw,kw. (1654)

9 (bone loss* adj5 "after" adj5 menopaus*).tw,kw. (475)

10 (osteoporo* adj5 age-related).tw,kw. (1221)

11 (bone loss* adj5 age-related).tw,kw. (1727)

12 (osteoporo* adj5 senil*).tw,kw. (1864)

13 (bone loss* adj5 senil*).tw,kw. (55)

14 or/1-13 (45303)

15 Osteoporosis/ (158815)

16 osteoporo*.tw,kw. (200650)

17 Bone Density/ (142862)

18 (bone? adj3 densit*).tw,kw. (137288)

19 bmd.tw,kw. (78820)

20 bone loss*.tw,kw. (67392)

21 or/15-20 (379669)

22 Menopause/ (77798)

23 Postmenopause/ (91320)

24 (postmenopaus* or post-menopaus*).tw,kw. (164951)

25 or/22-24 (233689)

26 21 and 25 (59403)

27 14 or 26 [POST-MENOPAUSAL OSTEOPOROSIS] (71504)

28 Etidronic Acid/ (10046)

29 (etidronate or editronic acid or anfozan or biotredine or bonemass or dequest or detidron or diadronel or didrocal or didrokit or didro kit or didronal or didronat* or didronel or difosfen or dinol or diphos or diphosphonate or dralen or dronate-os).tw,kw,rn. (30324)

30 (ehdp or ethanehydroxydiphosphonate or emoform total or eopon or etibon or etidrate or etidrel or etidron or etiplus or feminoflex or gen-eti-cal or hedp or maxibral or oflocin or osfo or ostedron or osteodidronel or osteodrug or osteoto* or osteum or ostogene or ostopor).tw,kw,rn. (83328)

31 (somaflex or squam or sterodome or sviroxit or tilferan or tiloetca combi or turpinal or xidifon or xidiphon*).tw,kw,rn. (221)

32 or/28-31 [ETIDRONATE] (109832)

33 27 and 32 [ETIDRONATE IN POSTMENOPAUSAL OSTEOPOROSIS] (3992)

34 (controlled clinical trial or randomized controlled trial or pragmatic clinical trial).pt. (1128994)

35 clinical trials as topic.sh. (220409)

36 exp Randomized Controlled Trials as Topic/ (295398)

37 (randomi#ed or randomi#ation* or randomly or RCT? or placebo*).tw,kw. (3155455)

38 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (665659)

39 trial.ti. (755130)

40 or/34-39 (3965361)

41 33 and 40 [ETIDRONATE IN POSTMENOPAUSAL OSTEOPOROSIS - RCTS] (1443)

42 Male/ not (Female/ and Male/) (5515219)

43 41 not 42 [MALE-ONLY REMOVED] (1422)

44 exp Animals/ not (exp Animals/ and Humans/) (18276792)

45 43 not 44 [ANIMAL-ONLY REMOVED] (1354)

46 (comment or editorial or interview or news or newspaper article).pt. (1954050)

47 (letter not (letter and randomized controlled trial)).pt. (2094952)

48 45 not (46 or 47) [OPINION PIECES REMOVED] (1333)

49 (2017082* or 201709* or 201710* or 201711* or 201712* or 2018* or 2019*).dt. (2308886)

50 48 and 49 (12)

51 50 use medall [MEDLINE RECORDS] (12)

52 postmenopause osteoporosis/ (13835)

53 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (24380)

54 (bone loss* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (4353)

55 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (207)

56 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (209)

57 (osteoporo* adj5 "after" adj5 menopaus*).tw,kw. (627)

58 (osteoporo* adj5 menopaus*).tw,kw. (5583)

59 (bone loss* adj5 menopaus*).tw,kw. (1654)

60 (bone loss* adj5 "after" adj5 menopaus*).tw,kw. (475)

61 (osteoporo* adj5 age-related).tw,kw. (1221)

62 (bone loss* adj5 age-related).tw,kw. (1727)

63 (osteoporo* adj5 senil*).tw,kw. (1864)

64 (bone loss* adj5 senil*).tw,kw. (55)

65 or/52-64 (40670)

66 osteoporosis/ (158815)

67 osteoporo*.tw,kw. (200650)

68 bone density/ (142862)

69 (bone? adj3 densit*).tw,kw. (137288)

70 bmd.tw,kw. (78820)

