SUPPLEMENTAL DIGITAL CONTENT APPENDIX A. LITERATURE SEARCH STRATEGY

ACOG CLINICAL PRACTICE GUIDELINE NUMBER 1
OSTEOPOROSIS PREVENTION, SCREENING, AND DIAGNOSIS

Database: Ovid MEDLINE(R) 1946 to March Week 4 2021 (August 2018; bridge search February 2021)

Osteoporosis general search

- Each of the questions below begins with this general search; all question searches below start with line 17
- Unless noted, all searches were limited to 2012–present

Line	Search	Results
1	osteoporosis, postmenopausal/ or ((osteoporosis/ or osteoporotic fractures/) and (premenopause/ or perimenopause/ or menopause/ or postmenopause/ or climacteric/))	16267
2	(postmenopaus\$ adj4 osteoporo\$).ti.	2867
3	postmenopaus\$.ti. and *osteoporosis/	815
4	1 or 2 or 3	16383
5	4 and female/	15943
6	*bone resorption/ or *osteogenesis/ or *bone density/ or *bone development/ or *bone remodeling/ or *bone density conservation agents/	74683
7	6 and female/	37652
8	7 and (postmenopause/ or menopause/ or premenopause/ or climacteric/ or postmenopaus\$.mp. or menopaus\$.mp.)	9878
9	5 or 8	19881
10	(osteopen\$ or osteopaen\$).ti.	1996
11	(osteopen\$ or osteopaen\$).mp. and 9	1591
12	10 or 11	3283
13	12 and (postmenopause/ or menopause/ or premenopause/ or climacteric/ or postmenopaus\$.mp. or menopaus\$.mp.)	1722
14	9 or 13	20013
15	limit 14 to (english language and humans)	17144
16	limit 15 to yr="2012 -Current"	4783

Questions 1-3 (prevention techniques, fracture risk reduction, supplements to reduce fracture risk)

Line	Search	Results
17	secondary prevention/ or primary prevention/ or tertiary prevention/ or exercise/ or diet/ or life style/ or (exercise\$ or prevent\$).ti. or prevention.mp.	1989953
18	16 and 17	1544
19	fractures, bone/ or fracture\$.ti.	152395
20	risk reduction/	13352
21	18 and (19 or 20)	442
22	exp vitamin d/ or exp calcium/ or (vitamin d or calcium).ti,ab.	521487
23	16 and 19 and 22	176
24	(calcium adj3 absor\$).mp.	4340
25	exp dietary supplements/	81062
26	"aged, 80 and over"/ or aged/	3219656
27	(exercise\$ or weight-bearing or muscle strength\$ or adverse effect\$ or side effect or hazard\$ or fall\$ or injur\$ or (home adj3 safe\$)).mp.	3573987
28	17 or 25 or 27	4966574
29	16 and 19 and 26 and 28	451

30	middle aged/ or perimenopause/ or premenopause/ or (perimenopause\$ or premenopause).ti,ab.	4482419
31	menopause/ or postmenopause/ or (postmenopaus\$ or menopaus\$).mp.	98611
32	30 not 31	4421479
33	18 not 31	30
34	18 and 30	905
35	33 or 34	905
36	menopause/ or postmenopause/ or (postmenopaus\$ or menopaus\$).ti,ab.	93596
37	35 not 36	168
38	menopause/ or menopaus\$.ti.	32357
39	18 and 38	184
40	(postmenopaus\$ or post-menopaus\$).ti.	22386
41	39 not 40	120
42	39 not 41	64
43	postmenopause/	25293
44	40 or 43	33017
45	18 and 44	706
46	menopaus\$.ti.	14422
47	45 not 46	639
48	45 not 47	67
49	18 not 26	743
50	homes for the aged/ or assisted living facilities/ or nursing homes/	42065
51	29 and 50	0
52	22 or 25	593153
53	prevent\$.ti.	270514
54	secondary prevention/ or primary prevention/ or tertiary prevention/	38829
55	20 or 53 or 54	306713
56	(reduce adj3 risk\$).ti,ab.	54217
57	55 or 56	354907
58	18 and 19 and 57	109
59	age factors/ or drug dosage calculations/	462265
60	(age or race or ethnic\$ or dose or interval\$ or (type adj3 fracture\$)).ti,ab.	3552806
61	59 or 60	3762218
62	58 and 61	46

Question 4 (screening—fractures) and Question 5 (screening—age)

Line	Search	Results
17	osteoporotic fractures/ or exp fractures, bone/ or fracture\$.ti,ab.	269352
18	exp Osteoporotic Fractures/pc or Osteoporosis/di or exp Absorptiometry, Photon/mt or Absorptiometry, Photon/ or mass screening/ or Area Under Curve/ or risk assessment/ or risk factors/ or multiphasic screening/ or (periodic assess\$ or periodic exam\$ or routine test\$).mp. or screen\$.ti,ab. or (fracture risk assessment or FRAX).ti.	1744028
19	16 and 17	2154
20	18 and 19	1207
21	aged/ or "Aged, 80 and over"/	3219656
22	20 and 21	863
23	middle aged/	4479080
24	16 and 23	3053
25	Reproducibility of Results/ or data accuracy/ or Predictive value of tests/ or Roc curve/ or "Sensitivity and specificity"/ or (accura\$ or reliable\$).ti.	883179
26	22 and 25	93
27	24 and 25	214
28	age factors/ or age of onset/ or predictive value of tests/	694049
29	20 and 28	122

30	16 and 18	2046
31	28 and 30	212
32	"Outcome and Process Assessment (Health Care)"/ or "Outcome Assessment (Health Care)"/ or patient outcome assessment/	107944
33	30 and 32	9
34	"Knowledge of Results (Psychology)"/	984
35	32 or 34	108919
36	16 and 35	22

Question 6 (pharmacotherapy and fractures—(bisphosphonates, partial estrogen agonists and antagonists, hormone therapy, denosumab, calcintonin, parathyroid hormone, other) and **Question 7** (pharmacotherapy monitoring—all years)

