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Title: Osteoporotic fractures, DXA and fracture risk assessment: Meeting future challenges in the Eastern Mediterranean Region

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Corresponding Author: Dr. RAFIC BADDOURA,

Corresponding Author's Institution: Hotel-Dieu Hospital, St Joseph University

First Author: RAFIC M BADDOURA, MD, MPH

Order of Authors: RAFIC M BADDOURA, MD, MPH; MAHA H HOTEIT, MS; GHADA A EL-HAJJ FULEIHAN, MD, MPH

Abstract: Objectives: To report on the burden of osteoporotic fractures in the Eastern Mediterranean Region (EMR) and the use of bone mineral density (BMD) DXA databases for osteoporosis diagnosis. Methods: PubMed electronic database was reviewed using the following MeSH terms: "Hip fractures", "Fractures, Compression", "Radius Fractures", "Osteoporosis", "Bone density" and "Middle East" up to July 2009.

Results: Incidence of hip fractures varied across the EMR between 100 to 295 per 100,000 person-years in women and 71 to 200 per 100,000 person-years in men. No data was found on other non-vertebral osteoporotic fractures. Prevalence of radiographic vertebral fractures above age 65 ranged between 15% to 25% in women and 7.3% to 18% in men. By 2020, the number of hip fractures above age 50 would increase by 20%. DXA manufacturer's reference curves for the spine were higher than population specific ones. At the hip, NHANES and population-based curves were comparable. Estimates of relative risk of vertebral fracture per SD decrease in BMD using NHANES and local dataset were similar, 1.61 [1.17-2.23] and 1.49 [1.14-1.95] respectively.

Conclusions: The EMR is similar to southern Europe regarding incidence rates of hip fracture, suggesting the health burden to be as significant. Using DXA at the hip, population specific reference databases did not perform better than NHANES on which the FRAX model has been developed highlighting the need for reviewing fracture risk assessment strategies in the EMR.

Journal of Clinical densitometry

While epidemiological evidence on osteoporosis health burden is high in developed countries and osteoporosis appears on the agenda of corresponding health authorities, similar data remain scattered in developing countries and particularly in the Eastern Mediterranean region.

This is to submit a review paper on osteoporosis in the Eastern Mediterranean Region titled: **“Osteoporotic fractures, DXA and fracture risk assessment: meeting future challenges in the Eastern Mediterranean Region”** aiming at filling the gap in this region and providing reference for further epidemiological research in the field.

The authors are **Rafic Baddoura**, MD, MPH¹, **Maha Hoteit** MSc² and **Ghada El-Hajj Fuleihan**, MD, MPH². The corresponding author is Rafic Baddoura MD, MPH¹

¹ Rheumatology department, Hotel Dieu de France Hospital, St Joseph University, Beirut, Lebanon

² Calcium Metabolism and Osteoporosis Program, American University of Beirut-Medical Center, Beirut, Lebanon

Looking forward,

Beirut, March 4, 2011

Rafic Baddoura, MD, MPH
Rheumatology department
Hotel Dieu de France Hospital, St Joseph University
Beirut, Lebanon

Running title: **Osteoporosis in Eastern Mediterranean Region**

Osteoporotic fractures, DXA and fracture risk assessment: Meeting future challenges in the Eastern Mediterranean Region

R. Baddoura, MD, MPH¹, M. Hoteit, MSc², G. El-Hajj Fuleihan, MD, MPH²

¹Division of Rheumatology, Hotel Dieu de France Hospital, Beirut, Lebanon

²Calcium Metabolism and Osteoporosis Program, American University of Beirut-Medical Center, Beirut, Lebanon

Corresponding author:

Rafic Baddoura, MD, MPH
Division of Rheumatology
Hotel Dieu de France Hospital
Beirut, Lebanon

Running title: **Osteoporosis in Eastern Mediterranean Region**

The authors report no conflict of interest.

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I would like to thank the reviewers for their valuable comments.

All of them have been addressed.

1. Tables and figures were revised for more clarity as recommended.
2. Tables and figures have been references in the results section and not only in the discussion section
3. Abbreviations were explained
4. Comparisons with references from the MEDOS and other relevant studies have been added.
5. The English grammar has been reviewed
6. The issue of rural versus urban was also mentioned in the discussion since data in the EMR are limited that respect.
7. Abbreviations for GE lunar and Hologic were made as recommended
8. Relevant explanations about the FRAX model were added
9. And finally all the typing errors referred to by the second reviewer were corrected

Once again I thank the reviewers for their input.

Sincerely,

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4 **Osteoporotic fractures, DXA and fracture risk assessment:**
5 **Meeting future challenges in the Eastern Mediterranean Region**
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9 R. Baddoura, MD, MPH¹, M. Hoteit, MSc², G. El-Hajj Fuleihan, MD, MPH²
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13
14 ¹Division of Rheumatology, Hotel Dieu de France Hospital, Beirut, Lebanon

15 ²Calcium Metabolism and Osteoporosis Program, American University of Beirut-Medical
16 Center, Beirut, Lebanon
17
18
19
20
21

