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Prevalence of osteoporosis in chronic diseases: an umbrella review of 283 observational studies from 13 systematic reviews

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Abstract

Introduction Osteoporosis is a disease characterized by decreased bone mineral density and deterioration of bone microarchitecture, which increases fracture risk. In the context of various chronic pathologies, this condition may present an even higher prevalence, impacting morbidity, mortality, and healthcare burden.

Objective To synthesize and compare available evidence from systematic reviews on the prevalence of osteoporosis across different chronic diseases.

Methodology An umbrella review following PRISMA guidelines was conducted, focusing on systematic reviews (with or without meta-analysis) reporting prevalence data of osteoporosis in adults with at least one chronic disease. Databases, including PubMed/MEDLINE, Scopus, Web of Science, and EMBASE, were searched, covering publications between 2009 and 2023, without language restrictions. Two independent reviewers performed study selection and data extraction, resolving discrepancies through consensus. A risk of bias assessment was conducted using the ROBIS tool. Prevalence estimates reported in each review were analyzed, classifying diseases according to the magnitude of the percentages found.

Results Thirteen systematic reviews were evaluated (twelve included meta-analyses). The highest prevalence of osteoporosis was observed in patients with Chronic Obstructive Pulmonary Disease (up to 36.8%) and diabetes mellitus (approximately 27.7%). Other conditions, such as rheumatoid arthritis, multiple sclerosis, liver cirrhosis, and celiac disease, showed variable prevalence but were equally relevant in clinical terms. Methodological heterogeneity, both in diagnostic criteria and populations, was a notable factor.

Conclusions The results highlight the need for systematic assessment of bone health in patients with chronic diseases, particularly those with a higher prevalence of osteoporosis. These findings underscore the importance of timely screening strategies and multidisciplinary approaches to prevent fractures and optimize comprehensive care.

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Introduction

Osteoporosis is a disease characterized by decreased bone mineral density and deterioration of bone microarchitecture, leading to an increased risk of fractures [1]. According to the International Osteoporosis Foundation (IOF), it is estimated that more than 200 million people worldwide suffer from this condition, representing a significant healthcare challenge [2]. The clinical relevance of osteoporosis is based not only on the morbidity and mortality associated with fractures [3, 4] but also on their functional and socioeconomic effects, such as loss of autonomy and increased healthcare costs [5, 6]. In the context of chronic diseases such as rheumatoid arthritis, diabetes mellitus, or chronic kidney disease, the impact of osteoporosis may be even greater, justifying the relevance of a comprehensive and updated synthesis addressing its prevalence in these scenarios [1].

In recent decades, the prevalence of osteoporosis has shown a sustained increase, partly due to population aging and lifestyle changes, such as reduced physical activity and adoption of diets deficient in essential nutrients [7]. Recent studies highlight the influence of risk factors such as sedentary behavior, smoking, excessive alcohol intake, and vitamin D deficiency, whose combination can accelerate bone mass loss, especially in people with comorbidities [8, 9, 10]. In addition to the clinical repercussions, such as chronic pain and increased susceptibility to fractures, this situation entails a high economic cost for healthcare systems due to increased hospitalizations and rehabilitation expenses [11]. Given this panorama, it is essential to have a comprehensive review of the literature that integrates and clarifies information on the prevalence of osteoporosis in different chronic diseases, facilitating clinical decision-making and the development of evidence-based guidelines.

Despite the growing volume of research on osteoporosis, relevant knowledge gaps persist, particularly regarding its actual prevalence in different groups of patients with chronic diseases [12]. While most available systematic reviews focus on risk measures, it is equally fundamental to analyze the effective prevalence of this condition in these populations. Knowing the specific proportion of patients who have osteoporosis, and not just those with a risk profile, offers a more immediate overview of the magnitude of the problem and the healthcare resources required. Methodological heterogeneity across studies, the use of divergent diagnostic criteria, and variability in the analyzed populations make it difficult to compare results, generating controversies and disparate conclusions [13].

Therefore, the main objective of this UR is to synthesize and compare evidence from systematic reviews regarding the prevalence of osteoporosis in different chronic diseases. It also aims to identify modulating factors and knowledge gaps that will allow the delineation of future recommendations for clinical practice and subsequent research. Given the importance of systematic reviews in evidence-based decision-making, this synthesis is expected to provide an integrative view of published findings and clarify reported inconsistencies, establishing more solid foundations for addressing osteoporosis in the context of multiple chronic diseases.

Methodology

Study design

An UR was conducted to evaluate the prevalence of osteoporosis across various chronic diseases, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and adhering to the recommendations by Belbasis et al. [14].

Search strategy

The search was performed in four electronic databases: PubMed (MEDLINE), Scopus, Web of Science (including the SciELO catalog), and EMBASE. It followed the Cochrane Collaboration's suggestions on covering sources with broad international coverage and thematic diversity. The SciELO platform was not used in isolation, as its records were included through Web of Science.

To define the search terms, keywords, and MeSH terms related to osteoporosis and the chronic diseases of interest, they were combined using Boolean operators (AND, OR) to optimize the strategy's sensitivity and specificity. A search period was established from January 2000 to February 2025, including studies published in the last decade. The complete search strategy and the text strings used in each database are detailed in Supplementary Material 1.

Selection criteria

Inclusion criteria

- Study design: Only systematic reviews (with or without meta-analysis) that aimed to provide prevalence data of osteoporosis.
- Population: Adult populations with at least one chronic disease.
- Chronic diseases: No a priori restrictions were placed on which chronic diseases would be included; our approach was deliberately comprehensive,

seeking to identify systematic reviews across the entire spectrum of chronic conditions from all medical specialties (including rheumatology, pulmonology, gastroenterology, endocrinology, nephrology, neurology, cardiology, and others).
- Diagnostic criteria for osteoporosis: Reviews that employed diagnostic definitions by international guidelines (e.g., T-score ≤ -2.5 in bone densitometry).
- Study types in reviews: Reviews based on observational studies (cross-sectional, cohort, or case-control) and those that included clinical trials if the prevalence of osteoporosis constituted a reported variable.
- Review selection: In cases where multiple reviews on the same topic were identified, the most recent one was selected after verifying that it included the primary studies from earlier reviews.
- Language: No restrictions if studies met the established methodological criterio.