Line	Search	Results
17	Diphosphonates/ or alendronate/ or Risedronate Sodium/ or etidronic acid/ or "Bisphosphonate-Associated Osteonecrosis of the Jaw"/	21676
18	(bisphosphonate\$ or alendronate or fosamax or fosavance or risedronate or actonel or atelvia or risedronic acid or ibandronate or boniva or etidronate or ibandronic acid or etidronic acid or zoledronate or zoledronic acid or reclast or didronel or pamidronate).ti,ab.	20728
19	17 or 18	26789
20	16 and 19	965
21	Osteoporotic Fractures/ or exp Fractures, Bone/ or fracture\$.ti,ab.	269352
22	20 and 21	559
23	Selective Estrogen Receptor Modulators/ or Raloxifene Hydrochloride/ or tamoxifen/ or Estrogen Receptor Modulators/ or Estrogen Antagonists/	28696
24	(selective estrogen receptor modulator\$ or serm\$1 or raloxifene or evista or bazedoxifene or lasofoxifene or ospemifene or tibolone or tamoxifen or tissue selective estrogen\$).ti,ab.	26138
25	((estrogen\$ or oestrogen\$) adj3 (agonist\$ or antagonist\$)).ti,ab.	4203
26	23 or 24 or 25	38473
27	16 and 26	259
28	21 and 27	139
29	Hormone Replacement Therapy/ or prasterone/ or estradiol/ or estriol/ or estrone/ or estrogens/ or estrogens, conjugated/ or testosterone/ or epitestosterone/ or hydroxytestosterones/ or methenolone/ or methyltestosterone/ or Dehydroepiandrosterone Sulfate/ or Androgens/	220986
30	(testosterone or dehydroepiandrosterone or prasterone).ti. or (estrogen replacement or hormone replacement therapy or premarin or Climara or femhrt or cenestin or Alora or estratest or esclim or estinyl or estrace or estring or vagifem or vivelle or aquest or premphase or menest or ortho-est or prempro).mp.	57055
31	29 or 30	234475
32	Estrogen Replacement Therapy/	15212
33	32 and male/	1217
34	32 and female/	14725
35	33 not 34	38
36	32 not 35	15174
37	(postmenopaus\$ or menopaus\$ or climacteric or premenopaus\$).mp.	109643
38	31 and 37	32791
39	36 or 38	36647
40	exp progestational hormones/ or exp Progestational Hormones, Synthetic/ or exp progesterone/ or (progesterone or progesta\$).ti.	88752
41	37 and 40	7393
42	39 or 41	38079
43	(ogen or Menostar\$ or Vivelle\$ or Estradot or Estraderm or Premphase or Activella or Prefest).mp.	1563
44	42 or 43	39530
45	16 and 44	446

46	21 and 45	125
47	Denosumab/ or (prolia or RANK ligand inhibitor\$ or RANKL inhibitor\$).mp.	1893
48	16 and 47	280
49	21 and 48	195
50	calcitonin/ or calcitriol/	29776
51	(calcintonin\$ or calcitriol).ti,ab. or (fortical or miacalcin).mp.	4573
52	50 or 51	31437
53	16 and 52	68
54	parathyroid hormone/ or teriparatide/	29646
55	(teriparatide or forteo).mp. or (parathyroid hormone or PTH).ti,ab.	37739
56	54 or 55	45262
57	16 and 56	540
58	21 and 57	267
59	exp *bone density conservation agents/	91333
60	16 and 59	1543
61	21 and 60	821
62	19 or 22 or 26 or 44 or 47 or 52 or 56	166656
63	61 not 62	162
64	19 or 22 or 26 or 44 or 47 or 52 or 56 or 59	202860
65	15 and 64	8976
66	bone mineral density/ or (dual-energy x-ray absorptiometry or dexa or dxa or absorptiometry).ti,ab.	66898
67	66 and monitor\$.ti,ab.	2395
68	physiologic monitoring/ or monitor\$.ti.	148518
69	67 or 68	150660
70	65 and 69	245
71	drug monitoring/ or (holiday\$ or monitor\$).ti,ab.	722638
72	65 and 71	428
73	70 or 72	433

Question 8 (referral to a specialist)

Line	Search	Results
17	"referral and consultation"/	68448
18	(referred or referral or referring or consult\$).ti,ab.	363759
19	17 or 18	392839
20	16 and 19	91

Question 9 (soy isoflavones and alternative therapies)

Line	Search	Results
17	soy foods/ or soy milk/ or soybean proteins/ or soybeans/ or isoflavones/ or phytoestrogens/ or exp complementary therapies/ or exp plants, edible/ or exp plants, medicinal/ or exp plant extracts/ or drugs, Chinese herbal/ or holistic health/ or holistic nursing/ or cimicifuga/ or curcuma/ or aromatherapy/ or autogenic training/ or exp behavior therapy/ or exp desensitization, psychologic/ or exp relaxation techniques/ or "biofeedback (psychology)"/ or color therapy/ or dance therapy/ or exp hypnosis/ or "imagery (psychotherapy)"/ or music therapy/ or yoga/ or boron/ or boron compounds/ or strontium/ or exp stem cell transplantation/ or bone marrow transplantation/ or bone transplantation/ or zinc/ or zinc acetate/ or zinc sulfate/ or zinc compounds/	781519
18	soy.ti. or soy isoflavone\$.ti,ab. or zinc.ti,ab.	103454
19	(turmeric or curcuma or ginseng or panax or dang gui or dong quai or angelica or cohosh or cimicifuga or damaina or golden seal or mother wort or dandelion or licorice root or chamomile or raspberry or sasparilla or spearmint or yerba or chamomile or valerian or remifenin or affirmation\$ or deep breathing or relaxation or	186813

	meditation or yoga or guided imagery or massage or hydrotherapy or ginkgo or licorice or primrose or biofeedback or t'ai chi or tai chi or boron or strontium or strothium or chlorocalcium or chloro calcium).mp.	
20	((alternative or complementary) adj (therap\$ or medicine\$ or treatment\$)).ti,ab.	40889
21	(bone marrow.ti,ab. or bone marrow cells/ or bone marrow/ or stem cell\$.ti,ab. or exp stem cells/) and (transplants/ or transplantation/ or cell transplantation/ or tissue transplantation/ or transplant\$.ti,ab.)	113024
22	*prasterone/ or *estradiol/ or *estriol/ or *estrone/ or *estrogens, conjugated/ or *estrogens/ or testosterone/ or epitestosterone/ or hydroxytestosterones/ or methenolone/ or methyltestosterone/ or dehydroepiandrosterone sulfate/ or *hormone replacement therapy/ or *androgens/	162185
23	(dehydroepiandrosterone or testosterone or prasterone or premarin or alora).ti.	26417
24	(climara or femhrt or cenestin or estratest or esclim or estinyl or estrace or estring or vagifem or vivelle or estrogen replacement or hrt or ert or hormone replacement therapy or aquest or premphase or menest or ortho-est or prempro).mp.	38278
25	22 or 23 or 24	188204
26	25 and (postmenopaus\$ or menopaus\$ or climacteric or premenopaus\$).mp.	28064
27	26 or *estrogen replacement therapy/	30286
28	(exp *progestational hormones/ or exp *progestational hormones, synthetic/ or exp *progesterone/ or progesterone.ti. or progesta\$.ti.) and (postmenopaus\$ or menopaus\$ or climacteric or premenopaus\$).mp.	4083
29	27 or 28	31580
30	exp plant preparations/ or phytotherapy/ or exp plant extracts/ or drug compounding/ or individualized medicine/	286845
31	(bioidentical\$ or bio-identical\$ or compounded or compounding).mp. or natural.ti.	127065
32	30 or 31	386608
33	29 and 32	987
34	17 or 18 or 19 or 20 or 21 or 33	1020137
35	16 and 34	355