71 bone loss*.tw,kw. (67392)

72 or/66-71 (379669)

73 menopause/ (77798)

74 postmenopause/ (91320)

75 (postmenopaus* or post-menopaus*).tw,kw. (164951)

76 or/73-75 (233689)

77 72 and 76 (59403)

78 65 or 77 [POST-MENOPAUSAL OSTEOPOROSIS] (68733)

79 etidronic acid/ (10046)

80 (etidronate or editronic acid or anfozan or biotredine or bonemass or dequest or detidron or diadronel or didrocal or didrokit or didro kit or didronal or didronat* or didronel or difosfen or dinol or diphos or diphosphonate or dralen or dronate-os).tw,kw,rn. (30324)

81 (ehdp or ethanehydroxydiphosphonate or emoform total or eopon or etibon or etidrate or etidrel or etidron or etiplus or feminoflex or gen-eti-cal or hedp or maxibral or oflocin or osfo or ostedron or osteodidronel or osteodrug or osteoto* or osteum or ostogene or ostopor).tw,kw,rn. (83328)

82 (somaflex or squam or sterodome or sviroxit or tilferan or tiloetca combi or turpinal or xidifon or xidiphon*).tw,kw,rn. (221)

83 or/79-82 [ETIDRONATE] (109832)

84 78 and 83 [ETIDRONATE - POST-MENOPAUSAL OSTEOPOROSIS] (3451)

85 randomized controlled trial/ (1037431)

86 controlled clinical study/ (463094)

87 exp "clinical trial (topic)"/ (294922)

88 (randomi#ed or randomi#ation* or randomly or RCT? or placebo*).tw,kw. (3155455)

89 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (665659)

90 trial.ti. (755130)

91 or/85-90 (3926497)

92 84 and 91 [ETIDRONATE - POST-MENOPAUSAL OSTEOPOROSIS - RCTs] (1228)

93 male/ not (female/ and male/) (5515219)

94 92 not 93 [MALE-ONLY REMOVED] (1213)

95 exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (49778412)

96 exp human/ or exp human experimentation/ or exp human experiment/ (39370483)

97 95 not 96 (10409650)

98 94 not 97 [ANIMAL-ONLY REMOVED] (1202)

99 editorial.pt. (1096605)

100 letter.pt. not (letter.pt. and randomized controlled trial/) (2094824)

101 98 not (99 or 100) [OPINION PIECES REMOVED] (1197)

102 (2017082* or 201709* or 201710* or 201711* or 201712* or 2018* or 2019*).dc. (3221271)

103 101 and 102 (3)

104 103 use emczd [EMBASE RECORDS] (3)

105 Osteoporosis, Postmenopausal/ (19645)

106 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).ti,ab,kw. (24380)

107 (bone loss* adj5 (postmenopaus* or post-menopaus*)).ti,ab,kw. (4353)

108 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).ti,ab,kw. (207)

109 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).ti,ab,kw. (209)

110 (osteoporo* adj5 "after" adj5 menopaus*).tw,kw. (627)

111 (osteoporo* adj5 menopaus*).ti,ab,kw. (5583)

112 (bone loss* adj5 menopaus*).ti,ab,kw. (1654)

113 (bone loss* adj5 "after" adj5 menopaus*).tw,kw. (475)

114 (osteoporo* adj5 age-related).ti,ab,kw. (1221)

115 (bone loss* adj5 age-related).ti,ab,kw. (1727)

116 (osteoporo* adj5 senil*).ti,ab,kw. (1864)

117 (bone loss* adj5 senil*).ti,ab,kw. (55)

118 or/105-117 (45303)

119 Osteoporosis/ (158815)

120 osteoporo*.ti,ab,kw. (200650)

121 Bone Density/ (142862)

122 (bone? adj3 densit*).ti,ab,kw. (137287)

123 bmd.ti,ab,kw. (78807)

124 bone loss*.ti,ab,kw. (67392)

125 or/119-124 (379658)

126 Menopause/ (77798)

127 Postmenopause/ (91320)

128 (postmenopaus* or post-menopaus*).ti,ab,kw. (164951)

129 or/126-128 (233689)

130 125 and 129 (59403)

131 118 or 130 [POST-MENOPAUSAL OSTEOPOROSIS] (71504)

