Major osteoporotic fracture to hip fracture incidence rate ratios: a systematic review of observational studies

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Review question

The objective of this review is to evaluate the incidence rate ratios of major osteoporotic fracture (MOF) to hip fracture, by gender and age categories across various countries in studies extending ? 1 year.

Searches

We conducted a systematic review on MEDLINE, PubMed, and Embase databases, without time or language restriction until December 2016 and an update until May 2018. We used the following MeSH terms and keywords: Hip Fractures; Non-Hip Fractures; Major Osteoporotic Fractures; Epidemiology; Osteoporosis.
We will perform manual search and review of references listed in the included studies and review papers on the topic. We will contact experts in the field for queries on potential fracture data that we may have missed.

Search strategy

https://www.crd.york.ac.uk/PROSPEROFILES/129259_STRATEGY_20190320.pdf

Types of study to be included

Inclusion:
- Observational studies

Given that our aim is to describe the incidence of fracture, MOF and hip, in the general adult population, cohort studies will be included.

- Duration at least one year duration

Exclusion:

- Review articles

Condition or domain being studied

Several fracture risk assessment tools have been developed to identify high-risk individuals (Kanis, et al. 2017). Such tools incorporate osteoporosis risk factors (El-Hajj Fuleihan, et al. 2017). The Fracture Risk Assessment Tool (FRAX) is the most widely used tool. It was developed to predict the 10-year fracture risk, for major osteoporotic fractures and for hip fracture, separately (Kanis, et al. 2008). Currently, 63 country-specific FRAX calculators are available. These calculators incorporate country specific fracture (MOF and/or hip) and mortality data, to derive subject specific 10-year estimates for the probability of hip and MOF fractures. However, MOF fracture data are only available for few countries, namely Mexico, UK, Switzerland, Canada, US, Japan and Sweden (Kanis, et al. 2011, Leslie, et al. 2011). In almost all other countries where MOF rates are not available, FRAX therefore uses country specific hip fracture data and assumes the MOF/Hip fracture ratio is the same worldwide as in Malmo Sweden, to derive country specific MOF rates, and provide 10-year FRAX probability estimates for MOF for subjects from these countries (Kanis, et al. 2011). However, recent publications revealed the above assumption may not always apply (El Hajj Fuleihan, et al, 2011; Leslie, et al. 2011).

Participants/population
Men or women over the age of 50 years

Intervention(s), exposure(s)
Not applicable

Comparator(s)/control
Not applicable

Context

Osteoporotic fracture risk varies worldwide, by geographic location, ethnicity and socio-economic status (Cauley, Fuleihan et al. 2011). Hip fracture risk is the highest in northern countries, such as Denmark and Sweden (Sibai, Nasser et al. 2011, Kanis, Oden et al. 2012), and the lowest rates are registered in countries such as China and Korea (Sibai, Nasser et al. 2011), Nigeria and South Africa (Kanis, Oden et al. 2012); difference in incidence rate being as high as 10 folds. Variability in the incidence of morphometric vertebral fractures is even wider (Cauley, Chalhoub et al. 2014, Ballane, Cauley et al. 2017). The highest rates are reported in Sweden and Switzerland, and the lowest in Hungary (Cauley 2014). Similarly, the highest incidence of forearm fracture is registered in Hungary and the lowest in Japan (Cauley, Chalhoub et al. 2014). Furthermore, discrepancies in hip fracture incidence were reported across various ethnicities within individual countries, such as the US, New Zealand and Singapore (Cauley, Chalhoub et al. 2014).

Country-specific and ethnicity-specific secular trends in fracture risk have been also described (Cooper, Cole et al. 2011, Ballane, Cauley et al. 2013, Ballane, Cauley et al. 2014, Cauley, Chalhoub et al. 2014, Ballane, Cauley et al. 2017). While a decline in hip fracture risk is reported in various countries from Europe, US and Canada over the second half of the 20th century, an increase in these rates is detected in Asian countries such as Japan, China, Taiwan (Cooper, Cole et al. 2011, Cauley, Chalhoub et al. 2014).

Main outcome(s)
Primary outcomes are MOF to hip incidence rate ratio at ? 1 year, MOF being defined as hip, vertebral, humerus, and distal forearm fractures.

