A Systematic Review

Prevalence of osteoporosis in Iran: A meta-analysis

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Background: Several studies have investigated the prevalence of osteoporosis among general population in several parts of Iran. However, the results have been inconsistent. This meta-analysis was conducted to estimate the overall prevalence of osteoporosis. **Materials and Methods:** International and national electronic databases were searched until April 2012, including Web of Knowledge, Medline, Scopus, Ovid, ScienceDirect, Science Information Database, IranMedex, MagIran, as well the relevant conference databases. The reference lists of included studies were screened as well. The cross-sectional studies addressing the prevalence of osteoporosis among Iranian general population were retrieved irrespective of age and sex. Bone mineral density (BMD) based on T-score was classified as follows: (a) normal (T-score ≥−1); (b) osteopenia (−2.5SD < T-score <−1SD); (c) osteoporosis (T-score ≤−2.5). Study quality was assessed using the recommended checklist of STROBE. **Results:** Of 2598 retrieved studies, 31 studies comprising 34,814 people was used for meta-analysis. The overall prevalence of osteoporosis in lumbar spine was 0.17 (95% CI: 0.13, 0.20) and that of osteopenia was 0.35 (95% CI: 0.30, 0.39). The prevalence was higher in older age groups, in women, and in the northern regions of the country, with an increasing trend in recent years. **Conclusion:** This meta-analysis indicated that osteoporosis and osteopenia are common problems among Iranian population older than 30 years. Furthermore, increasing trend of the diseases in recent years is promising a critical public health problem in Iran in the near future. However, due to the heterogeneity between the studies' results, further evidence based on a national survey is needed to estimate the exact prevalence of the diseases in the country.

Key words: Iran, meta-analysis, osteopenia, osteoporosis, prevalence, systematic review

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INTRODUCTION

Osteoporosis is a metabolic disease that is associated with increased bone porosity.[1] Indeed, osteoporosis is a disease of the skeletal system characterized by low bone mass and deterioration of bone tissue, which may lead to an increase risk of bone fractures, especially in the wrist, hip, and spine.[2] In osteoporotic patients, bone mineral density (BMD) is ≥2.5 standard deviation below the average mineral density of young adults.[3]

The prevalence of osteoporosis increases with age. The disease is a common old-age problem, especially among women.[4,5] Osteoporosis is a major leading cause of bone fragility fractures.[5] Fragility fracture may occur in any part of the body particularly in hip, spine, and forearm;[6] the most dangerous of which is hip fracture.[7] In 1990, the prevalence of fragility fracture was about 1.3-1.7 million worldwide. It is estimated to reach three million by 2025.[8,9] In addition to fragility fracture, osteoporosis may increase the rate of hospitalization due to secondary complications.[10]

With increase life expectancy, osteoporosis is emerging as a serious health problem worldwide, especially in developing countries. Several genetic and environmental factors may influence the development of osteoporosis,[11] the most important of which are low physical activity, smoking, alcohol consumption, wasting, calcium malabsorption, vitamin D deficiency, previous bone fractures, using corticosteroids, hormonal agents, genetic factors, and female sex.[5,12]

Like many developing countries, life expectancy has increased in Iran. Since osteoporosis increases with age, the disease may be considered as a health priority. Several studies have investigated the prevalence of osteoporosis among general population in several parts of Iran. However, the results have been inconsistent. This meta-analysis was conducted to estimate the overall prevalence of osteoporosis among Iranian general population.