Costs

Line	Search	Results
17	ec.fs. or exp economics/ or exp "costs and cost analysis"/ or cost-benefit analysis/ or exp health care costs/ or exp cost control/ or exp cost sharing/ or exp health expenditures/	751214
18	(cost-effectiveness or economic analysis or (expenditure\$ not energy)).mp. or (cost or costs or economic\$).ti.	193750
19	17 or 18	794393
20	16 and 19	141

Health equity—limited to 2000-present

Line	Search	Results
17	Vulnerable populations/ or medically underserved area/ or Socioeconomic factors/ or Social segregation/ or Race factors/ or Race relations/ or Racism/ or Prejudice/ or Poverty/ or Social class/ or Healthcare disparities/ or Health status disparities/ or Poverty areas/ or Urban population/ or Rural Population/ or Ethnic groups/ or *African Americans/ or *Hispanic Americans/ or *Asian Americans/	449817
18	(ethnic\$ or race or racial\$ or socio-economic or socioeconomic or Hispanic\$ or Latino\$ or Latina\$ or Latinx or Asian American\$).ti.	74566
19	(equit\$ or inequit\$ or inequalit\$ or disparit\$ or equality or racis\$ or prejudic\$ or race-relat\$ or disproportionate risk\$ or systemic barrier\$ or SES or SEP or sociodemographic\$ or socio-demographic\$ or income or wealth\$ or poverty or educational level or (level adj education\$) or educational attainment or well	345303

	educated or better educated or unemploy\$ or home owner\$ or tenure or affluen\$ or well off or better off or worse off).ti,ab.	
20	(implicit adj3 bias).ti,ab	603
21	((bias or prejudic\$ or racis\$) and (unconcious\$ or implicit\$ or institutional\$ or structural\$ or dismantl\$)).ti,ab.	6151
22	((social\$ or socio-economic or socioeconomic or economic or structural or material) adj3 (advantage\$ or disadvantage\$ or exclude\$ or exclusion or include\$ or inclusion or status or position or gradient\$ or hierarch\$ or class\$ or determinant\$)).ti,ab.	107847
23	(health adj3 (gap\$ or gradient\$ or hierarch\$)).ti,ab.	3211
24	((African or Black) adj3 American\$).ti.	16529
25	17 or 18 or 19 or 20 or 21 or 22 or 23 or 24	738086
26	15 and 25	486
27	limit 26 to yr="2000 -Current"	407
28	Developing Countries/ or Moldova/ or Botswana/ or Gabon/ or Paraguay/ or Egypt/ or Turkmenistan/ or Indonesia/ or Palestine.mp. or Vietnam/ or Philippines/ or El Salvador/ or Bolivia/ or South Africa/ or Kyrgyzstan/ or Iraq/ or Cabo Verde/ or Morocco/ or Nicaragua/ or Guatemala/ or Namibia/ or Guyana/ or Micronesia/ or Tajikistan/ or Honduras/ or India/ or Bhutan/ or (Timor adj Leste).mp. or Vanuatu/ or Congo/ or Equatorial Guinea/ or Kiribati/ or Laos/ or Bangladesh/ or Ghana/ or Zambia/ or "Sao Tome And Principe"/ or Cambodia/ or Nepal/ or Myanmar/ or Kenya/ or Pakistan/ or Swaziland/ or Syria/ or Angola/ or Tanzania/ or Nigeria/ or Cameroon/ or Papua New Guinea/ or Zimbabwe/ or Solomon Islands/ or Mauritania/ or Madagascar/ or Rwanda/ or Comoros/ or Lesotho/ or Senegal/ or Haiti/ or Uganda/ or Sudan/ or Togo/ or Benin/ or Yemen/ or Afghanistan/ or Malawi/ or Cote d'Ivoire/ or Djibouti/ or Gambia/ or Ethiopia/ or Mali/ or "Democratic Republic Of The Congo"/ or Liberia/ or Guinea-Bissau/ or Eritrea/ or Sierra Leone/ or Mozambique/ or South Sudan/ or Guinea/ or Burundi/ or Burkina Faso/ or Chad/ or Niger/ or Central African Republic/ or "Democratic People's Republic Of Korea"/ or somalia/	487339
29	(Developing adj3 Countr\$).ti,ab.	52987
30	(Third adj World adj Countr\$).ti,ab.	946
31	(low adj3 middle adj3 income\$).ti.	3729
32	28 or 29 or 30 or 31	511748
33	27 not 32	375

Database: PubMed

• Final results limited to English and in process citations: english[la] AND (publisher[sb] OR inprocess[sb] OR pubmednotmedline[sb] OR (pubstatusnihms AND publisher[sb]) OR (pubstatuspmcsd AND publisher[sb]))

Line	Search	Results
1	(osteoporos*[ti] OR osteopen*[ti] OR osteopaen*[ti] OR bone dens*[ti]) AND (postmenopaus*[tiab] OR post-menopaus*[tiab] OR menopaus*[tiab] OR pre-menopaus*[tiab] OR climacteric[tiab] OR perimenopaus*[tiab] OR peri-menopaus*[tiab])	8,001
2	osteopor*[ti] NOT (child*[ti] OR pediatr*[ti] OR paediatr*[ti] OR male[ti] OR males[ti] OR man[ti] OR men[ti])	30,634
3	equit*[tiab] OR inequiit*[tiab] OR inequalit*[tiab] OR disparit*[tiab] OR equality[tiab] OR dispropORt*[tiab] OR ethnic*[tiab] OR race[tiab] OR racial*[tiab] OR racis*[tiab] OR prejudic*[tiab] OR race-relat*[tiab] OR dispropORtionate risk[tiab] OR systemic barrier*[tiab] OR health gap*[tiab] OR health gradient*[tiab] OR health hierarch*[tiab] OR SES[tiab] OR SEP[tiab] OR sociodemographic*[tiab] OR income[tiab] OR wealth*[tiab] OR poverty[tiab] OR educational level[tiab] OR "level of education"[tiab] OR educational attainment[tiab] OR well educated[tiab] OR better educated[tiab] OR unemploy*[tiab] OR home owner*[tiab] OR tenure[tiab] OR affluen*[tiab] OR well off[tiab] OR better off[tiab] OR worse off[tiab] OR social*[ti] OR socio-economic[ti] OR socioeconomic[ti] OR economic[ti] OR structural[ti] OR material[ti] OR African American*[tiab] OR Black[ti]	1,780,650