22 Corresponding author:
23

24 Rafic Baddoura, MD, MPH
25 Division of Rheumatology
26 Hotel Dieu de France Hospital
27 Beirut, Lebanon
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33 Running title: **Osteoporosis in Eastern Mediterranean Region**
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47 Scientific Research, and the World Health Organization Eastern Mediterranean Region Office.
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4 **INTRODUCTION**
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7 The health burden of osteoporosis in developed countries has been acknowledged by
8 health authorities including the World Health Organization (WHO) leading to a series of
9 recommendations and guidelines on prevention, screening and management [1-8]. Demographic
10 prospects in developing countries with increased life expectancy, high prevalence of sedentary
11 lifestyle and smoking all lead to projections that the burden of osteoporosis will increase
12 significantly in the near future [9].
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15 The large variability in the incidence of non-vertebral fractures, and particularly hip
16 fractures, is well recognized and may reflect the contribution of additional risk factors beyond
17 bone mineral density, i.e. proximal femur anatomy, body mass index, daily living conditions and
18 the numerous risk factors of falling [10-14]. Information regarding the epidemiology of non-
19 vertebral osteoporotic fractures in the Eastern Mediterranean region (EMR) remains quite
20 limited.
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23 The WHO operational definition of osteoporosis that is based on a bone mineral density
24 (BMD) T-score ≤ -2.5 using central Dual Energy X-Ray Absorptiometry (DXA) [1] has raised a
25 debate in the literature regarding the appropriate reference database one should use, that is be it
26 “population specific”, or “universal”, a question that has direct bearing with regard to case
27 finding strategies and fracture risk assessment [15-20]. Although both the International
28 Osteoporosis Foundation (IOF) and International Society for Densitometry (ISCD) recommend
29 the use of a standard universal database, namely the National Health and Nutrition Examination
30 Survey (NHANES) database at the hip, this recommendation has not been implemented in many
31 countries in the Eastern Mediterranean Region (EMR).
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36 **OBJECTIVES:**
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38 The aim of this paper is to report on the epidemiologic evidence relevant to the health
39 burden of osteoporosis and the different reference DXA based datasets used for T-score
40 determination in the EMR.
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43 **METHODS**
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45 A literature review was done through the PubMed electronic database from 1966 until
46 September 2009. Keywords were selected from the MeSH thesaurus. The first query used the
47 following MeSH terms “**Hip fractures**”[MeSH] AND “**Middle-East**”[MeSH] and identified
48 73 papers. The second query “**Fractures, Compression**”[MeSH] AND “**Middle East**”[MeSH]
49 provided no results. The third query “**Radius Fractures**”[MeSH] AND “**Middle East**”[MeSH]
50 identified 4 papers not relevant to our study purposes. The fourth query “**osteoporosis**”[Mesh]
51 AND “**Middle East**”[MeSH] identified 186 papers. The fifth query “**bone density**”[Mesh]
52 AND “**Middle East**”[MeSH] identified 137 papers.
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55 All papers with a title and abstract relevant to the study were reviewed. Related
56 references, with titles relevant to the study objectives, were also reviewed.
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58 Demographic data prospects were obtained from the following website:
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7 8 **RESULTS** 9

10 *Incidence of osteoporotic fractures and basic characteristics* 11

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13 Six studies reported on hip fracture incidence and provided characteristics of subjects
14 with such fractures. In five studies, hip fracture cases were identified from hospital admissions,
15 and incidence rates estimated with reference to the population in the catchment's area as the
16 denominator, with extrapolation and adjustment for the general population at national level. One
17 study was based on a hip fracture registry within a ministry of public health [27], *Figure 1*.
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20 In Saudi Arabia, a retrospective review of case records of Saudi residents of Riyadh city,
21 who were 40 years or older and who were admitted to any of the local acute-care hospitals over a
22 period of 12 months was used to identify hip fracture cases. The estimated incidence of hip
23 fracture over the age of 50 years was 100 per 100,000 person-years for females and 71 per
24 100,000 person-years for males [21].
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26 In Kuwait, a prospective study was conducted at a specialized orthopedic hospital which
27 provides services to residents in the three governorates representing about 70% of the total
28 population of Kuwait. All new hip fracture patients who were operated on or treated
29 conservatively during a 4-year period (1992-1995) were included. The age-standardized
30 incidence rates of hip fractures were estimated at 295 per 100,000 for females [95% CI: 238.8-
31 350.8] and 200 per 100,000 for males [95% CI: 163.3-236.5], using the 1985 US population as a
32 reference [22].
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35 In Lebanon, a prospective survey that included all hospitals with orthopedic surgery
36 departments in the capital Beirut collected information on new hip fracture cases over a three-
37 month period. An extrapolation was made for the estimation of the annual incidence for the
38 population of Beirut and the Lebanese population at large. The estimated annual incidence rate
39 of hip fractures in Lebanese subjects aged 30 and above was 129 per 100,000 person-years
40 (women: 153 per 100,000 person-years and men: 100 per 100,000 person-years) [23]. More
41 recently, a population based study making use of the ministry of public health hip fracture
42 registry evaluated the incidence of hip fractures in individuals age 50 and above for years 2006,
43 2007 and 2008. Crude incidence rates in those years varied between 164 and 188 per 100,000 for
44 females and between 88 and 106 per 100,000 for males, with a female/male ratio of 1.6-2.1. The
45 overall mean age (SD) for hip fractures was 75.9 (9.2), 76.8(9.0) and 77.0(9.9) years in females
46 in 2006, 2007 and 2008, respectively; and 74.4(11.6), 76.3(10.3) and 74.0(12.1) years in males.
47 Using the US 2000 white population as a reference, the age-standardized rates for years 2006,
48 2007 and 2007 were 370.4, 335.1 and 329.0 in females, and 109.7, 134.1 and 128.7 in males;
49 estimates that approximated those calculated for Southern European countries, such as Spain
50 and Portugal, in the paper describing the study [27].
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53 In Iran, a multicenter population-based prospective study on accidental injuries was
54 conducted in nine provinces across the country, covering about 9.5 million individuals over a 4.5
55 months period. All patients aged ≥ 50 with radiographically confirmed proximal femur fractures
56 were included. A total of 555 new cases of hip fracture (284 males, 271 females) were recorded,
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4 leading to an estimated incidence of hip fractures of 115.2/100,000 person-years in men [95%
5 CI: 107.2-123.7] and 115.6/100,000 person-years in women [95% CI: 107.4-124.3], [24].

6
7 In Oman, data was prospectively collected on hip fracture cases in Sur hospital and the
8 age-adjusted incidence rate of hip fractures in Omani subjects above 40 years of age was
9 estimated at 140 per 100,000 person-years [25].

10 In Morocco, register and medical records data was collected from the five public
11 hospitals in the province of Rabat. Hip fracture was restricted to cervical or trochanteric types.
12 The age-adjusted one-year cumulative incidence of hip fracture was 52.1/100,000 in women
13 [95% CI: 40.9-63.3] and 43.7/100,000 in men [95% CI: 33.3-52.2], [26].

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15 No studies on non-vertebral osteoporotic fractures, other than hip fractures, could be
16 identified within the EMR.
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18 19 *Demographic and clinical characteristics of patients with osteoporotic hip fractures*

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21 Few case-series and case-control studies have provided information on demographic
22 characteristics of subjects with hip fractures in the EMR.