Exclusion criteria

- Study design: Works that did not meet the definition of a systematic review (e.g., narrative reviews, scoping reviews, bibliometric reviews, or meta-analyses of studies not oriented toward prevalence).
- Population: Reviews focused exclusively on pediatric populations.
- Diagnostic criteria: Studies using diagnostic criteria other than bone densitometry (e.g., self-reports of osteoporosis without clinical verification).
- Publication types: Letters to the editor, clinical cases, clinical practice guidelines, or articles that did not provide specific prevalence data.
- Redundancy: Duplicate reviews or updates that did not offer new information compared to previous versions.

Article selection process

After applying the search strategy in the selected databases, all retrieved records were imported into Rayyan software for organization and duplicate control. Once redundant records were eliminated, two independent reviewers (VJVP and JBC) evaluated the titles and abstracts of the identified systematic reviews, following the methodology recommended for URs. This peer review was conducted in a blinded and parallel manner to minimize the influence of personal biases. LEVR and LAMVS served as additional reviewers to verify the screening process by reviewing a random 20% sample of the initial records. Subsequently, the full text of those documents that preliminarily met the inclusion criteria was read by the same two primary reviewers (VJVP and JBC) to confirm or rule out their eligibility.

Any discrepancy between the two primary reviewers regarding the inclusion or exclusion of a study was resolved by consensus through detailed discussion. In cases where disagreements persisted (approximately 8% of the evaluated studies), a third reviewer (FEZM) independently assessed the disputed articles and provided a decisive opinion. For particularly complex methodological questions, SMC served as an additional consultant due to her expertise in research methodology. This process ensured the independence and objectivity of the selection while allowing for the systematic and exhaustive identification of reviews that provided data on the prevalence of osteoporosis in populations with chronic diseases. All selection steps, from importing to Rayyan to the critical reading of full texts, were rigorously documented by JALC to ensure the reproducibility and transparency of the process.

Data extraction process

Data extraction was done using a Microsoft Excel spreadsheet to capture relevant information from each systematic review included in this UR. Two reviewers worked independently to extract the data: team one (VJVP, LAMVS, and JALC) and team two (JBC, LEVR, and FEZM). A previous training session led by VJVP and RTL was held to ensure consistency and accuracy where fields and coding criteria were clearly defined and calibrated across both teams. The extraction sheet was designed by JALC and contained both numerical and qualitative fields, allowing for detailed categorization of key parameters and ensuring the reproducibility of results.

Data collected included the review's first author, year of publication, number of primary studies included, total sample size analyzed, countries or geographic regions covered, population characteristics, type of study (cross-sectional, cohort, etc.), and the specific chronic disease evaluated. Additionally, how chronic disease and osteoporosis were defined and diagnosed in each review was recorded to assess the homogeneity of methods and the relevance of subsequent quantitative synthesis. When disagreements arose between the two extraction teams (found in approximately 15% of extracted data points), these were initially discussed between team representatives (VJVP and JBC). For unresolved discrepancies, a third arbitration team consisting of SMC, RTL, and CIGC evaluated the conflicting extractions and made the final determination based on consensus after reviewing the original source documents. This rigorous extraction approach allowed for a complete and homogeneous database to carry out the final analysis of the evidence.

Risk of bias assessment

The risk of bias assessment of the included systematic reviews was conducted using the Risk of Bias in

Systematic Reviews (ROBIS) tool. Two independent reviewers (LAMVS and FEZM) applied this instrument in parallel, following the four main domains proposed by ROBIS: (1) eligibility criteria of primary studies, (2) methods of searching and identifying evidence, (3) data extraction and synthesis procedures, and (4) results and interpretation of findings. Each domain was rated based on concordance with established methodological standards, allowing for a final classification of risk of bias (high, low, or uncertain). Before beginning the formal assessment, a training session and pilot test were conducted with small reviews by SMC and CIGC to standardize the instrument's application and resolve doubts about its use.

Discrepancies between evaluators were discussed in consensus meetings facilitated by JBC; if an agreement could not be reached (which occurred in approximately 12% of assessed reviews), a third reviewer (RTL, SMC, or CIGC, depending on the specific chronic disease being evaluated) with experience in systematic review methodology intervened to provide the definitive assessment. This process ensured the objectivity and reliability of the risk of bias assessment, as it reduced the possibility of biased individual judgments and promoted transparency in the final classification. The results of the ROBIS application were subsequently used to determine the robustness of the overall findings in the meta-analysis and to guide the interpretation of the final results of this UR. VJVP and JALC conducted the final integration of the risk of bias assessments into the analytical framework of the UR.

Data analysis

The global prevalence estimates and their confidence intervals reported in the meta-analyses of each included systematic review were used as the starting point for data analysis; consequently, no new independent meta-analysis was performed. When more than one meta-analysis was available for the same chronic disease, we first assessed methodological coherence (population, diagnostic criteria, study quality, and statistical synthesis methods) to confirm comparability and then retained the most representative pooled estimate. This procedure ensured that data extracted from different reviews were integrated without duplications or inconsistencies, while preserving the reliability of the original calculations.

To verify that prevalence figures were not artificially influenced by the repeated use of identical primary studies, we quantified overlap across the 13 reviews. A 13×13 cross-tabulation matrix of primary-study inclusions was constructed. The corrected covered area (CCA) was calculated using $CCA = (N - r)/(r\ c - r)$, where N is the number of study inclusions (416), r the number of unique primary studies (411), and c the number of reviews (13). The resulting CCA of 0.10% falls within the "light overlap" category (< 5%), indicating that the evidence bases of the reviews are largely independent; the few duplications detected were restricted to rheumatology-focused reviews.