132 Etidronic Acid/ (10046)

133 (etidronate or editronic acid or anfozan or biotredine or bonemass or dequest or detidron or diadronel or didrocal or didrokit or didro kit or didronal or didronat* or didronel or difosfen or dinol or diphos or diphosphonate or dralen or dronate-os).ti,ab,kw. (10299)

134 (ehdp or ethanehydroxydiphosphonate or emoform total or eopon or etibon or etidrate or etidrel or etidron or etiplus or feminoflex or gen-eti-cal or hedp or maxibral or oflocin or osfo or ostedron or osteodidronel or osteodrug or osteoto* or osteum or ostogene or ostopor).ti,ab,kw. (74833)

135 (somaflex or squam or sterodome or sviroxit or tilferan or tiloetca combi or turpinal or xidifon or xidiphon*).ti,ab,kw. (61)

136 or/132-135 [ETIDRONATE] (90570)

137 131 and 136 [ETIDRONATE IN POSTMENOPAUSAL OSTEOPOROSIS] (2319)

138 Male/ not (Female/ and Male/) (5515219)

139 137 not 138 [MALE-ONLY REMOVED] (2292)

140 ("201708" or "201709" or "201710" or "201711" or "201712" or 2018* or 2019*).up. (34609819)

141 139 and 140 (1048)

142 141 use cctr [CENTRAL RECORDS] (271)

143 51 or 104 or 142 [ALL DATABASES] (286)

144 remove duplicates from 143 (281) [TOTAL UNIQUE RECORDS]

145 144 use medall [MEDLINE UNIQUE RECORDS] (12)

146 144 use emczd [EMBASE UNIQUE RECORDS] (2)

147 144 use cctr [CENTRAL UNIQUE RECORDS] (267)

Risedronate

Database: Embase Classic+Embase <1947 to 2019 June 04>, Ovid MEDLINE(R) ALL <1946 to June 04, 2019>, EBM Reviews - Cochrane Central Register of Controlled Trials <April 2019>

Search Strategy:

1 Osteoporosis, Postmenopausal/ (19645)

2 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (24380)

3 (bone loss* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (4353)

4 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (207)

5 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (209)

6 (osteoporo* adj5 "after" adj5 menopaus*).tw,kw. (627)

7 (osteoporo* adj5 menopaus*).tw,kw. (5583)

8 (bone loss* adj5 menopaus*).tw,kw. (1654)

9 (bone loss* adj5 "after" adj5 menopaus*).tw,kw. (475)

10 (osteoporo* adj5 age-related).tw,kw. (1221)

11 (bone loss* adj5 age-related).tw,kw. (1727)

12 (osteoporo* adj5 senil*).tw,kw. (1864)

13 (bone loss* adj5 senil*).tw,kw. (55)

14 or/1-13 (45303)

15 Osteoporosis/ (158815)

16 osteoporo*.tw,kw. (200650)

17 Bone Density/ (142862)

18 (bone? adj3 densit*).tw,kw. (137288)

19 bmd.tw,kw. (78820)

20 bone loss*.tw,kw. (67392)

21 or/15-20 (379669)

22 Menopause/ (77798)

23 Postmenopause/ (91320)

24 (postmenopaus* or post-menopaus*).tw,kw. (164951)

25 or/22-24 (233689)

26 21 and 25 (59403)

27 14 or 26 [POST-MENOPAUSAL OSTEOPOROSIS] (71504)

28 Risedronate Sodium/ (8732)

29 (risedronate or risedronic acid or acrel or actokit or actonel or atelvia or aventis or alesone or atelvia or avestra or benet or boneact or ductonar or juverital or miosen).tw,kw,rn. (22128)

30 (ne 58095 or ne58095 or norifaz or norsed or nurrid or optinate or osteonate).tw,kw,rn. (79)

31 (racidrix or rentop or retonel or ribastamin or ridron or risedon or risedross or risemyl or risendros or riseos or riseratio or risofos or resonate or rizat or seralis or tevanel or vionate).tw,kw,rn. (4672)

32 or/28-31 [RISEDRONATE] (26784)

33 27 and 32 [RISEDRONATE IN POSTMENOPAUSAL OSTEOPOROSIS] (3350)

34 (controlled clinical trial or randomized controlled trial or pragmatic clinical trial).pt. (1128994)

35 clinical trials as topic.sh. (220409)

36 exp Randomized Controlled Trials as Topic/ (295398)