	OR Black American*[tiab] OR Hispanic*[tiab] OR Latino*[tiab] OR Latina*[tiab] OR Latinx[tiab] OR Asian American*[tiab] OR poverty[tiab] OR disparit*[tiab] OR urban[tiab] OR rural[tiab] OR vulnerable[tiab] OR underserved[tiab] OR ((bias[tiab] or prejudic*[tiab] or racis*[tiab]) AND (unconcious*[tiab] or implicit*[tiab] or institutional*[tiab] or structural*[tiab] or dismantl*[tiab])) OR ((social*[tiab] or socioeconomic[tiab] or economic[tiab] or structural[tiab] or material[tiab]) AND (advantage*[tiab] or disadvantage*[tiab] or exclude*[tiab] or exclusion[tiab] or include*[tiab] or inclusion[tiab] or status[tiab] or position[tiab] or gradient*[tiab] or hierarch*[tiab] or class*[tiab] or determinant*[tiab])) - Saved search	4 400 455
4	meta analysis[tiab] OR meta-analysis[tiab] OR systematic review[tiab] OR quantitative review[tiab] OR quantitative overview[tiab] OR randomized controlled[tiab] OR randomised controlled[tiab] OR randomised controlled[tiab] OR case controlled[tiab] OR case controlled[tiab] OR case-controlled[tiab] OR cross-sectional[tiab] OR case-controlled[tiab] OR cross-sectional[tiab] OR prospective study[tiab] OR prospective studies[tiab] OR non-randomised[tiab] OR non-randomised[tiab] OR non-randomised[tiab] OR guidelines[tiab] OR review[tiab] OR standard[tiab] OR standards[tiab] OR consensus[tiab] OR recommendation statement*[tiab] OR committee opinion*[tiab] OR observational stud*[tiab] OR observational trial*[tiab] OR observation stud*[tiab] OR observation stud*[tiab] OR observation trial*[tiab] - Saved search	4,400,155
5	(#1 OR #2) AND #3	2,008
6	#5 AND #4	967
7	#5 NOT #6	1,041
8	#1 AND #4	2,795
9	#1 NOT #8	5,206

Osteoporosis and breast cancer

Database: Ovid MEDLINE(R) <1946 to May Week 3 2021>

Line	Search	Results
1	osteoporosis, postmenopausal/ or ((osteoporosis/ or osteoporotic fractures/) and (premenopause/ or perimenopause/ or menopause/ or postmenopause/ or climacteric/))	16332
2	(postmenopaus\$ adj4 osteoporo\$).ti.	2885
3	postmenopaus\$.ti. and *osteoporosis/	822
4	1 or 2 or 3	16448
5	4 and female/	16007
6	*bone resorption/ or *osteogenesis/ or *bone density/ or *bone development/ or *bone remodeling/ or *bone density conservation agents/	75195
7	6 and female/	37861
8	7 and (postmenopause/ or menopause/ or premenopause/ or climacteric/ or postmenopaus\$.mp. or menopaus\$.mp.)	9917
9	5 or 8	19960
10	(osteopen\$ or osteopaen\$).ti.	2010
11	(osteopen\$ or osteopaen\$).mp. and 9	1598
12	10 or 11	3303
13	12 and (postmenopause/ or menopause/ or premenopause/ or climacteric/ or postmenopaus\$.mp. or menopaus\$.mp.)	1731
14	9 or 13	20094
15	limit 14 to (english language and humans)	17221
16	limit 15 to yr="2012 -Current"	4860

17	(breast neoplasms/ and (survivors/ or neoplasm recurrence, local/)) or (breast neoplasms/ and survivor\$.ti,ab.) or breast cancer survivor\$.ti,ab. or (survivor\$ adj2 breast adj3 (cancer or neoplasm\$)).ti,ab. or (survivor\$ adj2 (cancer or neoplasm\$) adj2 breast).ti,ab.	20807
18	*breast neoplasms/ or (breast\$ adj3 (cancer\$ or neoplas\$)).ti.	263284
19	17 or 18	264529
20	16 and 19	197

Database: PubMed

Line	Search	Results
1	(osteopor*[ti] OR osteopen*[ti] OR osteopaen*[ti] OR bone density[ti] OR bisphosphonate*[ti] OR alendronate[ti] OR risedronate[ti] OR pamidronate[ti] OR ranelate[ti] OR teriparatide[ti] OR zoledron*[ti] OR ibandronate[ti] OR fosamax[ti] OR actonel[ti] OR boniva[tiab] OR reclast[ti] OR zometa[ti])	49,786
2	(postmenopaus*[tiab] OR post-menopaus*[tiab] OR premenopaus*[tiab] OR perimenopaus*[tiab] OR perimenopaus*[tiab] OR menopaus*[tiab])	105,069
3	(breast*[ti] AND (cancer*[tiab] OR neoplas*[tiab] OR carcinoma*[ti])	239,265
4	#1 AND #2 AND #3	262
5	#1 AND #2 AND #3 from 2012 - 2021	139
6	english[la] AND (publisher[sb] OR inprocess[sb] OR pubmednotmedline[sb] OR (pubstatusnihms AND publisher[sb]) OR (pubstatuspmcsd AND publisher[sb])) - Saved search	4,615,052
7	#5 AND #6	39

