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Review Article

What traditional, complementary, and integrative medicine recommendations exist across osteoporosis clinical practice guidelines? A systematic review and quality assessment

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ABSTRACT

Background: Traditional, complementary and integrative medicine (TCIM) is sought by more than 50% of patients with osteoporosis. Despite this, many healthcare providers lack the knowledge to adequately counsel patients on safe and effective TCIM use. The purpose of this study was to determine the quantity and quality of TCIM recommendations in clinical practice guidelines (CPGs) for the treatment and/or management of osteoporosis.

Methods: MEDLINE, EMBASE and CINAHL databases, in addition to the Guidelines International Network, and the National Center for Complementary and Integrative Health website were searched from 2009–2020. CPGs making TCIM recommendations for the treatment/management of osteoporosis were assessed with the AGREE II instrument.

Results: Of 536 unique search results, 27 osteoporosis CPGs made mention of TCIM therapies. From highest to lowest, scaled domain percentages of all eligible CPGs averaged to 92.59% for scope and purpose, 88.79% for clarity in presentation, 55.04% for stakeholder involvement, 47.84% for editorial independence, 46.53% for rigor of development, and 36.96% for applicability. Of the 27 CPGs assessed, 4 CPGs were recommended as is by both appraisers, while 23 CPGs were recommended with modifications.

Conclusions: Recommendations pertaining to calcium and vitamin D supplementation and exercise were favorably recommended across nearly all CPGs. In the case of other TCIM interventions, recommendations varied greatly, which may present challenges for CPGs target users due to a lack of consistency. Given the varying quality of osteoporosis CPGs found, those requiring improvement may benefit from their guideline development panel utilizing the AGREE II instrument to inform future updates.

1. Introduction

Osteoporosis is a skeletal disorder characterized by structural deterioration of bone tissue, low bone mass, and is associated with an increased risk of fracture.[1] The two types of osteoporosis are primary and secondary. The most common form of osteoporosis is primary osteoporosis, in which a loss of androgens and estrogens induce increased bone turnover such that the rate of bone resorption exceeds that of bone formation, ultimately resulting in increased fracture susceptibility.[2] This is a consequence of the normal human aging process.[3] In contrast, secondary osteoporosis is characterized by bone loss due to specific, well-defined clinical conditions including, but not limited to, gastrointestinal disorders, endocrine disorders, and various forms of cancer.[3] One study estimated that this debilitating condition affects between 24 to 49 million people aged 50 years or older in Australia, Japan, five countries in Europe (United Kingdom, France, Germany, Italy, Spain), the USA and Canada.[4] Another study estimates a prevalence of more than 200 million patients impacted globally.[5] Commonly, patients with osteoporosis experience poor health-related quality of life compared to those with a normal bone mineral density.[6,7]

The current standard of care for osteoporosis includes the prescription of antiresorptive or anabolic medications. Antiresorptive medications, such as bisphosphonates, decrease the bone resorption rate while anabolic medications increase bone formation.[8] Not all of the medications that fall into these categories will treat all individuals with osteoporosis and may cause severe side ef-

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fects when used for the wrong target population.[8] For example, post-menopausal osteoporosis can be treated with teriparatide (anabolic) followed by antiresorptive medication, however, combination therapy of these medications is not recommended due to the limited evidence available, increased costs, and possible side effects.[8] Another study also reported limitations in their therapeutic recommendations for men, noting that the preferred treatment with bisphosphonates was a conclusion extrapolated from women with similar bone mineral densities, due to the sparse evidence applicable solely to men with osteoporosis.[8, 38] With the multitude of side effects of these medications, limited evidence for certain pharmacological interventions, and decreased accessibility to conventional therapies due to the burden caused by osteoporotic fractures, many older patients also opt to use TCIM therapies.[9] These complementary approaches often include sufficient calcium and vitamin D intake, as well as exercising and fall-prevention techniques.[9]