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24 *The mean age* at hip fracture was quite similar across different cases series and case-
25 control studies in the EMR, with values between 70 and 79 years. In Saudi Arabia, a
26 retrospective study of 43 subjects who sustained a proximal femoral fracture and were admitted
27 to the orthopedic department of the King Fahd University Hospital in al-Khobar city between
28 January 2001 and December 2006, reported a mean age of 72.1 years [28]. A similar
29 retrospective study from Al-Riyadh city, reported a mean age of 73 years [21]. In Turkey, a
30 retrospective study of 107 female patients who experienced hip fractures after the age of 60 years
31 revealed a mean age of 74 years, with a range from 63 to 100 years [29]. In the case-control
32 study of 274 patients with hip fractures from Lebanon, the mean age for hip fracture subjects was
33 72.1 (8.5) years [30].

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36 *Gender ratio* consistently showed predominance of females, as expected, across the
37 various studies from Iran, Jordan, Kuwait, Lebanon, Oman, and Saudi Arabia. The female to
38 male ratio among hip fracture cases above the age of 50 years was reported as 1.1 in Iran, 1.2 in
39 Morocco 1.3 in Oman, 1.4 in Saudi Arabia and Jordan, and 1.5 in Kuwait and Lebanon [22-30].

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41 *The anatomic distribution* of hip fractures was reported in three studies. In the study from
42 Kuwait, the proportions were as follows: intertrochanteric fractures 59%, femoral neck fractures
43 34%, and subtrochanteric fractures 7%, with no gender difference [22]. In the study from
44 Morocco, hip fracture data was restricted to cervical and trochanteric fractures. No significant
45 difference was found between genders in terms of cervical to trochanteric ratio; it was 0.97 in
46 women and 1.03 in men. In the Lebanese ministry of health registry study, the proportions for
47 femoral neck fractures was 73.9%, 71.5%, and 78.8% for years 2006, 2007 and 2008,
48 respectively; 24.6%, 25.3%, and 18.9% for per-trochanteric fractures (both inter-trochanteric
49 and trochanteric); and 1.4%, 3.2%, 2.2% for sub-trochanteric fractures [27].

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52 *Comorbidity* in hip fractures was addressed in two studies, whereby up to 70% had two or
53 more co-morbid medical conditions [30-31].
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55 56 *Burden of osteoporotic fractures in the EMR*

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58 *Mortality* as it related to osteoporotic hip fractures was documented in three case-series.
59 The case-series from Turkey included 92 hip fracture patients (56 females, 36 males) who were
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4 operated with a 36 months follow-up, and reported a 3-year mortality rate of 61% in females and
5 50% in males [32]. Another retrospective study from Saudi Arabia reported an average 2-year
6 mortality rate of 27% [33]. In the case-control retrospective study from Lebanon, the average
7 mortality rate was 47%; most deaths occurred within the first year post-operatively, and
8 mortality was significantly higher in men compared to women [30].
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11 The *global burden* of osteoporotic fractures in terms of disability-adjusted life-years
12 (DALYs) following fracture has been addressed in a single large population-based study in Iran,
13 the Multicenter Study on Accidental Injuries [24]. Hip fractures generated 16,708 DALYs,
14 comprising 8,812 (52.7%) years of life lost (YLL) and 7,896 (47.3%) years of life with disability
15 (YLD). The authors estimated that Iran accounted for 0.85% of the global burden of hip fracture
16 and 12.4% of that burden in the Middle East [34].
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20 *Prevalence of osteoporosis using DXA with regard to reference datasets*