SUPPLEMENTAL DIGITAL CONTENT APPENDIX B. PRISMA FLOW DIAGRAM

ACOG CLINICAL PRACTICE GUIDELINE NUMBER 1
OSTEOPOROSIS PREVENTION, SCREENING, AND DIAGNOSIS

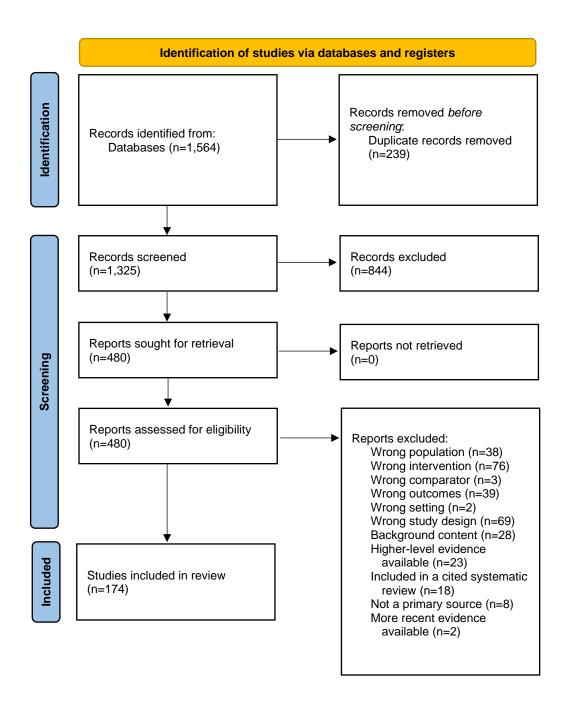


Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram summarizing the literature search and selection process for ACOG Clinical Practice Guideline No.1. *Osteoporosis Prevention, Screening, and Diagnosis*.

SUPPLEMENTAL DIGITAL CONTENT APPENDIX C. EVIDENCE TABLES

ACOG CLINICAL PRACTICE GUIDELINE NUMBER 1
OSTEOPOROSIS PREVENTION, SCREENING, AND DIAGNOSIS

Physical Activity									
Author, Year	Setting	Design/ Approach	Participants	Intervention	Comparator	Sample Size	Outcomes	Risk of Bias	Results
Basat 2013	Istanbul, Turkey	Prospective, randomized controlled 6- month interventional trial	Postmenopausal women with osteopenia	Daily calcium (1,200 mg) and vitamin D (800 international units [IU]) Training groups were prescribed strengthening or high-impact exercises	Daily calcium (1,200 mg) and vitamin D (800 IU) Control group was asked not to participate in any exercise training programs	42 postmenopau- sal women with osteopenia	Bone mineral density (BMD), bone turnover markers and health-related quality of life (HRQoL)	Low risk of bias, no blinding mechanism	Our data suggest that 6-month supervised high-impact exercise training can be effective in prevention of bone loss at lumbar spine and femoral neck. These data also indicate that both supervised training programs improve HRQoL in postmenopausal women.
Fratini 2016	Global	Systematic review and meta-analysis	Postmenopau- sal women	Whole body vibration treatments	Exercise training or absence of interventions	Nine studies including 527 postmenopau- sal women	BMD values for lumbar spine, total hip, femoral neck, trochanter, and whole body	High quality review	Whole-body vibration treatments in elderly women can reduce BMD decline, however, many factors (eg, amplitude, frequency and subject posture) affect the capacity of the vibrations to propagate to the target site; the adequate level of stimulation required to produce these effects has not yet been defined.
Garcia Gomariz 2018	Spain	Randomized clinical trial	Postmenopausal women without osteoporosis taking calcium plus vitamin D supplements	High impact and high resistance training program for 60 minutes, 2x per week	Walking 6 km in 1 hour, 3– 5x per week	34 postmenopau- sal women	T-score at femoral neck and lumbar spine	Low risk of bias	Calcium plus vitamin D supplementation combined with specifically oriented exercises had a higher impact in the femoral neck than walking at an intense pace. As there were no differences at the lumbar spine level, the results were, however, inconclusive concerning which type of exercise was the most convenient.

Gonzalo Encabo 2019	Canada	Two-center, Two-arm, 12- month randomized controlled trial	Postmenopausal women aged 50–74 years	300 minutes/week high intensity aerobic exercise	150 minutes/week moderate intensity aerobic exercise	379 included in analyses	BMD and BMC measured baseline, 12- and 24- months by DXA	Low risk of bias, except for "selective outcome reporting" category	BMD was slightly higher (0.006 g/cm²) in HIGH dose group at 12-months. Statistically significant difference remained at 24-months. No differences for BMC.
Howe 2011	Global	Systematic review	Healthy, postmenopau- sal women aged 45–70 years	Exercise program (eg walking, calisthenics, resisted strengthening)	Usual activity or placebo with or without pharmacolog- ical consumption	43 RCTs with 4,320 participants included in qualitative analysis	Number of incident fractures and BMD, BMC, or calcium bone index	Moderate quality review	Increase in BMD of the neck of the femur with non-weight bearing high force exercises (mean difference 1.03 (95% CI, 0.24–1.82) and a benefit for the spine BMD with combination exercise programs (MD, 3.22, 95% CI, 1.80–3.64).
Jepsen 2019	Denmark	Randomized controlled trial	Postmenopausal women 50 years of age or older with either one or more vertebral fractures within last 3 years	Whole body vibration and teriparatide	Teriparatide alone	33 included in analyses (15 EG, 18 CG)	BMD of lumbar spine and total hip by DXA at baseline, 6- and 12- months	Low risk of bias	The WBV and teriparatide group had significantly increased BMD at lumbar spine compared to teriparatide alone group. No other treatment effects were observed in hip BMD, bone microarchitecture parameters, or sclerostin levels in either group.
Marín- Cascales 2018A	Global	Systematic review	Postmenopausal and/or older women (age mean of 65 years or older)	Multicomp- onent training (MT)	No MT	15 studies met the inclusion criteria and were included	BMD or BMC of different sites or muscle mass	Moderate quality review	Studies showed contrasting results, likely due to ranges in participant age, and different training methods. Overall, appears that exercise programs that combine resistance, weight-bearing, and impact-aerobic activities may increase or prevent muscle and skeletal mass loss during aging process.
Marín- Cascales 2018B	Global	Systematic review and meta-analysis	Postmenopausal women or women older than 65 years	Whole body vibration	No whole body vibration	10 studies included in meta-analysis	Total, femoral neck, or lumbar spine BMD	High quality review	Significant pre-post improvements in BMD of the lumbar spine were identified following WBV protocols (<i>P</i> =.03). Significant differences in femoral neck BMD (<i>P</i> =.03) were also found between intervention and control groups when analyzing studies that included postmenopausal women younger than 65 years.
Martyn-St James 2008	Global	Systematic review and meta-analysis	Sedentary postmenopau- sal women	Walking as sole exercise	No walking	Eight studies included in meta-analysis	BMD at lumbar spine, femoral neck and total hip	High quality review	Walking programs alone may positively impact BMD of the hip, although the results were inconclusive.