TCIM can be broken down into three definitions; a "traditional" therapy is described as a total sum of historical knowledge and beliefs unique to different ethnic groups, "complementary" therapy is defined as a non-mainstream practice used together with conventional medicine, while an "integrative" therapy is defined as a combination of complementary approaches used in conjunction with conventional medicine.[10–12]. Few studies have been conducted on the prevalence of TCIM use across patients with osteoporosis, however, one Canadian study reported it to be 57% across those attending academic osteoporosis clinics in Toronto, Ontario.[13] The study found that the most commonly used TCIM therapies included megavitamins, massage therapy, herbal medicine, relaxation techniques, and lifestyle diets.[13] An Australian study reported that 51.5% of patients at an osteoporosis clinic used TCIM, with multivitamins, acupuncture, tai chi, and yoga being the most frequently used TCIM therapies.[14] Despite the common use of TCIM interventions, the rate of non-disclosure among patients with osteoporosis are reported to be high. One study found that of 360 patients, 56% did not disclose TCIM use to a medical doctor.[13] Another study found that among 202 osteoporosis patients, 73% of individuals using TCIM interventions did not consult a medical doctor beforehand; twenty-three percent of patients reported that their treating specialists were unaware of their TCIM use.[15] Given that the majority of patients with osteoporosis use TCIM therapies, it is important for healthcare practitioners to possess fundamental knowledge about this topic, in order to appropriately counsel their patients. Accessible resources such as clinical practice guidelines (CPGs), for example, can help guide practitioners in making evidence-informed decisions.

CPGs are important tools that healthcare professionals rely on to guide their decision-making.[16] While several studies have examined the quality of osteoporosis CPGs using appraisal instruments,[17–20] to date, there exists limited research that has systematically summarized the degree of consistency and agreement of TCIMs across osteoporosis CPGs. Given that many patients with osteoporosis use TCIM, it is important that healthcare providers lacking sufficient knowledge are aware of the TCIM therapy recommendations made across osteoporosis CPGs. Therefore, the purpose of this study is to determine the quantity and quality of TCIM recommendations in CPGs for the treatment and/or management of osteoporosis.

2. Methods

2.1. Approach

A systematic review was conducted to identify CPGs for the treatment and/or management of osteoporosis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria.[21] A protocol was not registered. Eligible CPGs were assessed using the Appraisal of Guidelines for Research & Evaluation II (AGREE II) instrument, which is a tool that assesses the methodological rigor and transparency of the guideline developmental process. The instrument consists of 23 key items that are organized into 6 overarching domains which include: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence. In addition, the tool includes 2 global rating items under "Overall Assessment", which include an overall rating of the guideline quality and a recommendation status for practical use. Details regarding the AGREE II tool can be found on the AGREE website [www.agreetrust.org].

2.2. Eligibility criteria

The criteria for eligible osteoporosis CPGs were based on the Population, Intervention, Comparison, and Outcomes (PICO) framework.[22] Eligible *populations* included adults aged 19 years and older diagnosed with osteoporosis. With respect to *interventions,* evidence-based CPGs were only included if they made at least one TCIM therapy recommendation for the treatment and/or management of osteoporosis. For the purpose of this review, TCIM therapies were identified based on the operational definition of complementary medicine published by Cochrane Complementary Medicine.[23] Additionally, all vitamin/mineral supplementation recommendations were included in the definition of TCIM due to the difficulties of standardizing what constitutes a "megadose", however, it is acknowledged that these also comprise conventional care in the context of osteoporosis. No *comparisons* were made. The *outcomes* included the type and recommendation status (i.e. for, against, or uncertain) of each TCIM therapy reported in each eligible CPG. The following additional selection criteria were used to define eligible CPGs: developed by non-profit organizations (i.e. academic institutions, government agencies, disease-specific foundations, or professional associations or societies); published in 2009 or later; written in the English language; and either available publicly or through the McMaster University library system, or orderable via interlibrary loan.. Protocols, abstracts, conference proceedings, primary research articles, letters, editorials, and CPGs that had newer updates were excluded.

2.3. Searching and screening

MEDLINE, EMBASE, and CINAHL were searched on May 3, 2020 from 2009 to May 1, 2020. The search strategies included indexed headings and keywords that reflect terms commonly used in the literature to refer to osteoporosis. A sample search strategy is provided in Supplementary File 1. The Guidelines International Network website[24], a repository of guidelines, was searched using keyword searches reflective of our eligibility criteria including "osteoporosis." Next, a search was conducted on the National Center for Complementary and Integrative Health website which contained a single list of TCIM CPGs.[25]

2.4. Data extraction and analysis

For each CPG, the following data were extracted and summarized: date of publication; country and World Health Organization (WHO) region (of first author); type of organization that published the CPG (academic institutions, government agencies, disease-specific foundations, or professional associations or societies); TCIM(s) recommended by the CPG; TCIM funding sources; whether any TCIM providers were part of the CPG panel; and whether modifying factors were acknowledged in each CPG. In addition, the types of TCIM therapies recommended and their respec-