After confirming minimal redundancy, prevalence estimates for each chronic disease were classified into four predefined ranges (very low, low, moderate, high) according to the percentage of affected individuals. These categories, together with their confidence intervals, were displayed graphically to facilitate visual comparison across conditions. This approach provides a clear overall picture of disease burden, highlights chronic diseases most strongly associated with osteoporosis, and helps to prioritise future research and clinical strategies.

Results

Article selection

In total, 1597 references were identified from the search in Scopus (398), EMBASE (369), PubMed (488), and Web of Science (342). After removing 549 duplicates, 1048 records remained for title and abstract review, of which 400 were excluded for not meeting the inclusion criteria (25 were not systematic reviews, 397 did not address populations with chronic disease or included pediatric populations, 536 did not report specific data on osteoporosis prevalence, and 42 applied inadequate diagnostic criteria). Subsequently, 48 potentially eligible articles were evaluated in full text, discarding 36 for presenting insufficient or nonspecific prevalence data ($n = 14$), inadequate methodology for a systematic review ($n = 9$), duplication or update without additional information ($n = 7$), or employing diagnostic criteria incompatible with international guidelines ($n = 6$). Finally, 13 systematic reviews (12 had meta-analyses) met the requirements for inclusion in the qualitative synthesis [15–27] (Fig. 1).

Characteristics of selected studies

The thirteen selected systematic reviews were published between 2010 and 2023, with a notable increase from 2019 onward, during which ten of the included reviews were published [17–27] (Table 1). These reviews encompassed primary studies from various geographical regions, including North America, South America, Europe, Asia, Africa, and Oceania. No specific predominance of a particular area was observed. All reviews were published in English, and most studies were incorporated without original language restrictions.

The reviews evaluated 416 primary studies, varying between 5 and 153 studies per review. The total population analyzed reached 372,102 participants, with individual sample sizes ranging from 563 to 227,812 subjects per review. Although the degree of overlap of primary studies between reviews was not explicitly detailed,

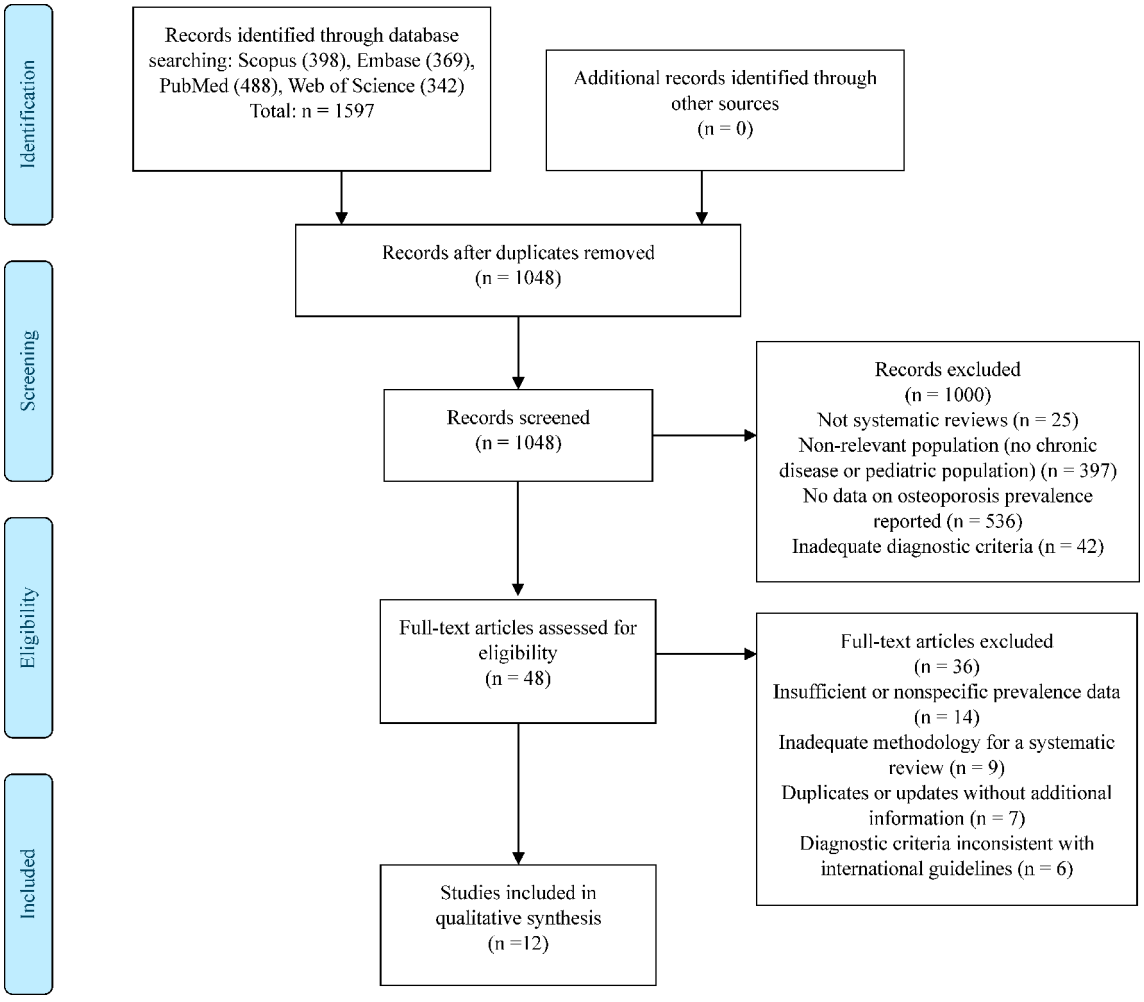

Fig. 1 Flowchart of study selection

these covered different clinical settings and diverse methodologies.