Oliveira 2016	Global	Systematic review and meta-analysis	Postmenopau- sal women	Whole-body vibration exercise	No whole- body vibration exercise	15 studies included in quantitative analysis	Change between pre- and post- intervention in the areal BMD (aBMD) or trabecular volumetric BMD (vBMDt)	High quality review	No differences were observed in the primary analysis. WBV was found to improve aBMD compared with the control group after exclusion of studies with low-quality methodology.
Sun 2016	Global	Systematic review and meta-analysis	Perimenopau- sal and postmenopau- sal women aged 45 years or older	Tai chi exercise or tai chi and calcium (Ca) supplement	No tai chi exercise, or Ca supplement only	Seven studies included in meta-analysis	Efficacy of tai chi exercise on BMD of lumbar spine and bone turnover markers	High quality review	Significant effect of tai chi exercise on BMD change at the spine compared with no treatment in perimenopausal and postmenopausal women; when tai chi exercise combined with a Ca supplement was compared with the Ca supplement alone the result of BMD change at the spine showed no significant effect.
Watson 2018	Australia	Randomized controlled trial	Postmenopausal women older than 58 years with low bone mass (T-score <-1.0)	8-month, twice-weekly, 30-minute, supervised HiRIT program (high-intensity, progressive resistance and impact weight- bearing training)	8-month, twice-weekly, 30-minute, unsupervised low-intensity home-based exercise	101 participants	Height, body mass, bone- relevant lifetime and current physical activity participation scores; BMD for femoral neck and lumbar spine	Low risk of bias	HiRIT was efficacious and induced no adverse events and effects were superior to control group for lumbar spine, femoral neck, height, and all functional performance measures.
Watson 2019	Australia	Subanalysis of randomized controlled trial	Postmenopausal women older than 58 years with low bone mass (T-score <-1.0)	8-month, twice-weekly, 30-minute, supervised HiRIT program (high-intensity, progressive resistance and impact weight- bearing training)	8-month, twice-weekly, 30-minute, unsupervised low-intensity home-based exercise	51 participants	Lateral thoracolumbar DXA scans; Cobb angle; vertebral fracture identification; Clinical kyphosis measure- ments	Low risk of bias, except for selective outcome reporting	Supervised HiRIT was not associated with an increased risk of vertebral fracture in postmenopausal women with low bone mass. Clinically relevant improvement in thoracic kyphosis was observed following 8 months of supervised HiRIT.
Wayne, 2012	USA	Pilot pragmatic, randomized trial	Postmenopausal osteopenic women, aged 45–70	9 months of Tai Chi (TC) training in addition to usual care	Usual care alone	43 in TC group and 43 in usual care group. 26 in TC were	DXA measures of BMD of femoral neck, total hip, and	Low risk of bias	No intent-to-treat analyses were considered statistically significant for BMD. Per protocol analyses of femoral neck BMD changes were significantly

						considered per protocol	lumbar spine, and serum levels of C- terminal telopeptide of type I CTX and OSC		different between TC and UC (+0.04 vs0.98%; <i>P</i> =0.05).
Xu 2016	Global	Systematic review	Female participants (girls to postmenopausal or older women)	Exercise	No exercise	12 reviews included in synthesis	Effect of exercise on bone status	Moderate quality review	Combined-impact exercise protocols (impact exercise with resistance training) are the best choice to preserve/improve BMD in pre- and postmenopausal women; WBV exercises have no beneficial effects on bone in postmenopausal or elderly women.
Zhao 2014	Global	Meta-analysis	Premenopau- sal women	Jumping exercise	No jumping exercise	Six studies included	BMD at femoral neck, trochanter, and lumbar spine	Moderate quality review	Jumping exercise significantly increased BMD in the femoral neck (<i>P</i> <.001) and trochanter (<i>P</i> <.001); however, the lumbar spine seemed to benefit less from such high-impact exercise (<i>P</i> =.181).
Zhao 2015	Global	Meta-analysis	Healthy postmenopau- sal women	Resistance- alone or combined resistance training	Non-exercise control or sham exercise	24 studies	Change in BMD at femoral neck and lumbar spine determined by DXA or DPA on the preand postexercise interventions	High quality review	Overall analysis suggested that resistance training significantly increased femoral neck BMD and lumbar spine BMD; however subgroup analysis indicated that combined resistance training programs significantly affected both the hip BMD and spine BMD, whereas resistance-alone protocols only produced nonsignificant positive effects both on femoral neck and lumbar spine BMD.
Zhao 2017	Global	Systematic review and meta-analysis	Postmenopausal women	Combined exercise interventions	Non-exercise group	11 studies with 1,601 postmenopau- sal women	Lumbar spine, femoral neck, total hip, and total body BMD	High quality review	Exercise integrating different physical activities significantly increased lumbar spine (<i>P</i> =.019), femoral neck (<i>P</i> =.018), total hip (<i>P</i> =.016), and total body (<i>P</i> =.014) BMD; combined exercise interventions generated a beneficial effect on femoral neck BMD (<i>P</i> =.020) in groups with women aged younger than 60 years and significantly improved lumbar spine BMD (<i>P</i> =.016) in groups with women aged 60 years or older.