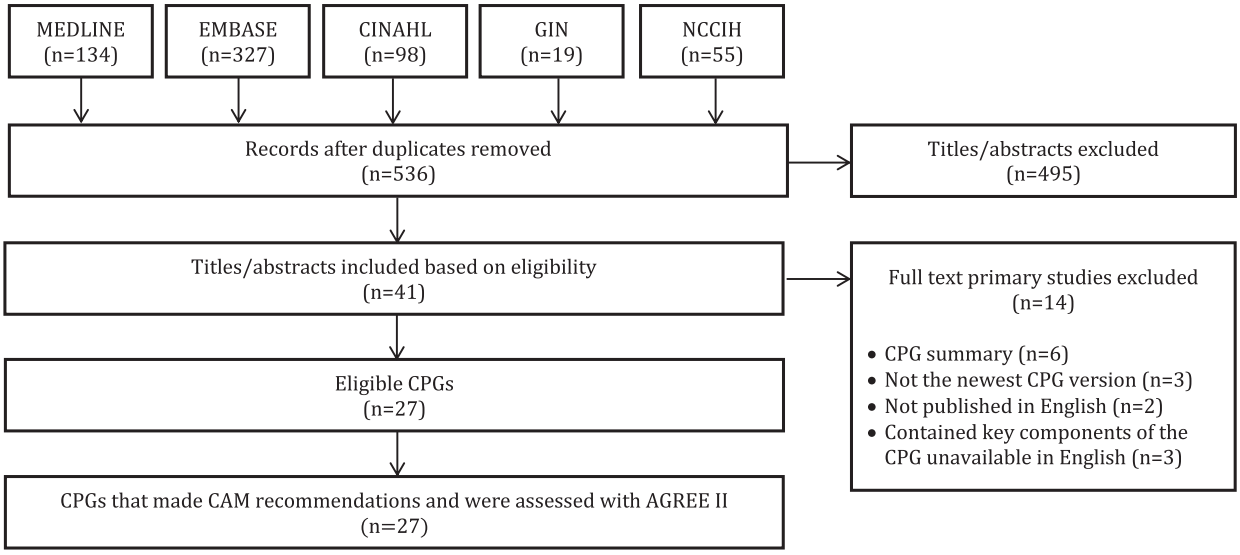

Fig. 1. PRISMA Diagram.

tive recommendation status (i.e. for, against, uncertain) were also collected.

3. Results

3.1. Search results

Searches retrieved 632 items, 536 of which were unique. Following title/abstract screening, 495 items were eliminated, leaving 41 full-text articles for further consideration. Of those, 14 were not eligible for the following reasons: CPG summary ($n = 6$), not the newest CPG version ($n = 3$), not published in English ($n = 2$), and contained key components of the CPG unavailable in English (i.e. such as supplementary materials) that would affect the AGREE II score ($n = 3$). The remaining 27 items comprised CPGs eligible for review, all of which made at least one TCIM therapy recommendation.[26–53] A PRISMA Diagram depicting this process is shown in Fig. 1.

3.2. Characteristics of included CPGs

Eligible CPGs were published from 2009 to 2020, and originated from various WHO regions, including the European Region (EUR, $n = 11$), Region of the Americas (AMR, $n = 10$), Western Pacific Region (WPR, $n = 4$), Eastern Mediterranean Region (EMR, $n = 1$), and the South-East Asian Region (SEAR, $n = 1$). The CPGs were funded and/or developed by professional associations or societies ($n = 26$) and one disease-specific foundation ($n = 1$). All 27 CPGs made mention and recommendations of TCIM, which included: nutrient supplementation ($n = 27$), lifestyle interventions ($n = 23$), traditional Chinese medicine ($n = 6$), and electric field therapy ($n = 1$). Only 1 CPG had TCIM practitioners who served on the CPG development panel.[44] Detailed characteristics associated with each CPG can be found in Table 1. A summary of TCIM therapies and their respective recommendations across all CPGs are presented for the benefit of clinicians and researchers in Table 2.

3.3. Average overall assessments, recommendations regarding use of CPGs

The average overall assessment scores for the 27 CPGs assessed ranged from 3.5 to 6.5 on a seven-point Likert scale (with seven signifying that the item's criteria have been fully met). Twenty-four CPGs out of the 27 achieved or surpassed an average overall assessment score of 4.0, while 10 CPGs achieved or surpassed an average overall assessment score of 5.0.