37 (randomi#ed or randomi#ation* or randomly or RCT? or placebo*).tw,kw. (3155455)

38 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (665659)

39 trial.ti. (755130)

40 or/34-39 (3965361)

41 33 and 40 [RISEDRONATE IN POSTMENOPAUSAL OSTEOPOROSIS] (1313)

42 Male/ not (Female/ and Male/) (5515219)

43 41 not 42 [MALE-ONLY REMOVED] (1297)

44 exp Animals/ not (exp Animals/ and Humans/) (18276792)

45 43 not 44 [ANIMAL-ONLY REMOVED] (1007)

46 (comment or editorial or interview or news or newspaper article).pt. (1954050)

47 (letter not (letter and randomized controlled trial)).pt. (2094952)

48 45 not (46 or 47) [OPINION PIECES REMOVED] (997)

49 (2017082* or 201709* or 201710* or 201711* or 201712* or 2018* or 2019*).dt. (2308886)

50 48 and 49 (12)

51 50 use medall [MEDLINE RECORDS] (12)

52 postmenopause osteoporosis/ (13835)

53 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (24380)

54 (bone loss* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (4353)

55 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (207)

56 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (209)

57 (osteoporo* adj5 "after" adj5 menopaus*).tw,kw. (627)

58 (osteoporo* adj5 menopaus*).tw,kw. (5583)

59 (bone loss* adj5 menopaus*).tw,kw. (1654)

60 (bone loss* adj5 "after" adj5 menopaus*).tw,kw. (475)

61 (osteoporo* adj5 age-related).tw,kw. (1221)

62 (bone loss* adj5 age-related).tw,kw. (1727)

63 (osteoporo* adj5 senil*).tw,kw. (1864)

64 (bone loss* adj5 senil*).tw,kw. (55)

65 or/52-64 (40670)

66 osteoporosis/ (158815)

67 osteoporo*.tw,kw. (200650)

68 bone density/ (142862)

69 (bone? adj3 densit*).tw,kw. (137288)

70 bmd.tw,kw. (78820)

71 bone loss*.tw,kw. (67392)

72 or/66-71 (379669)

73 menopause/ (77798)

74 postmenopause/ (91320)

75 (postmenopaus* or post-menopaus*).tw,kw. (164951)

76 or/73-75 (233689)

77 72 and 76 (59403)

78 65 or 77 [POST-MENOPAUSAL OSTEOPOROSIS] (68733)

79 risedronic acid/ (8902)

80 (risedronate or risedronic acid or acrel or actokit or actonel or atelvia or aventis or alesone or atelvia or avestra or benet or boneact or ductonar or juverital or miosen).tw,kw,rn. (22128)

81 (ne 58095 or ne58095 or norifaz or norsed or nurrid or optinate or osteonate).tw,kw,rn. (79)

82 (racidrix or rentop or retonel or ribastamin or ridron or risedon or risedross or risemyl or risendros or riseos or riseratio or risofos or resonate or rizat or seralis or tevanel or vionate).tw,kw,rn. (4672)

83 or/79-82 [RISEDRONATE] (26786)

84 78 and 83 [RISEDRONATE - POST-MENOPAUSAL OSTEOPOROSIS] (3598)

85 randomized controlled trial/ (1037431)

86 controlled clinical study/ (463094)

87 exp "clinical trial (topic)"/ (294922)

88 (randomi#ed or randomi#ation* or randomly or RCT? or placebo*).tw,kw. (3155455)

89 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (665659)

90 trial.ti. (755130)

91 or/85-90 (3926497)

92 84 and 91 [RISEDRONATE - POST-MENOPAUSAL OSTEOPOROSIS - RCTs] (1384)

93 male/ not (female/ and male/) (5515219)

94 92 not 93 [MALE-ONLY REMOVED] (1368)

95 exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (49778412)

96 exp human/ or exp human experimentation/ or exp human experiment/ (39370483)

97 95 not 96 (10409650)

98 94 not 97 [ANIMAL-ONLY REMOVED] (1358)

99 editorial.pt. (1096605)

100 letter.pt. not (letter.pt. and randomized controlled trial/) (2094824)

101 98 not (99 or 100) [OPINION PIECES REMOVED] (1343)

102 (2017082* or 201709* or 201710* or 201711* or 201712* or 2018* or 2019*).dc. (3221271)

103 101 and 102 (62)

104 103 use emczd [EMBASE RECORDS] (62)