Vitamin D and Calcium

Author, Year	Setting	Design/ Approach	Participants	Intervention	Comparator	Sample Size	Outcomes	Risk of Bias	Results
Grossman 2018 (USPSTF) Supplementa- tion	USA	Guideline	Community dwelling adults, 65 years or older without osteoporosis or vitamin D deficiency	Vitamin D, calcium, and combined supplementa- tion	Other interventions and supplementations or placebo	Systematic reviews, RCTs, and observational studies	Falls and fall- related morbidity and mortality	5.8 out of 7 (target users are not clearly defined and the procedure for updating guideline is not discussed)	USPSTF recommends against daily supplementation with 400 IU or less of vitamin D and 1,000 mg or less of calcium for the primary prevention of fractures in community-dwelling, postmenopausal women. USPSTF concludes that the current evidence is insufficient to assess the balance of the benefits and harms of vitamin D and calcium supplementation, alone or combined, for the primary prevention of fractures in community-dwelling, asymptomatic men and premenopausal women.
Holick 2011 (endocrine society)	USA	Guideline	Individuals at risk for vitamin D deficiency	Screening for vitamin D deficiency, supplementa- tion, and prevention	Other screening and treatments for vitamin D deficiency	Studies on vitamin D deficiency	Recommenda- tions for evaluation, treatment, and prevention of vitamin D deficiency	5 out of 7 (did not describe methods of systematic review/litera- ture search nor how the literature was selected)	Task Force recommended supplementation at suggested daily intake and tolerable upper limit levels, depending on age and clinical circumstances.
IOM 2011	USA	Guideline	All life stage groups except infants up to 12 months of age	Calcium and vitamin D	Different doses and intakes of calcium and vitamin D	Various systematic reviews on calcium and vitamin D dosages and intake	Health outcomes related to calcium and vitamin D, including falls and skeletal health	6 out of 7 (no information on future updating procedures)	Women 51 through 70 years of age: RDA 1,200 mg/day Calcium; Adults 51–70 years of age: RDA 600 IU/day vitamin D; Adults older than 70 years : RDA 800 IU/day vitamin D.
Kahwati 2018 (USPSTF)	Global	Systematic review	Community dwelling adults	Supplementation with vitamin D and/or calcium	No supplementa- tion, placebo, lower- or higher-dose regimens	11 RCTs (N=51,419)	Incident fracture, fracture- related morbidity and mortality, kidney stones, cardiovascular events, and cancer	Moderate quality review	Vitamin D supplementation alone or with calcium was not associated with reduced fracture incidence among community-dwelling adults without known vitamin D deficiency, osteoporosis, or prior fracture. Vitamin D with calcium was associated with an increase in the incidence of kidney stones.

Krist 2021	USA	Guideline	Community- dwelling, nonpregnant adults aged 18 years or older	Screening for vitamin D deficiency	Other screening methods	Articles about vitamin D deficiency	Benefits and harms of screening for vitamin D deficiency	6 out of 7	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for vitamin D deficiency in asymptomatic adults. (I statement).
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Screening a	Screening and Diagnosis										
Author, Year	Setting	Design/ Approach	Participants	Intervention	Comparator	Sample Size	Outcomes	Risk of Bias	Results		
Camacho 2020 (AACE)	USA	Guideline	Postmenopausal women	Screening and pharmacologic treatment for osteoporosis	Other screening methods and treatments	Articles about screening for and treating osteoporosis	Recommenda- tions for screening for and treating osteoporosis	6 out of 7 (no information on public comment or the role of the funding body)	The Executive Summary of this 2020 updated guideline contains 52 recommendations.		
Cosman 2014 (NOF)	Global	Guideline	Postmenopausal women and men age 50 and older	Treatments and risk assessments of osteoporosis	Other treatments or placebo	Systematic Reviews, RCTs, and Observational studies	Prevention, diagnosis, and management of osteoporosis	5 out of 7 (does not explain methodology)	Recommendations for vitamin D and calcium intake, weight-bearing exercise, diagnostic assessment, monitoring patients, and pharmacological treatment.		
Curry, 2018 (USPSTF)	USA	Guideline	Postmenopau- sal women and older men	Screening and treatment for osteoporotic fractures	Other screening methods and treatments	Systematic Reviews, RCTs, and observational studies	Efficacy of screening and treatment of osteoporotic fractures	5.8 out of 7 (target users are not clearly defined and the procedure for updating guideline is not discussed)	The USPSTF recommends screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in women 65 years and older.		
Hillier 2012	USA	Cohort study	Community- dwelling women age 65 or older	Height loss in older women or vertebral fractures	No height loss or vertebral fractures	3,124 women	Risk of hip fractures, non- spine fractures, and mortality.	Moderate risk of bias due to recruitment of participants	Height loss greater than 5 cm was associated with a marked increased risk of hip fracture [hazard ratio (HR) 1.50, 95% confidence interval (CI), 1.06–2.12], non-spine fracture (HR 1.48; 95% CI, 1.20–1.83), and mortality (1.45; 95% CI, 1.21–1.73)		

Kanis 2010	Global	Review	Adult women with osteoporosis	Use of FRAX	Other screening tools for osteoporosis	Various studies on treatment and assessment of osteoporosis	Development and use of FRAX in osteoporosis	N/A	The FRAX tool integrates information on fracture risk from clinical risk factors with or without the use of BMD and can be used to improve the targeting of individuals at high fracture risk.
Kanis 2011	Global	Review	Patients and clinicians	Resource documents and joint position statements of ISCD and IOF	N/A	Various guidelines and documents	Use of FRAX in clinical practice, details on clinical risk factors in FRAX	N/A	While FRAX does not define intervention thresholds, which depend on country-specific considerations, it provides a platform to assess fracture probability which is needed to make rational treatment decisions by clinicians and public health agencies.
NAMS 2010	Global	Guideline	Postmenopau- sal women	Evaluation and treatment for osteoporosis	Evaluation and treatment for osteoporosis	Various systematic reviews	Management of osteoporosis	6.3 out of 7	Management strategies for postmenopausal women involve identifying those at risk for fracture, followed by instituting measures that focus on reducing modifiable risk factors through dietary and lifestyle changes, and if needed, pharmacologic therapy.
NICE 2017	Global	Guideline	Adult patients	Assessment of fragility fracture risk in adults	Various assessment strategies for fracture risk	Systematic reviews, clinical studies, and observational studies	Assessment of fragility fracture risk	6.4 out of 7	Recommendations on risk assessment for when, who, and how.
Siminoski 2005	North America	Prospective analysis of placebo arm of two randomized controlled trials	Postmenopausal women up to the age of 85 years with vertebral fractures and low spinal BMD	Placebo plus calcium and vitamin D (as needed)	N/A	985 women	Height loss	High risk of bias in incomplete outcome data, unclear for selective reporting	Strong relationship between amount of height loss and the risk of a new vertebral fracture. Height loss of 2.0 cm or less over 1–3 years has acceptable accuracy for ruling out an incident fracture.