3.4. Overall recommendations

Out of the 27 CPGs assessed, only four were recommended without any modifications by both appraisers[30,33–35,44] 44, 33, 34 35, 30. Appraisers agreed in their overall recommendation with modifications for the rest of the 23 CPGs assessed.

3.5. Scaled domain percentage quality assessment

Across all CPGs, scaled domain percentage scores for scope and purpose ranged from 63.89 to 100.00%, with an average of 92.59% overall. Domain scores for stakeholder involvement ranged from 22.22 to 100.00%, with an average of 55.04%. Domain scores for rigor of development ranged from 12.50 to 89.58%, with an average of 46.53%. Domain scores for clarity of presentation ranged from 55.56 to 100.00%, with an average of 88.79%. Domain scores for applicability ranged from 2.08 to 87.50%, with an average of 36.96%. Domain scores for editorial independence ranged from 0.00 to 100.00%, with an average of 47.84%.

3.6. Scope and purpose

The overall objectives of each CPGs were explicitly stated with the exception of one.[52] The remaining CPGs included the health intents and expected outcomes of their recommendations. The health questions covered by each CPG were also generally well-defined in all but one.[36] The target populations of each CPGs were described in sufficient detail.

3.7. Stakeholder involvement

All of the included CPGs thoroughly detailed characteristics of the individuals involved in CPG development, which generally included name, field of expertise, institution, and geographical location.[26–52] Twelve of these CPGs also included brief descriptions of author and development group roles.[30,31,33–35,38,41,43,44,46–49] A few CPGs also took patient values and preferences into account,[26,27,30,33–35,44] while the remainder of the CPGs did

Table 1
Characteristics of eligible CPG.

CPG	Country (of First Author)	WHO Region	Developer	Type of Recommended TCIM Intervention(s)	CPG Topic
Eastell 2019[26]	United Kingdom	European Region	European Society of Endocrinology	Nutritional supplements	Pharmacological management of osteoporosis in postmenopausal women
Hernandez 2019[27]	Spain	European Region	Spanish Society of Rheumatology	Nutritional supplements, lifestyle interventions	Management of osteoporosis
Makras 2019[28]	Greece	European Region	International Osteoporosis Foundation and National Osteoporosis Foundation	Nutritional supplements, lifestyle interventions	Diagnosis and treatment of osteoporosis in Greece
Nuti 2019[29]	Italy	European Region	Inter-Society Commission for Osteoporosis	Nutritional supplements, lifestyle interventions	Management of osteoporosis and fragility fractures
Shapiro 2019[30]	United States	Region of the Americas	American Society of Clinical Oncology	Nutritional supplements, lifestyle interventions	Management of osteoporosis in survivors of adult cancers with nonmetastatic disease
Briot 2018[31]	France	European Region	French Society for Rheumatology	Nutritional supplements, lifestyle interventions	Management of postmenopausal osteoporosis
Rodrigues 2018[32]	Portugal	European Region	Portuguese Society of Rheumatology	Nutritional supplements, lifestyle interventions	Prevention, diagnosis, and management of primary osteoporosis
Allen 2017[33]	United States	Region of the Americas	Institute for Clinical Systems Improvement	Nutritional supplements, lifestyle interventions, traditional Chinese medicine	Diagnosis and treatment of osteoporosis