Regarding population characteristics, the reviews primarily focused on adults, with broad age ranges, from young adults (mean age around 28 years in cystic fibrosis) (15) to older adults, with a mean age of 67.8 years in patients with chronic obstructive pulmonary Disease (COPD) [17]. The sex distribution was varied, with male predominance reported in patients with COPD (69% men) [17] and axial spondyloarthritis (axSpA) (57–85% men) [16]. In comparison, conditions such as systemic sclerosis (SSc) had a clear female predominance (90.6%) [23]. The clinical contexts where these studies were conducted were mainly hospital and specialized settings, without systematic primary or community care specifications.

The chronic conditions evaluated included LR [24], rheumatoid arthritis (RA) [21], multiple sclerosis (MS) [22], COPD [17], celiac disease (CD) [18], type 2 diabetes mellitus (T2DM) [25], axSpA [16], SSc [23], chronic pancreatitis (CP) [26], Systemic Lupus Erythematosus (SLE) [19], cystic fibrosis (CF) [15], inflammatory bowel disease (IBD) [20], and chronic kidney disease (CKD) [27]. The diagnostic criteria for these pathologies were varied, ranging from clinical and biochemical criteria to specific diagnostic criteria from international scientific societies.

Regarding osteoporosis, all reviews defined this condition using bone densitometry (DXA or DEXA), mainly applying the World Health Organization (WHO) criterion of T-score ≤ -2.5. Some studies additionally used the Z-score < -2 criterion in specific younger populations or with particular genetic conditions such as cystic fibrosis. The reviews did not address other secondary clinical outcomes, such as fractures or additional complications, limiting themselves exclusively to reporting the prevalence of osteoporosis by the chronic condition analyzed.

Table 1 Characteristics of 12 systematic reviews included in the general review investigating the prevalence of osteoporosis in chronic diseases

First author and year	Number of primary studies	Sample size	Countries evaluated	Population studied	Type of study	Chronic disease	Chronic disease assessment	Osteoporosis assessment
Paccou (2010)	10	888	United Kingdom, Canada, Australia, Italy, Germany, United States	Adult patients with cystic fibrosis, mean age 28.2 years (18.5–32) years	Systematic review and meta-analysis	Cystic Fibrosis	Diagnosis based on clinical and genetic criteria	Bone densitometry (DXA), T-score <= -2.5
Ramírez (2017)	5	905	Spain, France, Netherlands, Germany, Morocco, Turkey, Croatia, Sweden, India, China, Mexico, Canada, United Kingdom, Taiwan, Italy	Patients with Axial Spondyloarthritis, male predominance (57–85%), age between 29–50 years	Systematic review and meta-analysis	Axial Spondyloarthritis	Diagnosis based on ASAS or New York criteria	Bone densitometry (DXA), T-score < -2.5
Chen (2019)	57	8753	Japan, Brazil, Malaysia, Iran, Saudi Arabia, China, United States, Spain, Poland, Germany	Patients with Chronic Obstructive Pulmonary Disease (COPD), mean age 67.8 years, 69% of men.	Systematic review and meta-analysis	Chronic Obstructive Pulmonary Disease	Diagnosis by spirometry (FEV1 < 80% of predicted value)	Bone densitometry (DXA), T-score <= -2.5
Ganji (2019)	6	563	United Kingdom, Brazil, India, Hungary, Poland	Patients with Celiac Disease, premenopausal women and men under 55 years, mean age not specified	Systematic review and meta-analysis	Celiac Disease	Diagnosis based on positive serology and duodenal biopsy	Bone densitometry (DXA), T-score <= -2.5
Gu (2020)	31	3089	Japan, Germany, Netherlands, Italy, Malaysia, Mexico, Canada, Spain, Hungary, United Kingdom, China	For patients with Systemic Lupus Erythematosus, the mean age is not specified.	Systematic review and meta-analysis	Systemic Lupus Erythematosus	Diagnosis based on American Society of Rheumatology (ACR) criteria	Bone densitometry (DXA), T-score < -2.5
Kärnsund (2020)	12	3661	Denmark, United States, Norway, Canada, Netherlands, Taiwan	Patients with Inflammatory Bowel Disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC)	Systematic review	Inflammatory Bowel Disease	Diagnosis based on clinical criteria and laboratory tests	Diagnosis based on T and Z scores or ICD-10 codes
Moshayedi (2022)	57	227,812	Australia, Iran, Argentina, China, Germany, Tunisia, France, Thailand, Greece, Malaysia, South Korea, Kazakhstan, Romania, Italy, Pakistan, Mexico, India, Sweden, Turkey, Colombia, Ireland, United Kingdom, Norway, Brazil, United States, Morocco, Spain, Venezuela	For patients with rheumatoid arthritis, the mean age not specified	Systematic review and meta-analysis	Rheumatoid Arthritis	Diagnosis based on clinical and radiological criteria	Bone densitometry (DXA), T-score <= -2.5
Azadvari (2022)	31	13,906	Canada, Poland, Iran, Denmark, United Kingdom, Czech Republic, Italy, Norway, Turkey, United States, Egypt, Australia, Greece, Tunisia	Patients with Multiple Sclerosis, mean age between 25 and 56 years, female predominance.	Systematic review and meta-analysis	Multiple Sclerosis	Diagnosis based on clinical and radiological criteria	Bone densitometry (DXA), T-score <= -2.5
Tu (2022)	22	1839	Canada, Brazil, India, Egypt, Italy, Spain, Greece, China, France, Turkey, Morocco, Hungary, Thailand, Iceland, Russia, Australia	Patients with Systemic Sclerosis, mean age 57.3 years, 90.6% women	Systematic review and meta-analysis	Systemic Sclerosis	Diagnosis based on American Society of Rheumatology (ACR) criteria	Bone densitometry (DXA), T-score <= -2.5
Kang (2023)	10	836	United States, Spain, France, Morocco, China, Saudi Arabia	Patients with liver cirrhosis, mean age 52.12 years, 50.10% women	Systematic review and meta-analysis	Liver Cirrhosis	Diagnosis is based on clinical history, biochemical tests, and clinical criteria.	Bone densitometry (DEXA), BMD T-score <= -2.5