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23 Eight cross-sectional studies reporting osteoporosis prevalence by DXA, among
24 postmenopausal women and the elderly population, were identified. Osteoporosis prevalence was
25 often estimated using the manufacturer's reference curve, occasionally a population specific
26 reference dataset, and in a single study the NHANES reference dataset.
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29 In Iran, one cross-sectional survey collected data from 4188 individuals, 92% females,
30 with a mean (SD) age of 53.4(11.8) years, referred to a community-based outpatient osteoporosis
31 center in Tehran. Osteoporosis prevalence, using GELunar DPX-L (GE Lunar, Madison, WI,
32 USA) database was 24.7% at spine, 12.4% at the hip, and 27.8% at any of the two sites [35].
33 Another cross-sectional survey, community based, included 2085 healthy Iranian subjects (75%
34 women), aged 20-88 years, also using a GELunar DPX database, reported osteoporosis
35 prevalence at any site among subjects aged 50 years and older to be 36.1% in women and 24.5%
36 in men [36].
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38 In Turkey, a multicenter study of postmenopausal women, residing in five big cities, in
39 four different regions of Turkey, mean age (SD) 57.6 (9.6) years, reported 30% to be
40 osteoporotic at any site using a MetriScan Densitometer database (Alara Inc., CA, USA) [37].
41 Another community based study, among the elderly, including 783 females and 464 males aged
42 65 years and above and using a Hologic QDR 4500A densitometer database (Hologic, Bedford,
43 MA, USA), reported 63.5% of women and 45.9% of men as having osteoporosis at any site [38].
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46 In Saudi Arabia, a cross-sectional survey of 830 postmenopausal women, 50-80 years of
47 age, evaluated at King Khalid University Hospital, Riyadh, reported 39.5% to be osteoporotic at
48 any site using GELunar DPX densitometer [39]. Another study using simulation approach
49 estimated osteoporosis prevalence in women aged 50-70 years at around 23% [40].
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51 In Jordan, a study of 400 women who visited outpatient clinics at two community
52 hospitals in Amman City, with a mean (SD) age of 53 (12) years, reported 29.6% as
53 osteoporotic at any site using a GELunar DPX densitometer [41].
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55 In Lebanon, one study of a population-based random sample of elderly subjects aged 65
56 to 84 years, using the NHANES database, reported osteoporosis prevalence at total hip to be
57 33.0% [27.5-38.8] in women and 22.7% [16.2-30.2] in men [42].
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4 *Population specific datasets*
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7 Eleven studies [43-53] on premenopausal women and young adult populations reported
8 BMD and T-score distribution by site, age and gender providing estimates of mean peak bone
9 mass mainly at the spine and the hip. Eight provided relevant epidemiological information (*see*
10 *Figure 2 & Table 2*).
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12 Four of these studies [43, 48, 49, and 53] reported population-based reference datasets
13 with a properly selected random sample quite representative of the general population, including
14 young adults. The remaining studies [44, 45, 46, 47, 50, 51, and 52] reported no explicit
15 sampling frame or no proper random selection.
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18 Most studies determined the prevalence of osteoporosis, defined by BMD, in their
19 populations using peak bone mass as defined by the manufacturer's normative database and their
20 population specific normative database. Only one study [42] compared the performance of using
21 a population specific database versus an NHANES database to identify subjects with prevalent
22 radiographic vertebral fractures.
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25 In Iran, the *Iranian Multicenter Osteoporosis Study* included 5201 subjects aged from 20
26 to more than 70 years (2340 males, mean age 42.7 ± 13.8 years) by random cluster sampling from
27 civil status registries of five major cities. DXA was performed using a GELunar DPX
28 densitometer and the NHANES reference curve for proximal femur, with phantom cross
29 calibration between centers. Standardized peak bone mass values were comparable to reference
30 values from Western countries and to reported references from other Eastern Mediterranean
31 countries [43]. Another Iranian population-based cross-sectional survey was conducted in
32 Teheran and included 553 subjects (34% men, 66% women) randomly selected from 50 blocks
33 in the city. DXA was performed on also and using a GELunar DPX with the manufacturer's
34 database and reported similar findings [44], *Table 2*.
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39 In *Kuwait*, 623 healthy Kuwaiti women, aged 20-79 years, with no explicit sampling
40 frame, were evaluated using a GELunar DPX machine. Average peak bone mass at the spine was
41 1.238 ± 0.14 g/cm² and the hip was 1.022 ± 0.11 g/cm², slightly higher values than NHANES
42 reference values, but the difference was not statistically significant [45], *Table 2*.
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45 In *Saudi Arabia*, one study included 1,980 randomly selected subjects from 18 primary
46 health care centers in Jeddah area (age range 20-79 years, 915 males and 1065 females) using a
47 GELunar DPX machine. Average peak bone mass at total hip was estimated at 0.992 ± 0.17
48 g/cm² in females and 1.098 ± 0.19 g/cm² in males, values quite comparable to the NHANES
49 values, *Table 2*. However, using manufacturer's reference dataset, confidence interval for
50 osteoporosis prevalence was 6.3-7.8% at the total hip compared to 1.2-4.7% when using the
51 Saudi reference database [46]. Another study compared T-score distribution across four
52 reference curves, two from Saudi Arabia, one from Lebanon and one from Kuwait among 1653
53 women referred for DXA using a GELunar DPX machine at the Security Forces Hospital,
54 Riyadh, Saudi Arabia. Saudi reference curves were comparable, while on average Lebanese
55 reference values were lower and Kuwaiti reference values were higher than both Saudi reference
56 curves, however no testing for statistical significance of the difference was reported [47].
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4 In *Morocco*, a population-based survey was carried out on 569 Moroccan women and 592
5 Moroccan men, aged between 20 and 79 years, randomly selected in the area of Rabat, using a
6 cluster sampling frame [48-49]. DXA was performed with a GELunar Prodigy machine. Peak
7 BMD at the total hip was $1.029 \pm 0.11 \text{ g/cm}^2$ in women and $1.161 \pm 0.16 \text{ g/cm}^2$ in men [49],
8 *Table 2*. The use of the GELunar reference dataset classified 18.1% of men as osteoporotic at the
9 spine compared to 7.4% using the Moroccan, and 7.8% using a Lebanese reference dataset. The
10 proportion of men identified with osteoporosis at the hip were more comparable across
11 databases, it was 6% with the Moroccan, 3.9% with the US and 5.3% with the European
12 GELunar reference databases, [49].
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17 In *Turkey*, one study among 323 healthy young adults (171 women, 152 men), aged 19-
18 25 years, using Hologic QDR 4500A, reported T-scores distribution but no BMD values. Using
19 the manufacturer's reference dataset, average T-scores at the spine and proximal femur were
20 significantly lower than zero in both genders. Using the local population reference dataset for T-
21 score calculation, the prevalence of low BMD defined as a T-score < -1 was 14.0% at the lumbar
22 spine and 14.6% at the femoral neck in women, and 15.8% at the lumbar spine and 17.1% at the
23 femoral neck in men, proportions that were significantly lower than those derived using the
24 manufacturer's database, with corresponding numbers of 50.3% and 60.8% in women, and
25 42.8% and 30.9% in men [50]. Another study included 951 subjects (639 women and 312 men)
26 aged from 15 to 79 years who had their BMD was measured at the calcaneus using a dual X-ray
27 and laser Calscan (Demetech AB, Stockholm, Sweden) bone densitometer. Mean BMD value for
28 healthy young adults (20-39 years old) was $0.411 \pm 0.058 \text{ g/cm}^2$ in women and 0.504 ± 0.068
29 g/cm^2 in men. Values were on the average about 1 standard deviation lower in both genders, and
30 across all ages-groups, as compared to those from the densitometer Swedish database [51].
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35 In *Lebanon*, three studies were identified. The first study included 858 women and 165
36 men aged 20-79 years, with no explicit sample selection frame, and used GELunar DPX.
37 Lebanese BMD values were generally slightly lower than the US and European reference values
38 in younger age groups, with smaller differences in the older age groups [52], *Table 2*. The
39 authors reported similar age-related changes in BMD in the Lebanese in comparison to both US
40 and European reference databases. The second study reported BMD distribution in a randomly
41 selected young adult population using a cluster sampling frame from Beirut and its suburbs.
42 DXA was performed in three centers, one with a Hologic 4500W, one with Hologic 4500A and
43 the third one with GELunar DPX densitometer. Cross calibration across centers was performed
44 by having 45 women simultaneously tested at the three centers and a linear regression was
45 applied to allow conversion of densitometry measurements from one machine to the other. BMD
46 values were $1.01 \pm 0.11 \text{ g/cm}^2$ in women and $1.01 \pm 0.13 \text{ g/cm}^2$ in men at the lumbar spine, and
47 $0.84 \pm 0.10 \text{ g/cm}^2$ in women and $0.94 \pm 0.15 \text{ g/cm}^2$ in men at the total hip, on the Hologic
48 densitometer. The corresponding values were $1.18 \pm 0.12 \text{ g/cm}^2$ in women and $1.18 \pm 0.14 \text{ g/cm}^2$ in
49 men at the lumbar spine, and $0.97 \pm 0.11 \text{ g/cm}^2$ in women and $1.07 \pm 0.15 \text{ g/cm}^2$ in men at the total
50 hip, on GELunar DPX [53]. Whether measured on GELunar or Hologic, the T-scores derived
51 with reference to the NHANES database were significantly less than zero in women both the
52 spine and the hip. The NHANES-derived total hip mean T-score (SD) was -0.8 (0.9) for women,
53 and -0.7 (1.0) for men, both being significantly less than zero [53].
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58 The third study included a randomly selected sample of elderly subjects from Beirut and
59 its suburbs using the same sampling frame of the peak BMD study. DXA was performed in two
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4 centers, one with Hologic 4500W machine and the one with Hologic 4500A, with cross
5 calibration between both centers. In addition standard X-rays of the spine were performed, and
6 vertebral fractures were assessed using the Genant semi-quantitative technique, thus providing
7 the only published paper on the prevalence of radiographic vertebral fractures in the EMR, and
8 allowing for an estimation of the relative risk of vertebral fracture in association with BMD loss.
9 With reference to NHANES, the prevalence of osteoporosis by BMD at total hip was 33.0%
10 [27.5-38.8] in women and 22.7% [16.2-30.2] in men. Excluding grade I fractures, the prevalence
11 of vertebral fractures, was estimated at 19.9% [15.4-25.0] in women and 12.0% [7.3-18.3] in
12 men. Compared to the NHANES, the population specific database was less sensitive to identify
13 subjects with prevalent radiographic vertebral fractures. However, as expected, the relative risk
14 of vertebral fracture per SD decrease (RR/SD) in BMD was similar across the two databases. In
15 women, RR/SD was 1.61 [1.17-2.23] using the NHANES database and 1.49 [1.14-1.95] using
16 the local database. In men, the figures were 1.59 [0.94-2.72] using NHANES and 1.43 [0.95-
17 2.16] using the local dataset [42].
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23 DISCUSSION