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MATERIALS AND METHODS

Definitions

Dual-energy X-ray absorptiometry (DXA) is a means of measuring BMD. The DXA is used for diagnosis and screening of both osteoporosis and osteopenia.[1] World Health Organization (WHO) has classified BMD based on T-score as follows: (a) Normal: A value of BMD within 1 standard deviation of the young adult reference mean (T-score ≥−1); (b) osteopenia: A value of BMD >1 standard deviation below the young adult mean, but <2 standard deviations below this value (−2.5SD < T-score <−1SD); (c) Osteoporosis: A value of BMD 2.5 standard deviations or more below the young adult mean (T-score ≤−2.5).[3]

Searching

Major electronic databases were searched with the following keywords: Prevalence, incidence, osteoporosis, and Iran. The international databases, which were searched, included Web of Knowledge (January 1945 to April 2012); Medline (January 1950 to April 2012); Scopus (January 1973 to April 2012); ScienceDirect (January 1823 to April 2012); and Ovid (January 1860 to April 2012). In addition, the following national electronic sources were searched: Science Information Database (up to April 2012); MagIran (up to April 2012); and IranMedex (up to April 2012).

In order to obtain additional literatures, the reference lists of all included studies were scanned. The authors of included studies were contacted as well. The following conference databases were searched for unpublished data until April 2012:

- National Osteoporosis Society; available from: www.nos.org.uk
- International Conference on Osteoporosis and Bone Research; available from: www.csobmr.org.cn/icobr2010/en
- European Congress on Osteoporosis and Osteoarthritis; available from: http://www.iof-ecceo12.org
- National Osteoporosis Foundation Support Community; available from: www.inspire.com/groups/national-osteoporosis-foundation
- International Osteoporosis Foundation (IOF); available from: http://www.iofbonehealth.org

Criteria for including studies

All cross-sectional studies regarding the prevalence of osteoporosis in Iran using DXA method were retrieved irrespective of publication date and language. Iranian general population was considered as study population regardless of age and sex. The studies addressing osteoporosis in populations other than Iranian citizens were excluded. The primary outcome of interest was prevalence of osteoporosis and the secondary one was prevalence of osteopenia.

Data collection and validity assessment

Two authors (ZC and AD) independently screened the title and abstract of the retrieved studies and then reviewed the full texts to extract studies that met the inclusion criteria of this meta-analysis. The authors were not blinded to the names of the studies' authors and journals. Any disagreements were resolved by adjudication with a third author (JP). The percent agreement of the two authors was 97% and the Kappa statistics for checking reliability was 84.5%. The variables that were extracted for data analysis included study design, year and location of study conduction, sample size, number of outcomes, mean age of participants, and gender.

Six selected items from the recommended checklist of STROBE[13] was used for assessing the quality of reporting. The items included (a) clearly define the outcome, i.e., osteoporosis and osteopenia; (b) give the eligibility criteria; (c) present key elements of study design; (d) report numbers of outcome events; (e) explain how the study sample was arrived at; and (f) describe the setting, locations, and relevant dates. The studies that fulfilled all criteria were classified as high quality. The studies that did not meet one criterion were classified as intermediate quality. The studies that did not fulfill more than one criterion were classified as low quality.

The studies with small sample size were excluded from the analysis. For this purpose, a minimum sample size of 96 was considered as cut-off point for estimating prevalence of osteoporosis by assuming P to be 50% with significance level of 5% and statistical power of 80%. Thus, the studies, with sample size <96, were considered as ineligible and were excluded from the analysis.

Heterogeneity and publication bias

We explored statistical heterogeneity using the chi-square (Chi^2) test at the 5% significance level ($P < 0.05$). We quantified inconsistency across studies results using I^2 statistic.[14] We also estimated the between-study variance using tau-square (Tau^2) statistic.[15] We used Begg[16] and Egger[17] statistical tests to assess publication bias quantitatively.

Both Review Manager 5[18] and statistical software Stata 11 (Stata Corp, College Station, TX, USA) were used for data analysis. Meta-analysis was performed to obtain summary measure of "prevalence" of osteoporosis and osteopenia in the general population. Data were analyzed and the results were reported using a random-effects model[19] with 95% confidence interval (CI).