Table 1 (continued)

First author and year	Number of primary studies	Sample size	Countries evaluated	Population studied	Type of study	Chronic disease	Chronic disease assessment	Osteoporosis assessment
Liu (2023)	21	11,603	Japan, Brazil, Malaysia, Iran, Saudi Arabia, China, United States, Spain, Germany	Patients with Type 2 Diabetes Mellitus, mean age not specified	Systematic review and meta-analysis	Diabetes Mellitus	Diagnosis based on clinical criteria and laboratory tests	Bone densitometry (DXA), T-score <= -2.5
Chhoda (2023)	21	20,155	United States, India, China, Argentina, United Kingdom, Ireland, Germany, Denmark, Netherlands, Czech Republic, Norway, Sweden, Italy	Patients with chronic pancreatitis	Systematic review and meta-analysis	Chronic Pancreatitis (CP)	Clinical, radiological, endoscopic, histological, ICD-9/10 codes	DXA (Dual X-ray Absorptiometry), T-score ≤ -2.5
Duarte (2023)	153	78,092	42 countries	Adults with chronic kidney disease (stages 3a–5D)	Systematic review with meta-analysis	Chronic Kidney Disease (CKD)	Clinical stages according to estimated glomerular filtration rate (eGFR), including renal replacement therapy (hemodialysis, peritoneal dialysis, or kidney transplantation)	Bone densitometry (DXA) with WHO criterion: T-score ≤ -2.5

Risk of bias analysis

The risk of bias assessment of the systematic reviews analyzed using the ROBIS tool showed that most reviewed studies presented a low risk in eligibility criteria, study identification and selection, and data extraction and evaluation. This suggests that all reviewed articles' basic methodological processes for conducting systematic reviews were rigorous and adequate (Table 2).

However, eight studies showed significant concerns in synthesizing and interpreting findings. These articles include those by Ganji et al. (2019) [18], Kärnsund et al. (2020) [20], Moshayedi et al. (2022) [21], Azadvari et al. (2022) [22], Kang et al. (2023) [24], Liu et al. (2023) [25], Chhoda et al. (2023) [26] and Duarte et al. (2023) [27]. The main reasons for these concerns were high heterogeneity among included studies, limited sample sizes, and variability in methodologies and populations studied, which affected the practical and clinical interpretation of the results. Consequently, these systematic reviews were rated with a high risk of bias.

The distribution of risk of bias among the chronic diseases studied shows that reviews on COPD [17], SLE [19], SSc [23], axSpA [16], and CF [15] presented a low risk, while reviews on T2DM [25], RA [21], MS [22], LC [24], CD [18], IBD [20], CP [26], and CKD [27] were classified as high risk. It is important to highlight that, despite these methodological limitations, these reviews represent the best evidence currently available on the prevalence of osteoporosis in these conditions, and their results remain valuable for understanding the magnitude of the problem in the context of various chronic diseases.

Prevalence of osteoporosis according to chronic disease

Figure 2 shows the prevalence of osteoporosis in twelve chronic diseases, categorized into three levels of prevalence. Of the 13 systematic reviews included, 12 contained meta-analyses from which this data could be extracted. COPD stands out with the highest prevalence (37.6%, 95% CI: 34.0–43.0) [17], being the only disease classified as high prevalence (≥ 30%). In the moderate range (20-29.9%) are: T2DM (27.7%, 95% CI: 21.4–34.0) [25], RA (27.6%, 95% CI: 23.9–31.3) [21], SSc (27.0%, 95% CI: 24.0–31.0) [23], CKD (24.5%, 95% CI: 21.3–27.8) [27], CF (23.5%, 95% CI: 16.6–31.0) [15], CP (23.4%, 95% CI: 16.6–32.0) [26], and axSpA (22.0%, 95% CI: 11.7–34.4) [16]. Finally, four diseases present low prevalence: MS (17.0%, 95% CI: 14.0–20.0) [22], SLE (16.0%, 95% CI: 12.0–19.0) [19], LC (14.8%, 95% CI: 14.2–15.5) [24], and CD (14.2%, 95% CI: 9.0-20.5) [18].

Overlapping of primary studies and the value of the CCA

Of the 416 primary inclusions distributed across 13 systematic reviews, only five studies were duplicated, yielding a corrected covered area (CCA) of 0.10%. According

Table 2 Presentation of the ROBIS assessment of the 13 systematic reviews included in the umbrella review

Systematic review (First author and year)	Phase 2				Phase 3
	1. Study eligibility criteria	2. Identification and selection of studies	3. Data collection and study appraisal	4. Synthesis and findings	Risk of bias in the review
Paccou (2010)	Low	Low	Low	Low	Low
Ramírez (2017)	Low	Low	Low	Low	Low
Chen (2019)	Low	Low	Low	Low	Low
Ganji (2019)	Low	Low	Low	High	High
Gu (2020)	Low	Low	Low	Low	Low
Kärnsund (2020)	Low	Low	Low	High	High
Moshayedi (2022)	Low	Low	Low	High	High
Azadvari (2022)	Low	Low	Low	High	High
Tu (2022)	Low	Low	Low	Low	Low
Kang (2023)	Low	Low	Low	High	High
Liu (2023)	Low	Low	Low	High	High
Chhoda (2023)	Low	Low	Low	High	High
Duarte (2023)	Low	Low	Low	High	High