105 Osteoporosis, Postmenopausal/ (19645)

106 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).ti,ab,kw. (24380)

107 (bone loss* adj5 (postmenopaus* or post-menopaus*)).ti,ab,kw. (4353)

108 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).ti,ab,kw. (207)

109 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).ti,ab,kw. (209)

110 (osteoporo* adj5 "after" adj5 menopaus*).ti,ab,kw. (627)

111 (osteoporo* adj5 menopaus*).ti,ab,kw. (5583)

112 (bone loss* adj5 menopaus*).ti,ab,kw. (1654)

113 (bone loss* adj5 "after" adj5 menopaus*).ti,ab,kw. (475)

114 (osteoporo* adj5 age-related).ti,ab,kw. (1221)

115 (bone loss* adj5 age-related).ti,ab,kw. (1727)

116 (osteoporo* adj5 senil*).ti,ab,kw. (1864)

117 (bone loss* adj5 senil*).ti,ab,kw. (55)

118 or/105-117 (45303)

119 Osteoporosis/ (158815)

120 osteoporo*.ti,ab,kw. (200650)

121 Bone Density/ (142862)

122 (bone? adj3 densit*).ti,ab,kw. (137287)

123 bmd.ti,ab,kw. (78807)

124 bone loss*.ti,ab,kw. (67392)

125 or/119-124 (379658)

126 Menopause/ (77798)

127 Postmenopause/ (91320)

128 (postmenopaus* or post-menopaus*).ti,ab,kw. (164951)

129 or/126-128 (233689)

130 125 and 129 (59403)

131 118 or 130 [POST-MENOPAUSAL OSTEOPOROSIS] (71504)

132 Risedronate Sodium/ (8732)

133 (risedronate or risedronic acid or acrel or actokit or actonel or atelvia or aventis or alesone or atelvia or avestra or benet or boneact or ductonar or juverital or miosen).ti,ab,kw. (7289)

134 (ne 58095 or ne58095 or norifaz or norsed or nurrid or optinate or osteonate).ti,ab,kw. (46)

135 (racidrix or rentop or retonel or ribastamin or ridron or risedon or risedross or risemyl or risendros or riseos or riseratio or risofos or resonate or rizat or seralis or tevanel or vionate).ti,ab,kw. (2106)

136 or/132-135 [RISEDRONATE] (14567)

137 131 and 136 [RISEDRONATE IN POSTMENOPAUSAL OSTEOPOROSIS] (3339)

138 Male/ not (Female/ and Male/) (5515219)

139 137 not 138 [MALE-ONLY REMOVED] (3304)

140 ("201708" or "201709" or "201710" or "201711" or "201712" or 2018* or 2019*).up. (34609819)

141 139 and 140 (1210)

142 141 use cctr [CENTRAL RECORDS] (309)

143 51 or 104 or 142 [ALL DATABASES] (383)

144 remove duplicates from 143 (353) [TOTAL UNIQUE RECORDS]

145 144 use medall [MEDLINE UNIQUE RECORDS] (12)

146 144 use emczd [EMBASE UNIQUE RECORDS] (50)

147 144 use cctr [CENTRAL UNIQUE RECORDS] (291)

Zoledronic

Database: Embase Classic+Embase <1947 to 2019 June 04>, Ovid MEDLINE(R) ALL <1946 to June 04, 2019>, EBM Reviews - Cochrane Central Register of Controlled Trials <April 2019>

Search Strategy:

1 Osteoporosis, Postmenopausal/ (19645)

2 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (24380)

3 (bone loss* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (4353)

4 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (207)

5 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (209)

6 (osteoporo* adj5 "after" adj5 menopaus*).tw,kw. (627)

7 (osteoporo* adj5 menopaus*).tw,kw. (5583)

8 (bone loss* adj5 menopaus*).tw,kw. (1654)

9 (bone loss* adj5 "after" adj5 menopaus*).tw,kw. (475)

10 (osteoporo* adj5 age-related).tw,kw. (1221)

11 (bone loss* adj5 age-related).tw,kw. (1727)

12 (osteoporo* adj5 senil*).tw,kw. (1864)

13 (bone loss* adj5 senil*).tw,kw. (55)

14 or/1-13 (45303)

15 Osteoporosis/ (158815)

16 osteoporo*.tw,kw. (200650)