Buckley 2017[34,35]	United States	Region of the Americas	American College of Rheumatology	Nutritional supplements, lifestyle interventions	Prevention and treatment of glucocorticoid-induced osteoporosis
Lorenc 2017[36]	Poland	European Region	Multidisciplinary Osteoporosis Forum	Nutritional supplements, lifestyle interventions	Diagnosis and management of osteoporosis in Poland
Loures 2017[37]	Brazil	Region of the Americas	Brazilian Society of Rheumatology	Nutritional supplements, lifestyle interventions	Diagnosis and treatment of osteoporosis in men
Qaseem 2017[38]	United States	Region of the Americas	American College of Physicians	Nutritional supplements	Treatment of low bone density or osteoporosis to prevent fractures in men and women
Radominski 2017[39]	Brazil	Region of the Americas	Brazilian Society of Rheumatology and Brazilian Medical Association	Nutritional supplements, lifestyle interventions	Diagnosis and treatment of postmenopausal osteoporosis
Yeap 2017[40]	Malaysia	Western Pacific Region	Malaysian Osteoporosis Society	Nutritional supplements, lifestyle interventions	Management of glucocorticoid-induced osteoporosis
Camacho 2016[41]	United States	Region of the Americas	American Association of Clinical Endocrinologists and the American College of Endocrinology	Nutritional supplements, lifestyle interventions, traditional Chinese medicine	Diagnosis and treatment of postmenopausal osteoporosis
Rossini 2016[42]	Italy	European Region	Italian Society for Osteoporosis, Mineral Metabolism and Bone Diseases	Nutritional supplements, lifestyle interventions	Diagnosis, prevention, and management of osteoporosis
Al-Saleh 2015[43]	Saudi Arabia	Eastern Mediterranean Region	Saudi Osteoporosis Society	Nutritional supplements, lifestyle interventions	Diagnosis and management of osteoporosis
SIGN 2015[44]	Scotland	European Region	Scottish Intercollegiate Guidelines Network	Nutritional supplements, lifestyle interventions, traditional Chinese medicine, electric field therapy	Management of osteoporosis and the prevention of fragility fractures
Briot 2014[45]	France	European Region	French Society for Rheumatology	Nutritional supplements, lifestyle interventions	Prevention and treatment of glucocorticoid-induced osteoporosis
Khan 2014[46]	Canada	Region of the Americas	Society of Obstetricians and Gynaecologists of Canada.	Nutritional supplements	Prevention, diagnosis, and clinical management of postmenopausal osteoporosis
Suzuki 2014[47]	Japan	Western Pacific Region	Japanese Society for Bone and Mineral Research	Nutritional supplements, lifestyle interventions	Management and treatment of glucocorticoid-induced osteoporosis
Compston 2013[48]	United Kingdom	European Region	National Osteoporosis Guideline Group	Nutritional supplements	Diagnosis and management of osteoporosis in postmenopausal women and older men in the UK
Taipang 2013[49]	Hong Kong	Western Pacific Region	Osteoporosis Society of Hong Kong	Nutritional supplements, lifestyle interventions, traditional Chinese medicine	Clinical management of postmenopausal osteoporosis
Pereira 2012[50]	Brazil	Region of the Americas	Brazilian Society of Rheumatology, Brazilian Association of Physical Medicine and Rehabilitation, Brazilian Medical Association	Nutritional supplements, lifestyle interventions, traditional Chinese medicine	Prevention and treatment of glucocorticoid-induced osteoporosis
Watts 2012[51]	United States	Region of the Americas	The Endocrine Society	Nutritional supplements, lifestyle interventions	Management of osteoporosis in men