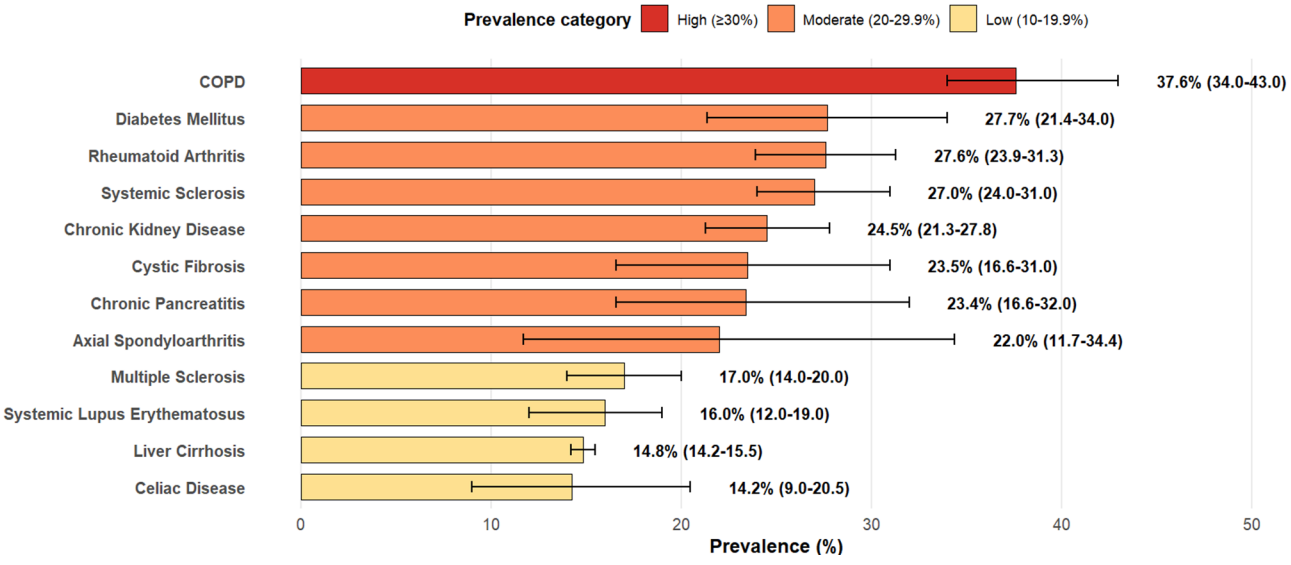

Fig. 2 Prevalence of osteoporosis (95% confidence intervals) in twelve chronic diseases

to established thresholds this represents light overlap, indicating that the umbrella review synthesises largely independent evidence bases. Duplications were confined to the rheumatology cluster—two ankylosing-spondylitis studies that also met rheumatoid-arthritis eligibility, one lupus study included for comparison in the rheumatoid-arthritis review, and one systemic-sclerosis cohort analysed together with rheumatoid-arthritis. No overlap was found between reviews addressing respiratory, gastrointestinal, hepatic, endocrine-metabolic or renal disorders. Therefore, the potential inflation of summary estimates or bias due to redundancy of primary data is minimal, supporting the robustness of our pooled prevalence synthesis across chronic-disease categories.

Discussion

Main findings

The findings of this UR show that the prevalence of osteoporosis varies notably among the different chronic diseases analyzed, with COPD occupying the first place (around 36.8%) and other pathologies such as celiac disease presenting lower values (approximately 11.9%). Likewise, conditions such as diabetes mellitus, rheumatoid arthritis, and systemic sclerosis exhibit prevalences close to the moderate range, around 25–30%. These data highlight the importance of considering systematic bone health assessment in patients with certain comorbidities, given that a relevant proportion could be at risk of fractures and complications associated with decreased bone mineral density.

It is important to note that the chronic diseases represented in our final selection, including chronic obstructive pulmonary Disease (COPD), type 2 diabetes mellitus (T2DM), rheumatoid arthritis (RA), multiple sclerosis (MS), liver cirrhosis (LC), celiac disease (CD), among others, reflect the available published systematic reviews that met our inclusion criteria at the time of our search, rather than a predetermined selection of conditions. Several prevalent chronic diseases (such as hypertension, coronary artery disease, and obesity) are not represented in our results because no systematic reviews meeting our inclusion criteria were identified for these conditions, highlighting an important gap in the current literature.

Pathophysiology and underlying mechanisms

The relationship between chronic diseases and osteoporosis is largely explained by shared pathophysiological mechanisms, mainly low-grade chronic inflammatory states, which promote bone resorption and alter bone formation. Chronic diseases have a common characteristic of persistent low-grade inflammation, which is characterized by excessive production of inflammatory mediators such as tumour necrosis factor Alpha (TNF-α), interleukin 1 (IL-1), and interleukin 6 (IL-6) that stimulate the differentiation and activation of osteoclasts, accelerating bone mass loss [28, 29]. This imbalance in bone remodeling constitutes the common pathogenic substrate that predisposes the development of osteoporosis in multiple chronic diseases.

Systemic inflammatory mediators play a central role in this process. Proinflammatory cytokines such as IL-6 and TNF-α induce greater osteoclastic activity, promoting bone resorption by activating the pathway based on the interaction between the receptor activator of nuclear factor kappa-B, its ligand, and osteoprotegerin (RANK/RANKL/OPG). Additionally, chronic inflammation can negatively affect osteoblast function, altering the balance between bone formation and resorption [28, 29]. This pathogenic mechanism is particularly relevant in autoimmune and chronic inflammatory diseases, but is also observed in various metabolic and endocrine conditions.

Autoimmune and inflammatory diseases

In autoimmune diseases such as SLE or systemic sclerosis, chronic inflammation and immune alterations promote significant imbalances in bone remodeling. In SLE, various studies have found that osteoporosis is mainly associated with activating the type I interferon pathway and dysregulating B lymphocytes, which alter bone metabolism [30]. In the case of SSc, additional mechanisms include vasculopathy and tissue fibrosis, which compromise bone microcirculation [31].