RESULTS

Description of studies

We retrieved 2492 studies up to April 2012, including 1732 references through searching international electronic

databases, 654 references through searching national electronic databases, 99 references through checking reference lists, and seven references through personal contact with the study authors [Table 1 and Figure 1]. Of 2492 retrieved references, 588 references were excluded because of duplication, 1766 references did not relate to the objective of this review, 102 references did not meet the eligibility criteria, and five references had small sample size. Eventually, we included 31 studies in the meta-analysis [20-50] that involved 34,814 participants; 4886 men with mean age of 49.2 years; and 29,928 women with a mean age of 52.5 years.

Estimated prevalence

We considered all studies addressed osteoporosis irrespective of the organ or body location, including spine, femur, hip, and arm. However, spine was the only organ of which osteoporosis was addressed by all studies. Femur was

Table 1: Characteristics of the included studies in meta-analysis; repeated references show the prevalence of osteoporosis and osteopenia among different subgroups

Study	Location	Sex	Menopause	Mean age	Sample	Prevalence of osteoporosis		Prevalence of osteopenia	
						Spinal	Femoral	Spinal	Femoral
Adinehpour *et al.*, 2010	Fars	Male	Male	46.0	263	0.02	0.06	0.42	0.48
Amiri *et al.*, 2004	Bushehr	Female	Post	–	174	0.08	0.04	0.51	0.38
Amiri *et al.*, 2004	Bushehr	Female	Pre	–	414	0.01	0.00	0.13	0.07
Amiri *et al.*, 2008	Bushehr	Female	Post	59.6	406	0.07	0.03	0.51	NR
Bayat *et al.*, 2008	Tehran	Female	Post	57.2	200	0.26	0.07	NR	0.48
Bayat *et al.*, 2010	Tehran	Female	Pre	43.1	644	0.30	NR	0.22	NR
Bazrafshan *et al.*, 2011	Gorgan	Female	Post	52.7	260	0.16	0.33	0.40	0.37
Bonakdar *et al.*, 2008	Isfahan	Female	Mix	44.0	1118	0.09	0.03	0.25	0.27
Dabbaghmanesh *et al.*, 2002	Tehran	Female	Post	58.0	420	0.31	0.14	NR	NR
Dabbaghmanesh *et al.*, 2008	Shiraz	Female	Post	57.2	5573	0.31	0.20	0.40	0.49
Derakhshan *et al.*, 2006	Kurdistan	Female	Post	57.7	305	0.17	0.31	0.56	0.48
Eghbali *et al.*, 2009	Bushehr	Female	Post	59.2	406	0.07	0.04	0.32	0.30
Hamidi *et al.*, 2004	Tehran	Female	Post	57.2	180	0.18	0.06	0.41	NR
Jamshidian *et al.*, 2004	Tehran	Female	Post	NR	354	0.28	0.05	NR	0.38
Jamshidian *et al.*, 2004	Tehran	Female	Pre	NR	389	0.05	0.01	0.29	0.16
Khojastehpour *et al.*, 2009	Shiraz	Female	Mix	53.6	114	0.32	0.18	0.37	0.46
Larijani *et al.*, 2005	Tehran	Female	Mix	43.5	364	0.09	0.02	0.29	0.22
Larijani *et al.*, 2006	Tehran	Male	Male	45.5	189	0.10	0.03	0.35	0.32
Larijani *et al.*, 2006	Tehran	Female	Mix	42.7	2861	0.26	0.07	0.50	NR
Larijani *et al.*, 2007	Tehran	Male	Male	43.2	2340	0.05	0.02	0.37	0.35
Larijani *et al.*, 2007	Tehran	Female	Mix	38.9	600	0.28	0.08	NR	0.49
Moayyeri *et al.*, 2006	Tehran	Male	Male	49.7	340	0.06	0.19	NR	NR
Moayyeri *et al.*, 2006	Tehran	Female	Mix	53.8	3848	0.25	0.12	NR	NR
Moghimi *et al.*, 2008	Urmia	Female	Post	54	225	0.06	0.17	0.06	0.72
Mojibian *et al.*, 2006	Yazd	Female	Post	60.6	502	0.21	NR	0.52	NR
Nazarnia *et al.*, 2005	Shiraz	Female	Mix	NR	250	0.12	NR	0.46	NR
Rajabian *et al.*, 2006	Mashhad	Male	Male	43.2	372	0.26	0.05	0.40	0.39
Rajabian *et al.*, 2006	Mashhad	Female	Mix	41.3	631	0.11	0.05	0.26	0.30
Ranjbar Omrani *et al.*, 2006	Shiraz	Male	Male	57.3	632	0.04	0.01	0.18	0.11
Ranjbar Omrani *et al.*, 2006	Shiraz	Female	Mix	57.2	760	0.17	0.04	0.13	0.19
Salamat *et al.*, 2009	Isfahan	Female	Post	51.8	174	0.05	0.40	0.50	0.45
Salehi *et al.*, 2009	Tehran	Male	Male	46.5	522	0.27	0.05	0.29	0.24
Salehi *et al.*, 2009	Tehran	Female	Mix	47.6	1563	0.10	0.06	0.25	0.18
Salimzadeh *et al.*, 2005	Karaj	Female	Post	59.4	268	0.35	0.16	NR	NR
Sedaghat *et al.*, 2003	Tehran	Female	Post	52.7	180	0.19	0.06	NR	NR
Soltani *et al.*, 2004	Tehran	Male	Male	53.4	347	0.24	0.19	NR	NR
Soltani *et al.*, 2004b	Tehran	Female	Post	53.4	3882	0.22	0.12	NR	NR
Taheripanah *et al.*, 2010	Tehran	Female	Mix	53.7	149	0.12	0.02	0.32	0.29
Touhidi *et al.*, 2011	Fars	Female	Mix	44.5	266	0.30	0.15	0.38	0.36
Yazdani *et al.*, 2009	Tehran	Female	Mix	54.5	1047	0.09	NR	0.44	NR