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26 Similarly to other large geographic areas worldwide, the incidence rate of hip fractures
27 varies across population studies in the EMR, although within a narrower range, estimates ranging
28 from 100 to 295/100,000 person-years in women and 71 to 200/100,000 person-years in men,
29 *Figure 1*.
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32 Limitations regarding hip fracture estimates in the EMR include the small number of
33 studies available, the frequent lack of clear inclusion criteria, the relative short time frame and
34 retrospective nature of the studies, as well as the lack of large epidemiologic population- based
35 cohorts, across the region. Despite these limitations, the currently available hip fracture
36 incidence rates in the EMR were similar to those reported in other Southern European and
37 Mediterranean countries, as reported in the Mediterranean Countries Osteoporosis Study
38 (MEDOS) study and lower than reported rates in Northern Europe, North America and Australia
39 [10, 11, 56-65]. Indeed, in the MEDOS study, hip fracture incidence rates in France varied
40 between 100 and 250 per 100,000 person-years and were below 100 per 100,000 person-years in
41 Southern European countries (56). In the European Prospective Osteoporosis Study (EPOS), hip
42 fracture incidence rates were 130 [(95% CI: 80-170] per 100,000 person-years in women and 80
43 [95% CI: 40-100] per 100,000 person-years in men (64). The US Women's Health Initiative
44 (WHI) study reported an annualized incidence rate of hip fractures 160 per 100, 000 person-
45 years (65), and the Dubbo cohort, which included subjects aged 60 and above, incidence rates of
46 hip fracture were 759 [95% CI: 647–871] per 100,000 person-years, in women and 329 [95% CI:
47 241–417] per 100,000 person-years in men (11).
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53 Female to male gender ratio among subjects with hip fracture ranged between 1.1 and
54 1.5, a ratio that is somewhat lower than what has been reported in US and European population,
55 possibly reflecting both regional epidemiological characteristics and different gender based life
56 expectancies [9], *Figure 3*. Mean age at hip fracture was similar across all surveys in the area,
57 ranging between 72 and 74 years, and was significantly lower than the mean reported age
58 reported in developed countries, again reflecting the shorter life expectancy in the EMR, in both
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4 genders. All reported age distributions of hip fracture incidence rates across the EMR show
5 consistently the exponential increase beyond age 70, *Figure 1*.
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8 In one study in Turkey authors addressed the issue of difference in incidence rates of hip
9 fracture between rural and urban areas as they found higher rates in rural versus urban
10 populations. Education as a social determinant was a significant confounding factor since
11 difference between rural and urban rates was significantly reduced when adjusted for educational
12 level. Higher energy fractures in rural areas was raised as a hypothetical explanation for their
13 findings which were opposite to common observations of higher incidence rates of hip fracture in
14 urban populations.
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17 The prevalence of radiographic vertebral compression fractures above age 65 was
18 estimated at around 20% in Lebanese women and 12% in Lebanese men by our group [42].
19 These figures are similar to those reported in European countries (13), providing some evidence
20 on the burden of osteoporosis in EMR countries. No epidemiological data on non-hip, non-
21 vertebral, osteoporotic fractures in the EMR could be identified.
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24 The prevalence of osteoporosis based on BMD at any skeletal site among
25 postmenopausal women and men above age 50 is quite comparable across EMR countries, and
26 was close to 30% in several studies in women and close to 20% in 2/3 studies in men, based on
27 manufacturer's database [36-42], *Table 1*. However manufacturer's reference values at the spine
28 were overall significantly higher than spine BMD values in population-based datasets across the
29 various studies in the EMR, and therefore osteoporosis prevalence could be overestimated or
30 underestimated depending on the reference dataset used. Interestingly, population-based
31 reference values at the hip were often closer to the NHANES reference values. Moreover, mean
32 BMD values were quite comparable across populations and showed a similar decline of BMD
33 with age, *Figure 2*. Finally, data relating BMD to radiographic vertebral fractures in a cohort of
34 elderly subjects in Lebanon revealed similar estimates for the relative risk of vertebral fracture
35 per SD decrease in BMD whether a population specific or the NHANES dataset were used.
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40 No evidence was found to support using local or regional databases instead of the
41 NHANES as a universal database. Based on the current evidence, we believe that along with the
42 IOF and ISCD recommendations [17,19], the NHANES database would be the most appropriate
43 database to be used in the EMR. This would help comparisons across populations in the EMR
44 and between the EMR and other parts of the world. In addition, the use of the NHANES would
45 ensure consistency in values obtained with those derived using the on-line fracture risk
46 assessment calculator, FRAX, a calculator that is now available for 3 countries in the EMR
47 region, namely Turkey, Lebanon and Jordan [55].
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51 From a public health perspective, mortality figures for hip fracture in the EMR although
52 limited are quite alarming. Mortality rates exceeded 25% at two years and reached 60% at three
53 years, despite a relatively younger mean age of individuals with hip fractures in the EMR
54 compared to developed countries [30-32-33]. Demographic prospects for the next decade suggest
55 a significant increase in the proportion of subjects above age 65 in the Middle East and North
56 Africa (MENA) region, *Figure 3*. The proportion of women above age 65 would rise by about
57 30%, from 4.8% in 2010 to 6.0% in 2020. Similarly for men the increase would be about 25%
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4 from 4.0% to 4.9%. Such demographic changes would translate in 17% increase in the number of
5 hip fractures over the next decade in both genders. Accordingly, the expected number of hip
6 fractures among subjects above age 65 in the MENA region in 2020 would be around 300,000 in
7 women and 250,000 in men, [9].
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10 **CONCLUSIONS**