(*continued on next page*)

Table 1 (*continued*)

CPG	Country (of First Author)	WHO Region	Developer	Type of Recommended TCIM Intervention(s)	CPG Topic
Krishnamurthy 2011[52]	India	South-East Asian Region	Indian Rheumatology Association	Nutritional supplements, lifestyle interventions	Management of glucocorticoid-induced osteoporosis
Xie 2011[53]	China	Western Pacific Region	Institute of Basic Research in Clinical Medicine, China Academy of Chinese Medical Sciences; Wangjing Hospital of China Academy of Chinese Medical Science; Fujian University of Chinese Medicine; Orthopedic Hospital of Guangzhou University of Traditional Chinese Medicine; China Traditional Chinese Medicine Publishing House; Beijing University of Chinese Medicine	Nutritional supplements, lifestyle interventions, traditional Chinese medicine	Traditional medicine for primary osteoporosis

Table 2
Summary of TCIM recommendations in clinical practice guidelines.

Guideline (Full Citation Provided in Table 1)	Nutritional Supplements					Lifestyle Interventions		Traditional Chinese Medicines		Electric Field Therapy
	Minerals (Magnesium/ Potassium)	Calcium Supplements	Vitamin D Supplements	Vitamin K Supplements	Vitamin A Supplements	Exercise	Sun Exposure	Tai Chi	Herbal Medicines	Acupuncture	
Eastell 2019[26]	N/A	+	+	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Hernandez 2019[27]	N/A	+	+	N/A	N/A	+	+	N/A	N/A	N/A	N/A
Makras 2019[28]	N/A	+	+	N/A	N/A	+	N/A	N/A	N/A	N/A	N/A
Nuti 2019[29]	N/A	+	+	N/A	N/A	+	N/A	N/A	N/A	N/A	N/A
Shapiro 2019[30]	N/A	+	+	N/A	N/A	+	N/A	N/A	N/A	N/A	N/A
Briot 2018[31]	N/A	+	+	N/A	N/A	+	N/A	N/A	N/A	N/A	N/A
Rodrigues 2018[32]	N/A	+	+	N/A	N/A	+	+	N/A	N/A	N/A	N/A
Allen 2017[33]	0	+	+	0	N/A	+	N/A	+	0	N/A	N/A
Buckley 2017[34, 35]	N/A	+	+	N/A	N/A	+	N/A	N/A	N/A	N/A	N/A
Lorenc 2017[36]	+	+	+	N/A	N/A	+	N/A	N/A	N/A	N/A	N/A
Loures 2017[37]	+	+	+	N/A	N/A	+	N/A	N/A	N/A	N/A	N/A
Qaseem 2017[38]	N/A	+	+	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Radominski 2017[39]	N/A	+	+	N/A	N/A	+	N/A	N/A	N/A	N/A	N/A
Yeap 2017[40]	N/A	+	+	N/A	N/A	+	N/A	N/A	N/A	N/A	N/A
Camacho 2016[41]	0	+	+	+	-	+	N/A	+	N/A	N/A	N/A
Rossini 2016[42]	N/A	+	+	N/A	N/A	0	N/A	N/A	N/A	N/A	N/A
Al-Saleh 2015[43]	N/A	+	+	N/A	N/A	+	+	N/A	N/A	N/A	N/A
SIGN 2015[44]	+	+	+	0	N/A	+	N/A	+	-	N/A	+
Briot 2014[45]	N/A	+	+	N/A	N/A	+	N/A	N/A	N/A	N/A	N/A
Khan 2014[46]	N/A	+	+	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Suzuki 2014[47]	N/A	+	+	0	N/A	+	N/A	N/A	N/A	N/A	N/A
Compston 2013[48]	N/A	+	+	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Taipang 2013[49]	+	+	+	N/A	N/A	+	N/A	+	N/A	N/A	N/A
Pereira 2012[50]	N/A	+	+	N/A	N/A	+	N/A	+	N/A	N/A	N/A
Watts 2012[51]	N/A	+	+	N/A	N/A	+	N/A	N/A	N/A	N/A	N/A
Krishnamurthy 2011[52]	N/A	+	+	N/A	N/A	+	+	N/A	N/A	N/A	N/A
Xie 2011[53]	N/A	+	+	N/A	N/A	+	N/A	N/A	+	+	N/A

+, recommendation for the therapy's use; -, recommendation against the therapy's use; 0, recommendation unclear/uncertain/conflicting; N/A, no recommendation provided.

not.[28,29,31,32,36–43,45–53] Target users of these CPGs were clearly defined in most cases with the inclusion of medical specialities and types of healthcare providers.[28,29,31,32,36–43,45–53] A few of the studies remained vague when referring to their intended users through the use of general descriptors such as "clinician" or implying that the CPGs are directed towards those who treat, diagnose, and manage osteoporosis.[29,37,42,48,50–53]

3.8. Rigor of development

Systematic methods were used and clearly defined by the majority of the CPGs,[27,28,30,32–36, 38, 40, 43,44,46,50,51,53] however, the remaining CPGs did not describe their search methodology in sufficient detail.[26,29,31,37, 39, 41,42,45,47–49,52] Of the CPGs with detailed systematic search methods, 6 also included detailed criteria

for selecting evidence.[28,30,34,35 38,40,46] The strengths and weaknesses of the body of evidence were clearly described in a few of the included CPGs.[27,30,34,35,38,40,41,44] The methods for formulating recommendations varied across the CPGs which included this process in their methodologies. A large majority utilized techniques involving expert consensus, in-depth discussion, and feedback over several meetings.[27,28,30,33–35, 38,41,44,51,53] Another study directly analyzed Japanese patients from three cohorts with varying treatment interventions.[47] One study commissioned two systematic reviews to support the development of the CPG.[26] All included CPGs took health benefits, side effects, and risks into consideration during the development process, although one lacked in detail.[46] Nearly all studies also included explicit links between the recommendations and the body of evidence to support these recommendations, with the exception of two CPGs that lacked both written text and references to link these two elements.[36,46] Eleven of the CPGs also included explicit statements of external review by experts prior to publication,[26–28,30,32,33, 42,44,45,51, 53] however, the majority of CPGs did not include this. The majority of the included CPGs also did not provide any criteria or methods for future updates. Four of the CPGs explicitly mentioned a time interval for an update.[33,38,30,53] One of the CPGs included methods for an update without a time interval for an update,[47] and two CPGs provided both a time interval for the updates as well as detailed methods.[34,35,44]