NR=Not reported

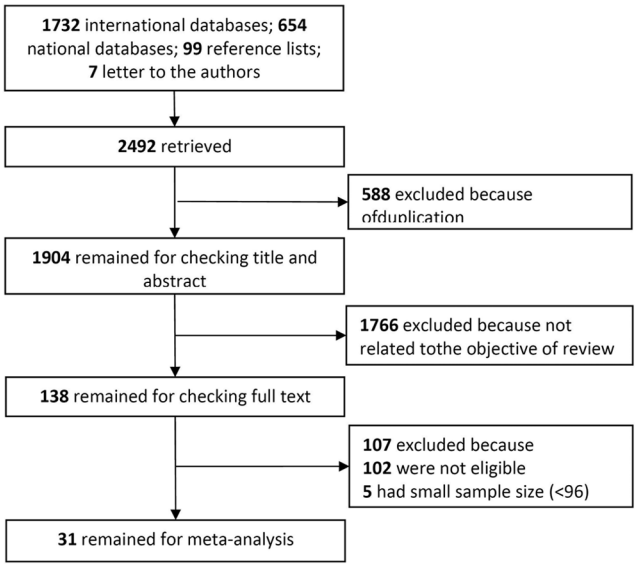

Figure 1: A flow diagram depicting the phases of retrieving articles, checking eligibility criteria, and including the articles into the meta-analysis

the second organ that most but not all studies had addressed. Osteoporosis of hip and arm was addressed by only few studies. In this review, we have reported the osteoporosis of spine that represents all studies and that of femur, which was reported by most studies [Table 1]. However, meta-analysis was performed based on osteoporosis of spine, which comprised all studies.

The overall prevalence of osteoporosis in the lumbar spine, based on the random-effects model, was 0.17 (95% CI: 0.13, 0.20). Furthermore, the prevalence of osteoporosis was 0.12 (95% CI: 0.08, 0.17) among men, 0.03 (95% CI: 0.01, 0.07) among premenopausal women, and 19% (95% CI: 14%, 24%) among postmenopausal women [Figure 2]. The overall prevalence of osteopenia in the lumbar spine, based on random-effects model, was 0.35 (95% CI: 0.30, 0.39). In addition, the prevalence of osteopenia was 0.33 (95% CI: 0.25, 0.42) in men, 0.21 (95% CI: 0.05, 0.37) in premenopausal women, and 0.40 (95% CI: 0.31, 0.49) in postmenopausal women [Figure 3].