Meanwhile, chronic autoimmune activity in multiple sclerosis alters bone homeostasis by increasing proinflammatory cytokines, T cell dysregulation, and excessive production of catabolic mediators. In this pathology, in addition to systemic inflammation, neurodegenerative factors and reduced mobility due to spasticity, fatigue, and muscle weakness contribute to insufficient mechanical stimulation for bone remodeling [32]. On the other hand, in axial spondyloarthritis, localized inflammation in the entheses and spine frequently leads to changes in skeletal architecture, activating osteoclastogenic pathways mediated by interleukin 17 (IL-17) and interleukin 23 (IL-23) [33].

Finally, RA represents a classic inflammatory osteoporosis model, combining local erosions and systemic osteoporosis due to the high inflammatory load. Cytokines such as TNF-α, IL-1, IL-6, and IL-17 promote osteoclastogenesis through the RANK/RANKL system while inhibiting osteoblast-mediated bone formation [34].

Digestive, hepatic, and renal diseases

Regarding liver cirrhosis, chronic liver disease leads to hepatic osteodystrophy, in which hormonal imbalance and dysfunction in vitamin D metabolism constitute the main pathogenic mechanisms. The reduction in the production of growth factors such as IGF-1 and alterations in hepatic hydroxylation of vitamin D compromise bone mineralization, a phenomenon that intensifies in the advanced stages of the disease [35].

Celiac disease generates malabsorption of calcium and vitamin D, altering bone homeostasis. Precisely, intestinal inflammation mediated by T lymphocytes specific against gluten and the consequent mucosal damage reduces the absorption of essential nutrients for the maintenance and formation of bone tissue [36]. Similarly, IBD, especially Crohn's disease, is associated with an elevated risk of osteoporosis, linked both to inflammation mediated by IL-23/IL-17 and to prolonged use of corticosteroids [37].

Concerning CKD, an entire system explains the appearance of osteoporosis, from the alteration in the production of the active form of vitamin D (1,25-dihydroxyvitamin D) to the elevation of fibroblast growth factor 23 (FGF-23), which triggers secondary hyperparathyroidism that promotes bone resorption. This condition, called renal osteodystrophy, is characterized by alterations in the quantity and quality of bone tissue, with a higher prevalence in patients on dialysis (30%) [38].

Pancreatic and pulmonary diseases

In chronic pancreatitis, enzyme deficiency reduces the absorption of essential nutrients such as proteins, calcium, and vitamin D, accelerating bone mass loss. Persistent pancreatic inflammation mediated by NF-κB and possible hormonal imbalances add to this; in advanced

cases, pancreatogenic diabetes may occur, which aggravates skeletal deterioration [39].

The etiology of osteopathy in cystic fibrosis is multifactorial: intestinal malabsorption due to exocrine pancreatic insufficiency causes deficiencies of vitamins D and K and decreased calcium absorption, which leads to secondary hyperparathyroidism; additionally, chronic inflammation and recurrent pulmonary infections elevate bone resorption markers, particularly during infectious exacerbations [40]. Hormonal alterations (relative hypogonadism, pubertal delay) and the direct effect of the CFTR mutation on bone tissue have also been observed [41]. Together, patients with CF show an imbalance with increased resorption and reduced bone formation, resulting in osteopenia or osteoporosis from an early age.

COPD and diabetes: particular mechanisms of their higher prevalence

One of the central elements of COPD is the frequent history of smoking, which not only constitutes the main risk factor for pulmonary disease but also accelerates bone loss by favoring osteoclastic activity and decreasing bone formation. Added to this is the systemic chronic inflammation characteristic of COPD, with elevation of mediators such as IL-6 or TNF-α, which promote bone resorption [42].

Additionally, many patients present functional limitations and a sedentary lifestyle due to dyspnea and fatigability, which reduces mechanical stimulation on the skeleton and, consequently, bone mineral density. The prolonged use of systemic and inhaled corticosteroids is another factor that can accelerate osteoporosis, as corticosteroids increase the apoptosis of osteoblasts and osteocytes and the half-life of osteoclasts. Moreover, the population with COPD tends to be older, which adds a risk factor since, with aging, there is a natural decline in bone mass [42].

Regarding diabetes mellitus, prolonged hyperglycemia plays a decisive role in damage to bone tissue through the formation of advanced glycation end products (AGEs), which reduce the quality of the bone matrix and its plasticity, promoting microfractures and progressive deterioration of the microarchitecture [43]. Additionally, alterations in the Wnt/β-catenin pathway, fundamental for the formation and maturation of osteoblasts, have been documented, which can decrease the capacity for bone regeneration [44].

Added to this are microvascular and neuropathic complications inherent to diabetes, which restrict physical activity (due to neuropathic pain, ulcers, or chronic infections), reducing the mechanical stimulus necessary to maintain bone mass. Even in T2DM, which is traditionally associated with a hyperinsulinemic profile (which could have a certain anabolic effect on bone), the negative impact of hyperglycemia and AGEs seems to predominate over time, resulting in a high prevalence of osteoporosis and an increased risk of fractures [45].

Importance of findings for public health

The prevalence of osteoporosis identified in this UR for different chronic diseases takes on special significance in public health. As mentioned, providing quantitative data on how many people already have osteoporosis beyond those at high risk generates valuable information for authorities and health professionals to establish resource allocation priorities and implement prevention and early detection programs. According to the IOF, fractures linked to osteoporosis constitute a significant public health problem, generating considerable costs in terms of hospital care and rehabilitation [2].

In many nations, health systems must face the consequences of the progressive aging of the population and the increase in chronic diseases, which multiplies the impact of osteoporosis at a socioeconomic level. When diseases such as COPD and T2DM show high prevalences of osteoporosis, it is foreseeable that the frequency of adverse events, such as hip or spine fractures, will increase in these patients, with the consequent need for more complex medical and socio-family interventions [2]. Furthermore, the fact that part of the disease burden falls on working populations can accentuate the cost of absenteeism and decreased productivity.