Viswanathan 2018 (USPSTF)	USA	Systematic review and meta-analysis	Adults 40 years and older	Screening, clinical risk assessment, and pharmacother- apy for treatment or prevention of osteoporosis	No screening group, other risk assessments, or placebo	168 studies included	Incident fractures and related morbidity and mortality, diagnostic and predictive accuracy, harms of screening or treatment	Moderate quality review	Two studies included participants with widely varying baseline BMD. Both suggest no advantage to repeated bone measurement testing (at 8 years and 3.7 years apart). However, three studies that developed prognostic models suggested that the optimal screening interval varies by baseline BMD. Age and use of hormone replacement therapy also influence optimal screening intervals.
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Screening Intervals										
Author, Year	Setting	Design/ Approach	Participants	Intervention	Comparator	Sample Size	Outcomes	Risk of Bias	Results	
Camacho 2020 (AACE)	USA	Guideline	Postmenopau- sal women	Screening and pharmacologic treatment for osteoporosis	Other screening methods and treatments	Articles about screening for and treating osteoporosis	Recommenda- tions for screening for and treating osteoporosis	6 out of 7 (no information of public comment or the role of the funding body)	The Executive Summary of this 2020 updated guideline contains 52 recommendations.	
Curry, 2018 (USPSTF)	USA	Guideline	Postmenopau- sal women and older men	Screening and treatment for osteoporotic fractures	Other screening methods and treatments	Systematic reviews, RCTs, and Observational studies	Efficacy of screening and treatment of osteoporotic fractures	5.8 out of 7 (target users are not clearly defined and the procedure for updating guideline is not discussed)	The USPSTF recommends screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in women 65 years and older.	

Gourlay 2015	USA	Cohort study	Postmenopausal women aged 50–64	BMD screening	BMD rescreening	4,068 women	Time interval for 1% of participants in three age groups to transition from baseline T-score categories to hip or clinical vertebral fracture before developing osteoporosis	Low risk of bias	Due to very low rates of major osteoporotic fracture, postmenopausal women aged 50–64 years without osteoporosis on a first BMD test are unlikely to benefit from frequent rescreening before age 65.
Gourlay 2012	USA	Cohort study	Ambulatory women 65 years of age or older	Normal BMD at baseline	Osteopenia at baseline	4,957 women	Estimated intervals for 10% of participants to make the transition from normal BMD or osteopenia at baseline to osteoporosis before fracture	Low risk of bias	Data indicate that osteoporosis would develop in less than 10% of older, postmenopausal women during rescreening intervals of approximately 15 years for women with normal bone density or mild osteopenia, 5 years for women with moderate osteopenia, and 1 year for women with advanced osteopenia.
Viswanathan 2018 (USPSTF)	USA	Systematic review and meta-analysis	Adults 40 years and older	Screening, clinical risk assessment, and pharmacother- apy for treatment or prevention of osteoporosis	No screening group, other risk assessments, or placebo	168 studies included	Incident fractures and related morbidity and mortality, diagnostic and predictive accuracy, harms of screening or treatment	Moderate quality review	Two studies included participants with widely varying baseline BMD. Both suggest no advantage to repeated bone measurement testing (at 8 years and 3.7 years apart). However, three studies that developed prognostic models suggested that the optimal screening interval varies by baseline BMD. Age and use of hormone replacement therapy also influence optimal screening intervals.
Ward 2017 (Expert Panel on Musculoskele- tal Imaging)	Global	Guideline	Women older than 65 years and men older than 70 years	Screening and monitoring methods for osteoporosis	Other screening and monitoring methods for osteoporosis	Various studies on screening and monitoring of osteoporosis	Determination of appropriate imaging examinations for diagnosis and treatment of osteoporosis and bone mineral density	5 out of 7 (evidence selection and methodology unclear)	Dual x-ray absorptiometry is the primary diagnostic modality by which to screen women older than 65 years and men older than 70 years for osteoporosis. Quantitative CT is useful in patients with advanced degenerative bony changes in their spines.

Fall Prevent	ion								
Author, Year	Setting	Design/ Approach	Participants	Intervention	Comparator	Sample Size	Outcomes	Risk of Bias	Results
Camacho 2020 (AACE)	USA	Guideline	Postmenopausal women	Screening and pharmacologic treatment for osteoporosis	Other screening methods and treatments	Articles about screening for and treating osteoporosis	Recommenda- tions for screening for and treating osteoporosis	6 out of 7 (no information on public comment or the role of the funding body)	R18: Provide counseling on reducing risk of falls, particularly among the elderly (Grade B; BEL 1, downgraded due to limited evidence). R19: Consider referral for physical therapy, which may reduce discomfort, prevent falls, and improve quality of life (Grade A; BEL 1).
Cosman 2014 (NOF)	Global	Guideline	Postmenopausal women and men aged 50 years and older	Treatments and risk assessments of osteoporosis	Other treatments or placebo	Systematic Reviews, RCTs, and Observational studies	Prevention, diagnosis, and management of osteoporosis	5 out of 7 (doesn't explain methodology)	Recommend regular weight-bearing and muscle-strengthening exercise to improve agility, strength, posture, and balance; maintain or improve bone strength; and reduce the risk of falls and fractures. Assess risk factors for falls and offer appropriate modifications (eg, home safety assessment, balance training exercises, correction of vitamin D insufficiency, avoidance of central nervous system depressant medications, careful monitoring of antihypertensive medication, and visual correction when needed).
Grossman 2018	USA	Guideline	Community dwelling	Vitamin D, calcium, and	Other interventions	Systematic reviews,	Falls and fall- related	5.8 out of 7 (target users	Recommendations for exercise and multifactorial interventions to prevent

(USPSTF) Falls			adults, 65 years or older without osteoporosis or vitamin D deficiency	combined supplementa- tion; exercise interventions.	and supplementa- tions or placebo	RCTs, and observational studies	morbidity and mortality	are not clearly defined and the procedure for updating guideline is not discussed)	falls in community-dwelling adults at increased risk for falls.
Guirguis-Blake 2018	Global	Systematic review and meta-analysis	Community- dwelling older adults (aged 65 years or older)	Multifactorial interventions, exercise, vitamin D supplementa- tion	Other multifactorial interventions; placebo; no intervention	Various trials on multifactorial, exercise, and vitamin D interventions	Falls, effectiveness of intervention, harms, mortality, fall related morbidity	High quality review	Multifactorial and exercise interventions were associated with fall-related benefit, but evidence was most consistent across multiple fall-related outcomes for exercise. Vitamin D supplementation interventions had mixed results, with a high dose being associated with higher rates of fall-related outcome.
Kanis 2019	Global	Guideline	Postmenopausal women	Calcium and vitamin D supplementa- tion; assessment of risk factors for fractures; diagnosis methods	Various assessment tools and treatment modalities	Various studies on the diagnosis and management of osteoporosis	Assessment and treatment of postmenopau- sal women at risk from fractures due to osteoporosis	4.82 out of 7 (methods are not described in detail, guideline development is not discussed, and committee involvement is not clear)	Recommendations for assessment, lifestyle and diet, interventions, and systems of care.