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12 The health burden of osteoporosis in the EMR is quite significant. Hip fracture incidence
13 ranged between 100 and 295 per 100,000 person-years across the EMR, in postmenopausal
14 women, with no major differences between countries in the EMR, and approximating rates in
15 Southern Europe. Female to male ratio among hip fracture subjects ranged between 1.1 and 2.4
16 and the mean age at the time of hip fracture ranged between 71 and 79 years. Mortality rates
17 exceed 25% by two years following fracture.
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21 Osteoporosis prevalence using DXA was quite similar across study populations in the
22 EMR, around 30% at the lumbar spine when BMD is measured using the manufacturer's
23 reference database. T-score derived from population specific databases was often slightly lower
24 than those obtained using wither the GELunar and or Hologic databases. Mean BMD were also
25 comparable between countries and the age-related decrease in BMD was similar across all
26 databases, in both genders and in all studies. Estimates of the relative risk of vertebral fracture
27 per SD decrease in BMD in an elderly Lebanese cohort were similar whether the NHANES or a
28 population specific database was used.
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32 Overall, population specific datasets seemed no better than the NHANES dataset for
33 fracture risk assessment using DXA, thus justifying the use of the universal NHANES database
34 for osteoporosis assessment in the EMR, as is recommended in other regions worldwide.
35 Furthermore, the FRAX calculator is based on the NHANES database, and is now available for
36 Turkey, Lebanon and Jordan, thus allowing absolute fracture risk assessment and health policy
37 decision making regarding osteoporosis treatment in several countries in the EMR.
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41 Demographic prospects in the MENA region suggest the burden of osteoporosis will rise
42 significantly by 2020, calling for cost-effective health policies to reduce the incidence of hip
43 fractures and fracture-related mortality and morbidity.
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Figure 1: Hip fracture annual incidence rates (per 100,000) in women among Eastern Mediterranean Countries.