The timely detection of reduced bone mineral density has become crucial for secondary prevention, so that this evidence could lead to more specific clinical guidelines. Establishing, for example, the indication for routine bone densitometry in patients with various chronic diseases according to their age and additional risk factors could anticipate the diagnosis of osteoporosis and facilitate an early approach. Such a strategy would not only reduce the number of fractures but would also alleviate the economic burden represented by long periods of hospitalization and rehabilitation following osteoporotic fractures.

On the other hand, implementing multidisciplinary interventions is essential to address the risk factors shared by these chronic diseases and osteoporosis. Pulmonary rehabilitation programs in COPD with a supervised exercise component, rigorous metabolic controls in diabetes, or more personalized therapeutic schemes in autoimmune pathologies could reduce bone loss. Such initiatives require the coordination of pulmonologists, endocrinologists, rheumatologists, physiotherapists, and nutritionists, who must work in an integrated manner to address the underlying disease and bone health simultaneously.

Equally important is health education for patients and the general population on the relevance of adopting healthy habits, such as reducing smoking, promoting

physical activity, and maintaining a balanced diet rich in calcium and vitamin D, and adherence to indicated treatments. These practices can mitigate the progression of the underlying chronic disease and reduce the risk of osteoporosis and associated fractures. In this sense, awareness campaigns driven by government bodies and medical entities could strengthen prevention, while helping to optimize the allocation of available resources.

In assessing the public health implications of our findings, it is important to consider some methodological aspects of our approach. Our UR methodology synthesizes prevalence data from existing systematic reviews rather than conducting a new meta-analysis of primary studies, aligning with the hierarchical structure of evidence where systematic reviews represent the highest level for informing health decisions and policy-making. While this approach provides a comprehensive overview of the current evidence landscape, we acknowledge that our results reflect the methodological choices, inclusion criteria, and statistical methods of the original review authors. This is particularly relevant given the variability in diagnostic criteria for osteoporosis across studies (although most used the WHO T-score ≤ -2.5 standard) and the heterogeneity of studied populations across different chronic diseases.

These findings highlight the need for more systematic reviews and meta-analyses on osteoporosis prevalence in other significant chronic conditions not represented in our analysis, such as hypertension, coronary artery disease, stroke, obesity, asthma, and various neurological disorders. From a public health perspective, standardized osteoporosis assessment methodology across chronic diseases would facilitate more robust prevalence comparisons and better resource allocation decisions. Future research should also focus on specific subpopulations (e.g., different age groups, disease severity levels, or treatment regimens) within each chronic disease to provide more granular prevalence data that could better inform targeted screening and preventive strategies at the population level. By providing this comprehensive overview of current evidence, we hope to stimulate more rigorous and methodologically consistent research in this important intersection of bone health and chronic disease management, ultimately improving public health outcomes through better-informed policy decisions.

Strengths and limitations

One of the main strengths of this work lies in the systematic application of recognized methodological guidelines and the use of the ROBIS tool for assessing the risk of bias in systematic reviews, strengthening the rigor and transparency of the procedures. Additionally, a broad search was conducted in multiple high-impact databases covering different geographical regions and disciplines, increasing the probability of identifying most published reviews. Similarly, including a high number of reviews reporting prevalences of osteoporosis in various chronic diseases offers a panoramic and updated view of the magnitude of this comorbidity, generating relevant evidence for clinical practice and public health.

Among the notable limitations is the methodological and clinical heterogeneity of the primary studies included in the analyzed reviews, particularly regarding diagnostic criteria for chronic disease and methods of measuring bone mass. Another critical aspect is the high risk of bias identified in eight of the thirteen included systematic reviews, mainly in synthesizing and interpreting findings. This largely responds to the lack of methodological standardization in the research on osteoporosis in chronic diseases and the inherent variability in the populations and clinical contexts studied.

Despite these methodological limitations, it is important to contextualize that the main objective of this UR was to provide a comprehensive synthesis of available prevalence data, responding to a clinical and public health need to quantify the magnitude of the osteoporosis problem across different chronic diseases. In this sense, even reviews with a higher risk of bias provide valuable information, representing the best evidence currently available for specific conditions. However, we recognize that prevalence estimates derived from these reviews should be interpreted with due caution, and it would benefit future primary research to improve methodological standardization in this field.

Finally, the disparity in the quality of primary studies may have affected the robustness of the consolidated results, especially in those reviews with less methodological rigor. This limitation underscores the need to consider both the magnitude of the reported prevalences and the quality of the evidence supporting them when formulating clinical or health policy recommendations.

Conclusions and recommendations

Collectively, the findings of this UR demonstrate a considerable prevalence of osteoporosis in various contexts of chronic diseases, highlighting pathologies such as COPD and diabetes mellitus. These results reinforce the importance of timely diagnostic evaluation and comprehensive management of osteoporosis in clinical practice, given the high burden of morbidity and the high healthcare costs that osteoporotic fractures pose in populations with underlying chronic conditions.

In light of these conclusions, implementing systematic bone health screening strategies in patients with chronic diseases highly prone to osteoporosis, such as COPD, T2DM, and rheumatic pathologies, is suggested. Likewise, it is recommended to promote future research that delves into shared pathophysiological mechanisms,

considering methodological aspects that address the heterogeneity of diagnostic criteria and disparities in the quality of primary studies. Finally, it is essential to adopt multidisciplinary intervention programs that combine monitoring of bone mineral density, pharmacotherapeutic adjustments, and education on healthy habits to reduce the incidence of fractures and improve the quality of life of affected individuals.

Supplementary Information

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Supplementary Material 1

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Data availability
Data are available upon request to the corresponding author.

Declarations

Ethics approval and consent to participate
Since this manuscript is a secondary database study, it was not required.

Consent for publication
Not applicable.

Informed consent
Since this is a secondary data analysis, informed consent was not required.

Competing interests
The authors declare no competing interests.

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