Timing and effect measures

Our primary outcome measure is the ratio of fracture incidence rates: major osteoporotic fracture incidence rate divided by hip fracture incidence rate stratified by age and gender, in each country.
When the fracture incidence is expressed in person years, two reviewers will derive the incidence rate using the following formula: Risk = [1- exp (-Rate x time)], using e base (2.718), where the risk is defined as incidence /count data and rate is defined as a person year measure

Additional outcome(s)
None

Data extraction (selection and coding)
One reviewer (NC) will screen the titles and abstracts of the retrieved citations based on the eligibility criteria.
One reviewer will screen the full text of the potential papers using a standardized form (MC).
Two reviewers will abstract data, in duplicate and independently (MC, HD and SS), on pertinent variables related to the population and outcomes, using data collection sheets, prepared a priori. These variables include: Author, year, study period, study design and sampling method, sample size, the number of sites, ethnicity, methods of identifying fractures, ICD code used, definition of osteoporotic fractures, and studies source of funding.
For the primary outcome, data collection will include the following by gender and age category:

- Hip incidence rate per 100, 000 person-years

- Major osteoporotic facture rate per 100, 000 person-years

- Hip to MOF ratio

If fracture rates are reported on each fracture individually, we will collect these rates and calculate the incidence of MOF as the sum of the incidences of hip, vertebral, humerus, and distal forearm fractures.

In case of missing data on a specific fracture or category, and before excluding the article, the corresponding authors will be contacted for queries about such data.

Risk of bias (quality) assessment

Two reviewers will independently assess the quality of the studies using a modified quality score, that was previously used for the rating of the quality of hip fracture incidence studies (Cauley, et al. 2011, Kanis, et al. 2012).
The latter tool evaluates the following domains:

- Population repetitiveness: Multi-center or Population based (Yes (=1)/No (=0))

- Study design (Prospective (=1)/retrospective (=0))

- Ethnicity (defined =1; not defined =0)

- Duration (for data collection 1 or more fractures > 1 year (=1), 1 year=0))

- Method used to define fracture (ICD =1)/other definition or no=0))

- All fractures collected during a period of 3 years (Yes =1, No=0)

- Definition of the included fractures as Osteoporotic (defined=1)/ Not defined=0)); all types of fractures included regardless of the severity of trauma, the score will be zero.

The last two items were added to the quality score for the purposes of this review.

A study will be rated of a good quality, if it has a score of at ? 6, fair if it has a score of 4-5 and poor if it scores ? 3

For each domain, judgment will be done qualitatively, and a summary score will be derived by summing up the individual items to allow comparability.

Strategy for data synthesis

Our primary outcome measure is the ratio of fracture incidence rates: major osteoporotic fracture incidence rate divided by hip fracture incidence rate stratified by age and gender, in each country.
When the fracture incidence is expressed in person years, two reviewers will derive the incidence rate using the following formula: Risk = [1- exp (-Rate x time)], using e base (2.718), where the risk is defined as incidence /count data and rate is defined as a person year measure (http://sphweb.bumc.bu.edu/otlt/MPH-Modules/EP/EP713_DiseaseFrequency/EP713_DiseaseFrequency5.html).

When the MOF and Hip incidence rates are reported in a graph form without corresponding table values, we will send an email to the corresponding author of each article requesting the raw incidence rate numbers corresponding to the graphs. Two reminders will be sent to each author. In case of no reply, two reviewers will use “Plotdigitizer”, a computer software that converts graph to numerical values (http://plotdigitizer.sourceforge.net/). The numbers derived by each reviewer will be compared. The difference (Delta) between same point values will calculated, and the average of the values derived by each reviewer will be calculated for each age category and gender. In case incidence data of more than one year are available for a given study, we will calculate the average across years.

We will calculate the confidence interval of the MOF/hip ratios, by gender and age category, across various countries. first we will calculate the point estimate, then we will derive the standard deviation of the log rate ratio, and accordingly, we will calculate the lower and upper limits of the rate ratio (Rothman KJ, Greenland S. Modern epidemiology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2008)

Analysis of subgroups or subsets
Not applicable
We will take into consideration studies quality score when assessing the implication of the results.

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Type and method of review
Epidemiologic, Narrative synthesis, Systematic review

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01 August 2019

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Conflicts of interest

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Lebanon

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Review Ongoing

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Subject indexing assigned by CRD

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Hip Fractures; Humans; Incidence; Osteoporotic Fractures; Pelvic Bones

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Details of any existing review of the same topic by the same authors

Stage of review at time of this submission

Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	No
Risk of bias (quality) assessment	Yes	No
Data analysis	No	No

Versions

16 April 2019