3.9. Clarity of presentation

Most CPGs offered recommendations that were specific, unambiguous, and easily identifiable. All 27 CPGs included various options for the treatment/management of osteoporosis and explicitly described the clinical situation or population most relevant for each option.[26–53]

3.10. Applicability

Nine CPGs clearly described the facilitators and barriers in place that impact its application[29,30,34,35,41–45,49] while 7 provided advice and/or tools on how to implement the recommendations made by the authors.[26,29,30,33–35,41,44] Five CPGs explicitly considered the potential resource implications of applying the recommendations described.[30,34,35,41,42,44] Nineteen of the CPGs presented monitoring and/or auditing criteria to measure the efficacy of suggested treatments.[26–36,39,41,42, 44, 45,48,49,51,53]

3.11. Editorial independence

Less than half of the 27 CPGs assessed fully described their editorial independence. While many CPGs specified a funding body, many did not explicitly mention whether the funding body influenced the development of the CPGs or not.[26,30,38,40,46,50] Some CPGs failed to mention a funding body.[27,28,31,32, 36, 37, 39,41–43,45,47,53] Additionally, while most CPGs listed competing interests, many failed to describe what interests were considered, and the manner by which interests were collected.

3.12. Modifying factors

The strength of the recommendations within the included CPGs is dependent upon whether these studies considered modifying factors, such as patient's values and preferences, the burden of disease, and equity. Of the 27 included CPGs, only 6 accounted for patients' cultural values and preference.[26,27,30,33,34,35,44] Seven of the CPGs also account for the resource implications and opportunity costs of their recommendations.[26,29,30,33–35,41,44] Almost all the CPGs had a developmental process that included the perspective of both physicians and patients, except for two, which only reported recommendations from the patient perspective.[52,53] Through further review of the AGREE II tool scores within the applicability domain, 10 CPGs were found to adequately address equity, feasibility, and burden of illness during the development of their respective CPGs.[29,30,34,35,41–45,49,51] The inclusion of these modifying factors in the development of these CPGs results in recommendations of greater strength, with three CPGs achieving the greatest strength of recommendations through the inclusion of all of the aforementioned factors.[30,34,35,44]

4. Discussion

With osteoporosis impacting over 200 million people globally, more than 50% of these patients seek out TCIM in hopes that such therapies will aid in the management of their disease. To identify credible, evidence-based resources that healthcare practitioners may utilize to make informed decisions about the use of TCIM therapies, the present review identified 27 CPGs published between 2009 and 2020 that contained at least one TCIM therapy recommendation for the treatment and/or management of osteoporosis. To our knowledge, this is the first study to date to determine the quantity and assess the quality of TCIM recommendations in CPGs for the treatment and/or management of osteoporosis.

The WHO regions from which the authors originate emphasize trends in the osteoporosis CPGs recommendations due to cultural similarities and differences between and within the regions. The majority of studies hailing from the Western world, from the AMR and EUR regions, focused on TCIM interventions that fall into the categories of nutritional supplements and lifestyle interventions. Four of the 21 total CPGs, or roughly 19%, which originate from the AMR or EUR regions also include mentions of traditional Chinese medicine, despite these practices not being native to these regions.[33,41,44 50] Of the 4 CPGs originating in the WPR, two CPGs, or 50%, include recommendations based on traditional Chinese medicine.[49,53] It is important to note that these two CPGs, by Xie et al.[53] and Tai-Pang et al.[49], are the only two which originate from China and Hong Kong respectively, where the practice of traditional Chinese medicine is comparatively more widespread and accepted.

The standard use of conventional medicine in osteoporosis involves the use of antiresorptive and anabolic treatments, which prevent bone resorption and encourage bone formation, respectively.[8] These treatments are prescribed differently depending on the patient's gender as well as whether they have comorbid conditions, due to the variable effectiveness of the medications and possible side effects.[8] This necessitates the availability of options outside of conventional care in order for patients and healthcare providers to make informed care decisions where there is a lack of evidence surrounding pharmacological treatments.