Subgroup analysis

The studies were divided into three categories based on the quality of reporting using STROBE checklist of items as follows: 10 studies (31.25%) had high quality; 10 studies (31.25%) had intermediate quality, and 12 studies (37.50%) had low quality. The prevalence of osteoporosis and osteopenia was estimated based on the different qualities of the studies. According to these results, the prevalence of osteoporosis and osteopenia was overestimated by the studies with low quality [Table 2].

The prevalence of osteoporosis and osteopenia was estimated based on the years of studies. According to the results, the overall prevalence of osteoporosis and osteopenia in the lumbar spine had increased significantly in recent years [Table 2].

The prevalence of osteoporosis and osteopenia was estimated based on the geographical regions of the country and the mean age of the participants [Table 2]. The prevalence of osteoporosis and osteopenia in the northern regions of the country was significantly higher than that in the southern regions. In addition, the prevalence of osteoporosis and osteopenia was much higher among people aged 50-69 years as compared to people aged 30-49 years.

Heterogeneity and publication bias

There was considerable heterogeneity among the included studies, so that the result of Chi^2 test for heterogeneity was highly significant ($P < 0.001$). In addition, the I^2 statistic was 98% to 99% [Figures 2 and 3]. In order to reduce the heterogeneity, we divided the studies into subgroups by gender and age groups to achieve homogeneity. Nonetheless, homogeneity was not achieved.

The results of statistical test for publication bias, including Begg and Egger tests, for osteoporosis were statistically significant for lumbar spine ($P = 0.008$ and $P = 0.033$, respectively). In addition, the results of Begg test for osteopenia of lumbar spine was statistically significant ($P = 0.011$), whereas the results of Egger test for osteopenia of lumbar spine was not statistically significant ($P = 0.327$). These results confirmed the presence of publication bias.

Further information

With increase in life expectancy, osteoporosis is becoming a major public health problem worldwide, particularly in developing countries. The results of this meta-analysis confirmed this issue. According to our results, 17% of the Iranian general population aged >30 years had osteoporosis and 35% had osteopenia. Furthermore, our findings indicated that prevalence of these diseases was increasing during the recent years. This means that the prevalence of osteoporosis and thus its associated complications is increasing with life expectancy and may become a critical public health problem in Iran in the near future.

The prevalence of osteoporosis and osteopenia was significantly higher during postmenopausal period than premenopausal period. This finding is mainly secondary to the nature of the disease and the fact that it mainly affects women after the menopause. Furthermore, the overall prevalence of osteoporosis and osteopenia has been increasing in recent years. One reason of this increasing trend may be the increase in life expectancy. Several evidences indicated the presence of a positive correlation between age and prevalence of osteoporosis.[4,5]