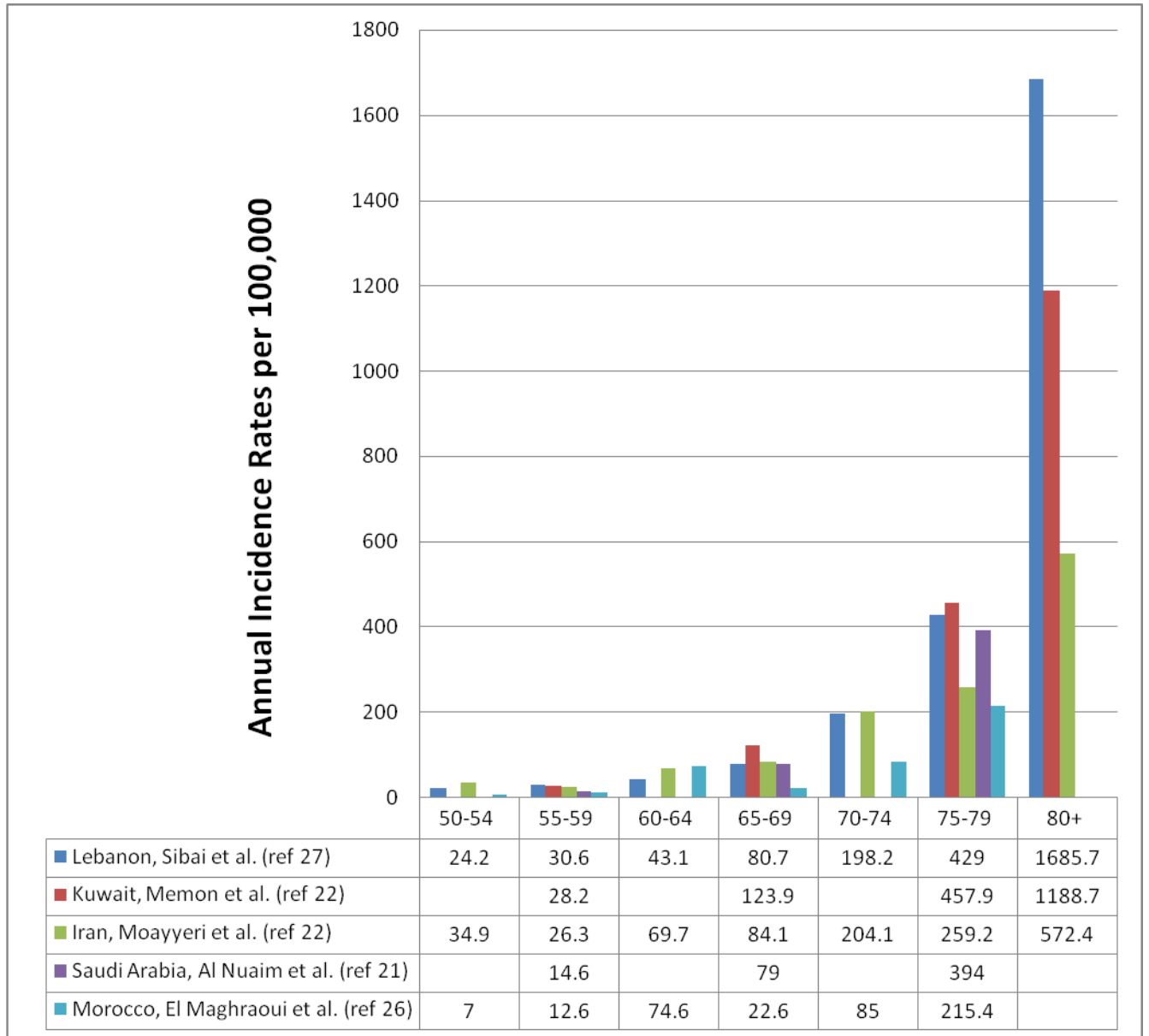


Figure 2: Mean total femur BMD (g/cm²) by 10-years age groups in both genders across various EMR countries. Data from studies using DPX-Lunar densitometers. The NHANES database values are as provided from Lunar manufacturer.

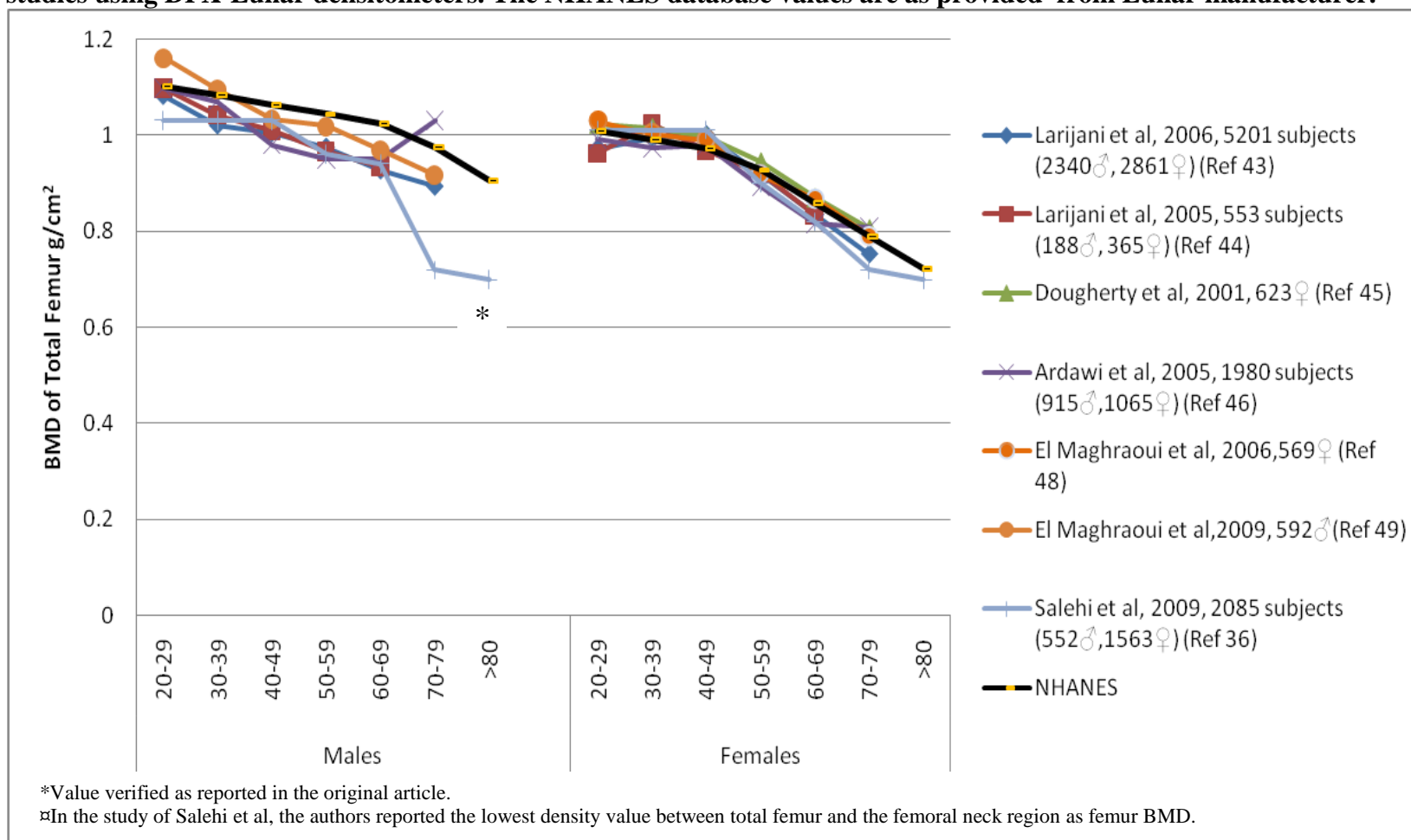
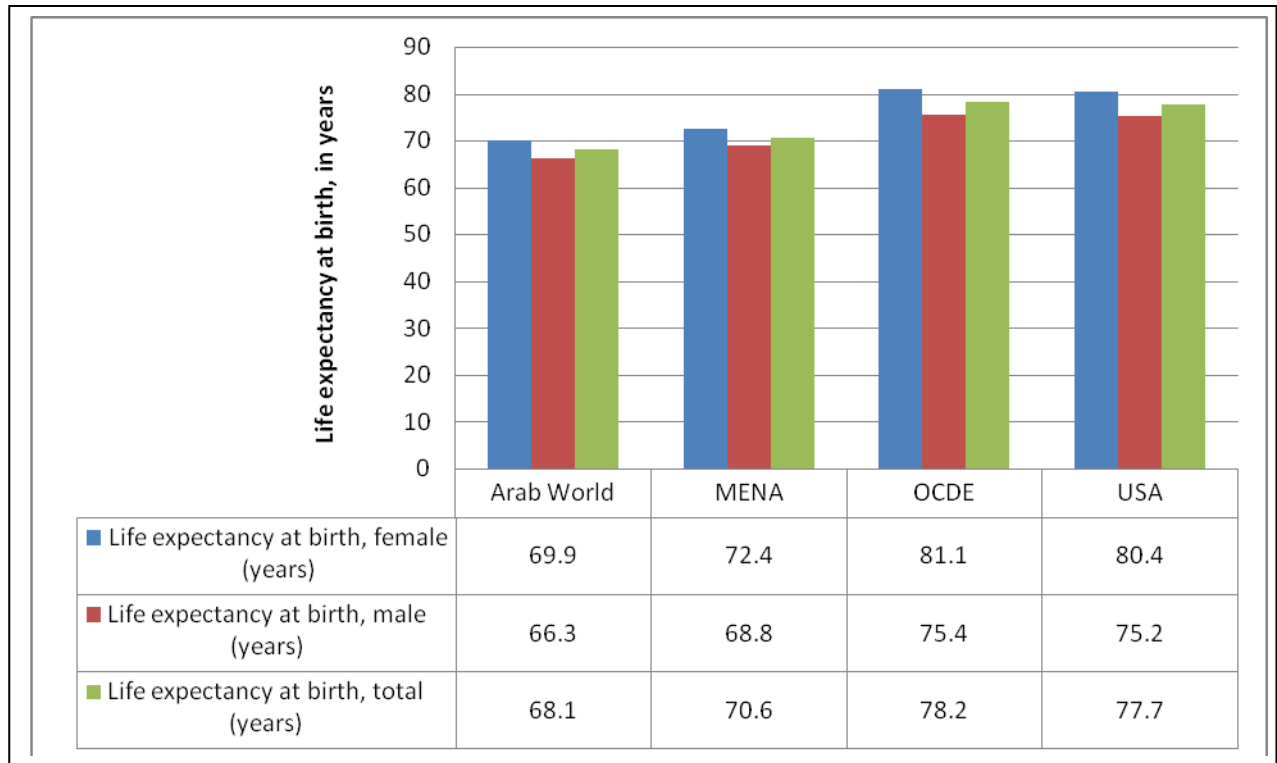