17 Bone Density/ (142862)

18 (bone? adj3 densit*).tw,kw. (137288)

19 bmd.tw,kw. (78820)

20 bone loss*.tw,kw. (67392)

21 or/15-20 (379669)

22 Menopause/ (77798)

23 Postmenopause/ (91320)

24 (postmenopaus* or post-menopaus*).tw,kw. (164951)

25 or/22-24 (233689)

26 21 and 25 (59403)

27 14 or 26 [POST-MENOPAUSAL OSTEOPOROSIS] (71504)

28 (zolendronate or zoledronic acid or aclasta).tw,kw,rn. (21019)

29 (cgp 42446 or cgp 42446a or cgp42446 or cgp42446a or db00399).tw,kw,rn. (40)

30 (orazol or reclast or zol 446 or zol446 or zolendron* or zometa or zomera).tw,kw,rn. (2280)

31 or/28-30 [ZOLEDRONIC ACID] (21299)

32 27 and 31 [ZOLEDRONIC ACID IN POSTMENOPAUSAL OSTEOPOROSIS] (2426)

33 (controlled clinical trial or randomized controlled trial or pragmatic clinical trial).pt. (1128994)

34 clinical trials as topic.sh. (220409)

35 exp Randomized Controlled Trials as Topic/ (295398)

36 (randomi#ed or randomi#ation* or randomly or RCT? or placebo*).tw,kw. (3155455)

37 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (665659)

38 trial.ti. (755130)

39 or/33-38 (3965361)

40 32 and 39 [ZOLEDRONIC ACID IN POSTMENOPAUSAL OSTEOPOROSIS] (966)

41 Male/ not (Female/ and Male/) (5515219)

42 40 not 41 [MALE-ONLY REMOVED] (947)

43 exp Animals/ not (exp Animals/ and Humans/) (18276792)

44 42 not 43 [ANIMAL-ONLY REMOVED] (627)

45 (comment or editorial or interview or news or newspaper article).pt. (1954050)

46 (letter not (letter and randomized controlled trial)).pt. (2094952)

47 44 not (45 or 46) [OPINION PIECES REMOVED] (625)

48 (2017082* or 201709* or 201710* or 201711* or 201712* or 2018* or 2019*).dt. (2308886)

49 47 and 48 (17)

50 49 use medall [MEDLINE RECORDS] (17)

51 postmenopause osteoporosis/ (13835)

52 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (24380)

53 (bone loss* adj5 (postmenopaus* or post-menopaus*)).tw,kw. (4353)

54 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (207)

55 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).tw,kw. (209)

56 (osteoporo* adj5 "after" adj5 menopaus*).tw,kw. (627)

57 (osteoporo* adj5 menopaus*).tw,kw. (5583)

58 (bone loss* adj5 menopaus*).tw,kw. (1654)

59 (bone loss* adj5 "after" adj5 menopaus*).tw,kw. (475)

60 (osteoporo* adj5 age-related).tw,kw. (1221)

61 (bone loss* adj5 age-related).tw,kw. (1727)

62 (osteoporo* adj5 senil*).tw,kw. (1864)

63 (bone loss* adj5 senil*).tw,kw. (55)

64 or/51-63 (40670)

65 osteoporosis/ (158815)

66 osteoporo*.tw,kw. (200650)

67 bone density/ (142862)

68 (bone? adj3 densit*).tw,kw. (137288)

69 bmd.tw,kw. (78820)

70 bone loss*.tw,kw. (67392)

71 or/65-70 (379669)

72 menopause/ (77798)

73 postmenopause/ (91320)

74 (postmenopaus* or post-menopaus*).tw,kw. (164951)

75 or/72-74 (233689)

76 71 and 75 (59403)

77 64 or 76 [POST-MENOPAUSAL OSTEOPOROSIS] (68733)

78 zoledronic acid/ (18990)

79 (zolendronate or zoledronic acid or aclasta).tw,kw,rn. (21019)

80 (cgp 42446 or cgp 42446a or cgp42446 or cgp42446a or db00399).tw,kw,rn. (40)

81 (orazol or reclast or zol 446 or zol446 or zolendron* or zometa or zomera).tw,kw,rn. (2280)

82 or/78-81 [ZOLEDRONIC ACID] (21771)

83 77 and 82 [ZOLEDRONIC ACID - POST-MENOPAUSAL OSTEOPOROSIS] (2792)