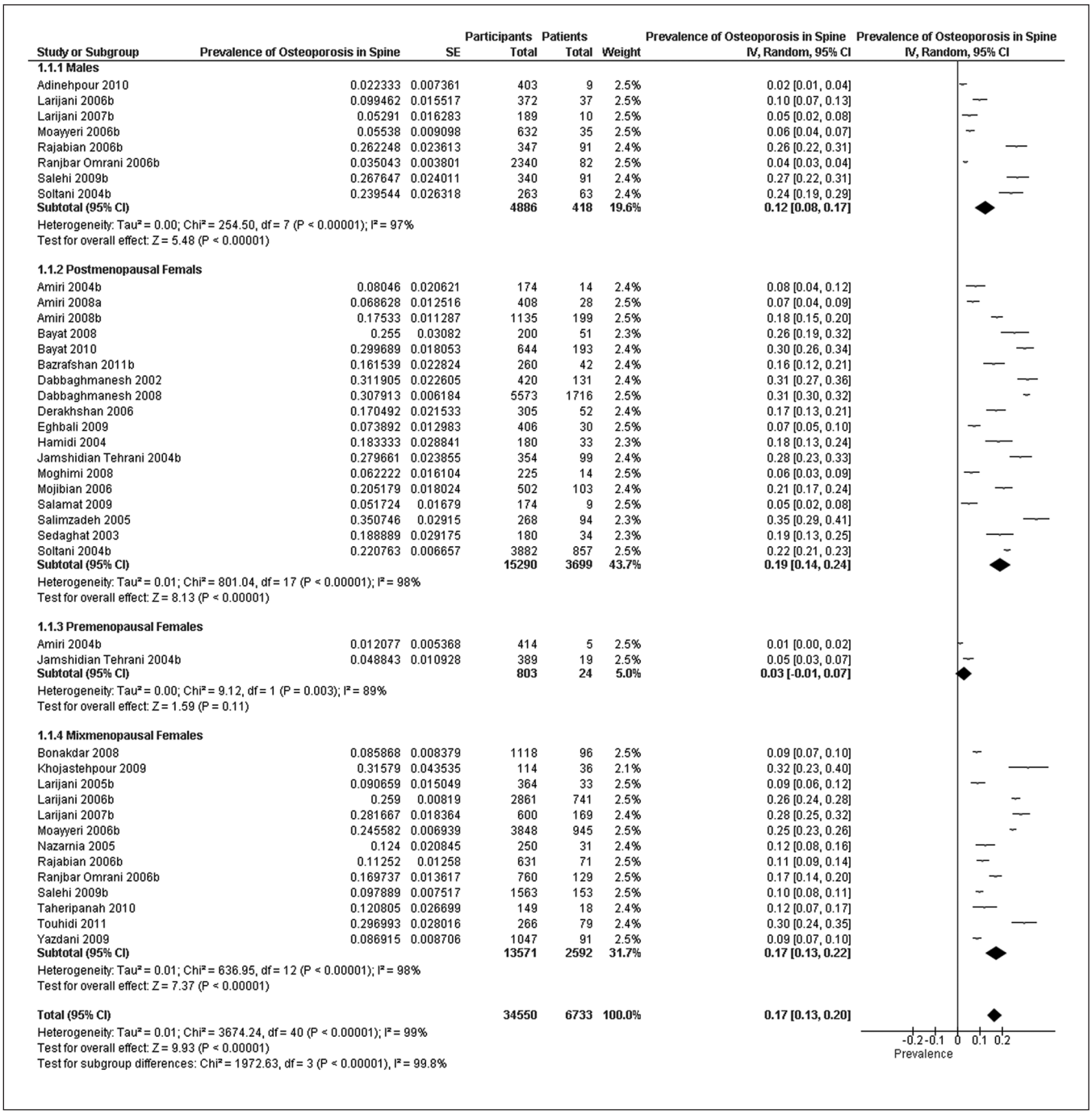

Figure 2: A forest plot for the prevalence of osteoporosis in spine among Iranian general population older than 30 years

The overall prevalence of osteoporosis and osteopenia was higher in women than in men. Nonetheless, the prevalence of osteoporosis and osteopenia was lower in women during premenopausal period compared to men. This issue may result from random error due to limited number of studies (two studies) conducted in women during premenopausal period. Another reason may be the mean difference of age between the two groups (45 years in premenopausal women versus 49 years in men). Previous investigations indicated that women are at higher risk of osteoporosis than men.[5,12]

The prevalence of osteoporosis and osteopenia in the northern regions of Iran was higher than in the southern regions. This issue may be due to the different geographical situation of the two regions. The northern parts of the country are mostly mountainous, while majority of the southern parts is covered by deserts. This issue may help the people who live in the southern parts of the country to receive more vitamin D than residences of the northern parts. Furthermore, there are several other factors that can play a role in coetaneous vitamin D synthesis and explain the difference between the two regions.