Figure 3: life expectancy at birth in the Arab World, MENA, OCDE and USA



MENA: Middle East and North Africa

OCDE: Organization for Cooperation and Economic development (European Countries)

USA: United States of America

Table 1: Osteoporosis prevalence in various EMR populations
Osteoporosis is defined as a T-score \leq -2.5 at any site (Spine, hip or forearm)

Ref	Country	Database	Study Population	N, (% women) Mean age (SD), Age range	% with OP by DXA any site	
					Women	Men
[35]	Iran	NHANES*	Community-based osteoporosis center	N=4188 (91.9%) Mean age: 53.4(11.8)	27.8 ^Δ [26.4-29.2]	
[36]	Iran	NHANES	Cross-sectional	N=2085 (75%) 50 years and above	36.1 [33.7-38.6]	24.5 [20.9-28.5]
[37]	Turkey	NHANES*	Multicenter study, five big cities	N=724 PM women Mean age: 57.6 (9.6)	30.2 [26.7-33.5]	NA
[38]	Turkey	NHANES*	Retrospective study,	N=1247 (62.8%) 65 years and above	65.0 [61.6-68.3]	45.9 [41.3-50.6]
[39]	Saudi Arabia	NHANES	King Khalid Hospital	N=830, PM women 50-80 years	39.5 [36.2-42.9]	NA
[40]	Saudi Arabia	NHANES*	Simulation approach	PM women 50-70 years	23.0	NA
[41]	Jordan	Spanish Reference	Community based outpatient clinics	N= 400, PM women Mean age: 53(12)	29.6 [25.1-34.2]	NA
[42]	Lebanon	NHANES	Population-based random sample	N= 460, (65%) 65 years and above	33.0 [27.5-38.8]	22.7 [16.2-30.2]

PM: postmenopausal.

* Presumed to be NHANES or manufacturer's database in view of the high prevalence of osteoporosis.

^ΔThis value is the frequency of osteoporosis diagnosis according to the site of assessment as an aggregate for both genders.

Table 2: Mean peak BMD (\pm SD) at the lumbar spine, total hip and femoral neck (FN) in both genders in various EMR populations.

Country ^{Ref}	DXA reference dataset	Age Group (year)	Women's peak BMD			Men's peak BMD		
			Spine	Hip*	FN	Spine	Hip	FN
Iran ⁴³	Lunar 7164, GE Madison, WI, USA	20-36	1.182 \pm 0.127	1.006 \pm 0.126		1.181 \pm 0.153	1.096 \pm 0.159	
Iran ⁴⁴	Lunar DPX-MD machine	20-29	1.198 \pm 0.132	0.962 \pm 0.132		1.209 \pm 0.132	1.098 \pm 0.15	
Kuwait ⁴⁵	Lunar DPX-IQ (Lunar, Madison)	30-39	1.238 \pm 0.14	1.022 \pm 0.11		NA**	NA**	
Saudi Arabia ⁴⁶	Lunar DPX-IQ (Lunar, Madison)	30-39	1.128 \pm 0.11	0.992 \pm 0.17	0.963 \pm 0.16	1.137 \pm 0.09	1.098 \pm 0.19	1.045 \pm 0.20
Morocco ^{8,49}	Lunar Prodigy Vision, GE	20-29	1.156 \pm 0.12	1.029 \pm 0.11		1.205 \pm 0.15	1.161 \pm 0.16	
Lebanon ⁵²	Lunar DPX-L	20-29	1.100 \pm 0.13		0.912 \pm 0.10	1.139 \pm 0.13		1.033 \pm 0.14
Lebanon ⁵³	Lunar DPX-L	20-29	1.180 \pm 0.12	0.97 \pm 0.11		1.18 \pm 0.14	1.07 \pm 0.15	

*The NHANES total hip BMD mean value (SD) among non-Hispanic whites is 1.101 g/cm² (0.144) in males and 1.008 g/cm² (0.126) in females within the age group 20-29 years; and 1.082 g/cm² (0.144) and 0.990 g/cm² (0.126) respectively within the age group 30-39 years.

** NA: Not Available