84 randomized controlled trial/ (1037431)

85 controlled clinical study/ (463094)

86 exp "clinical trial (topic)"/ (294922)

87 (randomi#ed or randomi#ation* or randomly or RCT? or placebo*).tw,kw. (3155455)

88 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (665659)

89 trial.ti. (755130)

90 or/84-89 (3926497)

91 83 and 90 [ZOLEDRONIC ACID - POST-MENOPAUSAL OSTEOPOROSIS - RCTs] (1134)

92 male/ not (female/ and male/) (5515219)

93 91 not 92 [MALE-ONLY REMOVED] (1111)

94 exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (49778412)

95 exp human/ or exp human experimentation/ or exp human experiment/ (39370483)

96 94 not 95 (10409650)

97 93 not 96 [ANIMAL-ONLY REMOVED] (1090)

98 editorial.pt. (1096605)

99 letter.pt. not (letter.pt. and randomized controlled trial/) (2094824)

100 97 not (98 or 99) [OPINION PIECES REMOVED] (1079)

101 (2017082* or 201709* or 201710* or 201711* or 201712* or 2018* or 2019*).dc. (3221271)

102 100 and 101 (65)

103 102 use emczd [EMBASE RECORDS] (65)

104 Osteoporosis, Postmenopausal/ (19645)

105 (osteoporo* adj5 (postmenopaus* or post-menopaus*)).ti,ab,kw. (24380)

106 (bone loss* adj5 (postmenopaus* or post-menopaus*)).ti,ab,kw. (4353)

107 (osteoporo* adj5 (perimenopaus* or peri-menopaus*)).ti,ab,kw. (207)

108 (bone loss* adj5 (perimenopaus* or peri-menopaus*)).ti,ab,kw. (209)

109 (osteoporo* adj5 "after" adj5 menopaus*).ti,ab,kw. (627)

110 (osteoporo* adj5 menopaus*).ti,ab,kw. (5583)

111 (bone loss* adj5 menopaus*).ti,ab,kw. (1654)

112 (bone loss* adj5 "after" adj5 menopaus*).ti,ab,kw. (475)

113 (osteoporo* adj5 age-related).ti,ab,kw. (1221)

114 (bone loss* adj5 age-related).ti,ab,kw. (1727)

115 (osteoporo* adj5 senil*).ti,ab,kw. (1864)

116 (bone loss* adj5 senil*).ti,ab,kw. (55)

117 or/104-115 (45296)

118 Osteoporosis/ (158815)

119 osteoporo*.ti,ab,kw. (200650)

120 Bone Density/ (142862)

121 (bone? adj3 densit*).ti,ab,kw. (137287)

122 bmd.ti,ab,kw. (78807)

123 bone loss*.ti,ab,kw. (67392)

124 or/118-123 (379658)

125 Menopause/ (77798)

126 Postmenopause/ (91320)

127 (postmenopaus* or post-menopaus*).ti,ab,kw. (164951)

128 or/125-127 (233689)

129 124 and 128 (59403)

130 117 or 129 [POST-MENOPAUSAL OSTEOPOROSIS] (71498)

131 (zolendronate or zoledronic acid or aclasta).ti,ab,kw. (10991)

132 (cgp 42446 or cgp 42446a or cgp42446 or cgp42446a or db00399).ti,ab,kw. (27)

133 (orazol or reclast or zol 446 or zol446 or zolendron* or zometa or zomera).ti,ab,kw. (1006)

134 or/131-133 [ZOLEDRONIC ACID] (11389)

135 130 and 134 [ZOLEDRONIC ACID IN POSTMENOPAUSAL OSTEOPOROSIS] (1392)

136 Male/ not (Female/ and Male/) (5515219)

137 135 not 136 [MALE-ONLY REMOVED] (1364)

138 ("201708" or "201709" or "201710" or "201711" or "201712" or 2018* or 2019*).up. (34609819)

139 137 and 138 (666)

140 139 use cctr [CENTRAL RECORDS] (197)

141 50 or 103 or 140 [ALL DATABASES] (279)

142 remove duplicates from 141 (251) [TOTAL UNIQUE RECORDS]

143 142 use medall [MEDLINE UNIQUE RECORDS] (17)

144 142 use emczd [EMBASE UNIQUE RECORDS] (52)

145 142 use cctr [CENTRAL UNIQUE RECORDS] (182)