Table 2: Subgroup analysis of prevalence of osteoporosis and osteopenia by anatomical site, quality of the included studies, year of studies conduction, geographical regions of the country and the mean age groups using Chi² test for heterogeneity

	Spinal osteoporosis			Spinal osteopenia		
	Prevalence	95% CI	*P* value	Prevalence	95% CI	*P* value
Quality of the included studies						
High	0.134	0.920, 0.177	0.001	0.383	0.307, 0.460	0.001
Intermediate	0.180	0.134, 0.225	0.001	0.313	0.248, 0.379	0.001
Low	0.174	0.111, 0.238	0.001	0.341	0.202, 0.480	0.001
Year of the studies conduction						
2002-2006	0.165	0.122, 0.209	0.001	0.343	0.260, 0.426	0.001
2007-2011	0.166	0.118, 0.214	0.001	0.350	0.294, 0.406	0.001
Geographical regions of the country						
South	0.149	0.087, 0.211	0.001	0.348	0.270, 0.426	0.001
North	0.176	0.140, 0.213	0.001	0.347	0.285, 0.408	0.001
Mean age groups (year)						
30-49	0.142	0.103, 0.181	0.001	0.329	0.280, 0.378	0.001
50-69	0.186	0.146, 0.226	0.001	0.360	0.272, 0.449	0.001