Recommendations pertaining to calcium and vitamin D supplementation and exercise were favorably recommended across nearly all CPGs. This is arguably unsurprising, as such therapies also comprise routine and standard conventional osteoporosis care. It is difficult to classify whether this supplementation is conventional or TCIM medicine, despite its routine use, as lifestyle modifications such as diet changes are often viewed as changes made in addition to pharmacological therapies.[10] It also presents as a conventional therapy as physicians regularly prescribe calcium and vitamin D supplementation at specific doses.[54] Beyond this, little consistency existed with regards to types of TCIMs mentioned and agreement across CPGs as to whether they should be recommended for use. Findings of a lack of consistency in the quantity and type of TCIM recommendations have been also reported in a systematic review assessing the quality of CAM CPGs focused on herbal medicines, acupuncture, and spinal manipulation.[55] Other studies concerning

musculoskeletal and pain-related conditions, including headaches and migraines,[56] low back pain,[57] arthritis,[58] multiple sclerosis,[59] and cancer-related pain[60] highlight a similar inconsistency.

Such differences can likely be attributed to the limited research conducted at the intersection of TCIM and osteoporosis and in particular the lack of clinical trial data. Several factors exist which impede TCIM research,[61] such as negative attitudes toward TCIM therapies,[62] a lack of dedicated funding,[63] and disagreement within the TCIM research community as to what constitutes best research evidence.[64,65] In addition, it has been observed that when contrasting TCIM professions to other health disciplines, many of the obstacles to other health disciplines have a primary emphasis on the application of research results in practice, while for TCIM, these barriers appear to apply to both conduct and application.[61] These findings in combination with those of the aforementioned comparative studies are especially important for CPG developers who seek to standardize recommendations across osteoporosis CPGs. At present, this lack of recommendation consistency undoubtedly presents a challenge for healthcare providers seeking knowledge about safe and effective TCIM use in the context of osteoporosis care. TCIMs beneficial to patients with osteoporosis may be better collected through the involvement of patient perspectives in the search strategies for common TCIM interventions or through the participation of a TCIM expert in the CPG development panel. Further research should explore why such inconsistencies exist, which may in part be achieved by assessing the quality of the TCIM recommendations found across this subset of osteoporosis CPGs; longer-term objectives include identifying strategies to harmonize TCIM types and recommendation statuses that are incorporated into osteoporosis CPGs.

Notable strengths of this study include the use of a comprehensive, systematic review methodology for data collection and analysis, as well as the use of the AGREE II instrument, which is widely regarded as the golden standard for CPG assessment. Additionally, while only two appraisers (instead of the recommended four) assessed the quality of eligible CPGs, we mitigated potential unreliability by having both appraisers participate in a pilot test to better standardize their assessments. This pilot test involved the evaluation of three separate CPGs using the AGREE II instrument. With respect to limitations, the consideration of protocol registration occurred after the inception of the review and collection of data, leaving us unable to retrospectively register a protocol on PROSPERO. An additional limitation includes the fact that this review did not capture CPGs published in languages outside of English.

In conclusion, the present review identified 27 CPGs for the treatment and/or management of osteoporosis each providing at least one TCIM recommendation. TCIM therapies identified across CPGs included: nutrient supplementation, lifestyle interventions, traditional Chinese medicine, and electric field therapy. Recommendations pertaining to calcium supplementation, vitamin D supplementation, and exercise were favorably recommended across nearly all CPGs. Beyond this, little consistency existed with regards to agreement across CPGs as to whether the other aforementioned TCIMs mentioned should be recommended for use. The use of the AGREE II instrument in the appraisal of these CPGs identified variations in quality across and within CPGs. Those that scored variably or lower overall may seek be improved in future updates by closely adhering to the guidance provided by the AGREE II instrument. Those which scored higher may be used to inform patients and healthcare providers of possible TCIM therapies which have the potential to be used in conjunction with conventional practices. Despite this, our findings indicate that healthcare providers are faced with a challenge in gaining knowledge surrounding the safe and effective TCIM use in the context of osteoporosis care, due to inconsistencies in recommendations made about various TCIM therapies across available osteoporosis CPGs.

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Author contributions

Conceptualization: JYN. Methodology: JYN. Formal investigation: JYN, AH, and IM. Data analysis: JYN, AH, and IM. Writing - original draft: JYN. Writing - review and editing: JYN, AH, and IM.

Conflict of interest

The authors declare that they have no competing interests.

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Ethical statement

Not applicable.

Data availability

All relevant data are included in this manuscript.

Supplementary materials

Supplement 1: MEDLINE Search Strategy for Osteoporosis Clinical Practice Guidelines.

Supplementary material associated with this article can be found in the online version, at doi:10.1016/j.imr.2021.100803.

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