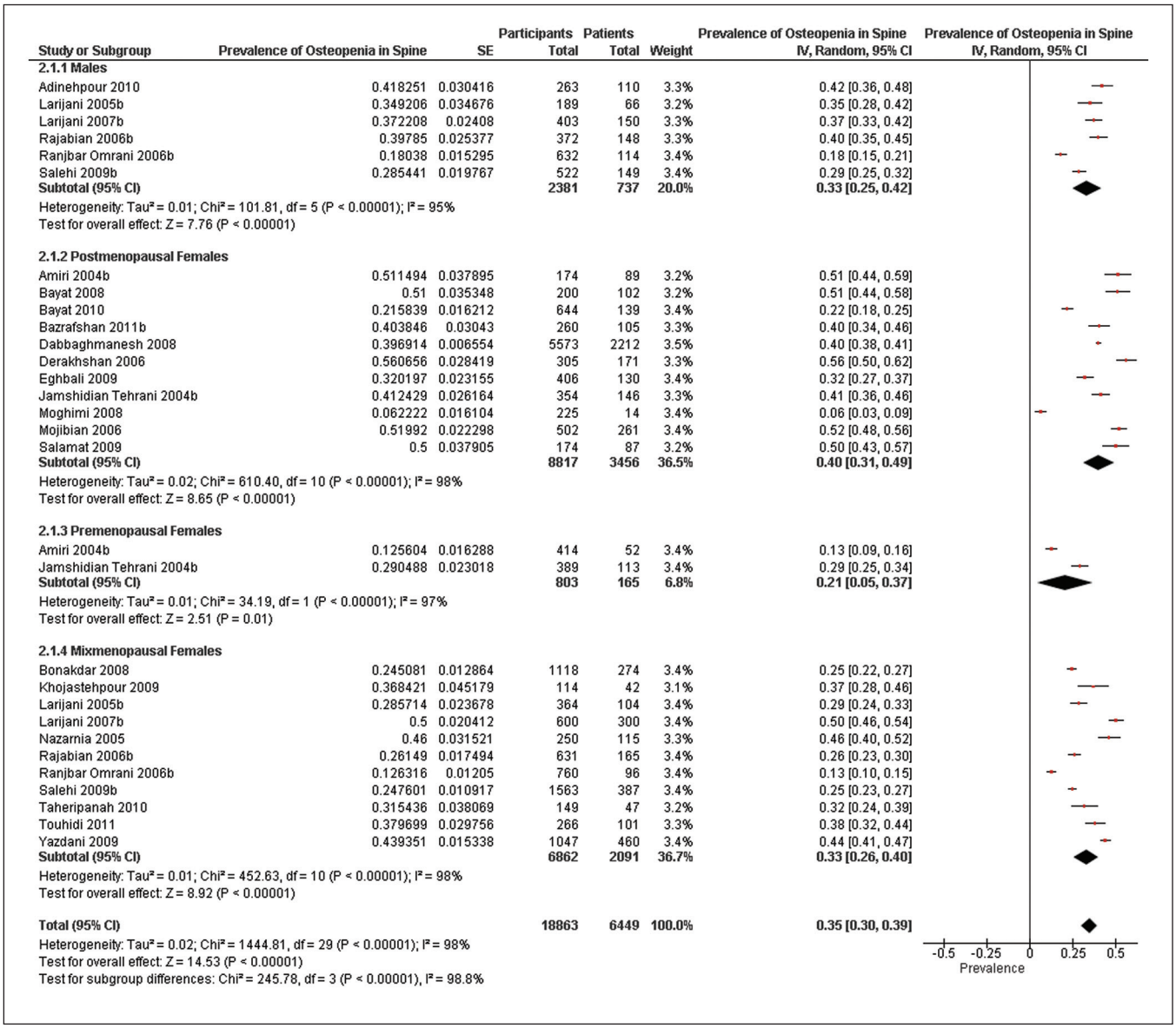

Figure 3: A forest plot for the prevalence of osteopenia in spine among Iranian general population older than 30 years

Vitamin D_3 is produced endogenously in the skin of humans when ultraviolet rays from sunlight strike the skin and trigger vitamin D synthesis.[51,52] The extent of coetaneous vitamin D production is dependent on latitude, altitude, time, total ozone, clouds, aerosols, and surface reflectivity. For clear atmospheric conditions, no endogenous vitamin D production occurs at 51° latitude and higher during some periods of the year. At 70° latitude, vitamin D synthesis may be absent for some months. Clouds, aerosols, and thick ozone events reduce the duration of vitamin D synthesis considerably and can suppress vitamin D synthesis completely.[53] Thus, these factors may explain the difference between the prevalence of osteoporosis in the northern and southern parts of the country.

There was evidence of heterogeneity (small *P* value of Chi^2 test and large I^2 statistic) among the results of the included studies. The studies were conducted in different settings and hence different densitometry devices and the related measurement errors may be a major source for the prevalence variation. However, care must be taken in the interpretation of the statistical tests for heterogeneity. The Chi^2 test has low power when the sample size is small. On the other hand, the test has high power in detecting a small amount of heterogeneity that may be clinically unimportant when there are many studies in a meta-analysis.[15] Therefore, we can attribute part of the observed heterogeneity to the great number of studies (31 studies) included in the meta-analysis and the large sample size (34,814 participants). Another reason that may explain the observed heterogeneity is the presence of inconsistency between the studies' results. Despite several studies that have been conducted recently to address the prevalence of osteoporosis in the general population, the results were however different even in age and sex subgroups.

Limitations

There were several limitations and potential biases in this meta-analysis as follows: First, only 31% of the included studies had high quality; this issue may raise the possibility of the information bias. Second, a considerable numbers of studies (34 studies) reported the prevalence of osteoporosis without specifying the anatomical region of the disease; these studies were excluded from this meta-analysis as this issue might have introduced selection bias in our results. Third, there were more women than men in the study (29,928 women versus 4886 men). Since the prevalence of osteoporosis was higher in women than in men, this issue might have lead to overestimation of the prevalence of osteoporosis and osteopenia in the Iranian general population.

CONCLUSION

The results of this meta-analysis indicated that osteoporosis and osteopenia are common problems among Iranian general population older than 30 years, particularly among women living in the northern parts of the country. Furthermore, the prevalence of these diseases has been increasing in recent years. This evidence promises that osteoporosis and thus its associated complications will become a critical public health problem in Iran in the near future. This issue should be the focus of special attention of policy maker who plan preventive and controlling programs. In addition, because of the considerable heterogeneity between the studies' results, further evidence based on a national survey is needed to estimate the exact prevalence of osteoporosis and osteopenia the country.

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