

Name of Journal: *World Journal of Orthopedics*

ESPS Manuscript NO: 23189

Manuscript Type: EDITORIAL

Since there have been 7 reviewers because the paper, owned to the computer system, has passed twice the peer-review process, we respond to the two set of reviewers. Some of the comments contradict to each other; anyhow we think we have reach changes satisfying all views

Responds to reviewer:

We are very grateful to the reviewer for his/her neat correction. We do appreciate the hard work performed. We think the text has been improved according to the suggestions.

Page 3-1: Many thanks for the comment!

Page 3-2: We have changed “traumatism” by “fall”. We want to emphasize –in fact that is the main idea of this editorial – that if patients did not have a fall the fracture would not exists. We kindly ask to leave the rest of the sentence as it is, otherwise the meaning would be distorted. What we want to emphasize is that in elderly patients sensorial deficits impede to land properly; trauma is onto the greater trochanter (that is the foundation of hip protectors, ineffective because patients reject to wear them as stated below following the reviewer’s suggestion). We think the problem with a soccer goalkeeper is different: when he has a fall, the trauma is not onto his hip (trochanter); rather, conversely to an elderly person, they have the fast proprioception of preparing themselves to land properly. The same comes true for problems in knee ACL injuries in a soccer player: the lesion comes always when the knee is not “expecting” to have a twist. In order to avoid lesions, a usual part of the training for a goal-keeper is to land with the ball on hands. Also ACL lesions are more frequent at the beginning or at the end of the season when muscle building and proprioception are diminished (I have been a soccer player in the Spanish first division from 1976 to 1984 – Malaga CF, not a very top team but at least first division-, 2 years as the team captain). We beg to keep the sentence as it is. Thank you.

Page 3-3: Following reviewer’s suggestions, reference has been changed to an already published one.

Page 3-3: We understand the point of the reviewer, but what we kept in our sentence is that no drug so far has come out by diminishing the prevalence of hip fracture in general population together with avoiding secondary effects. Our sentence is related to both: to diminish the prevalence of hip fracture (bisphosphonates have not diminished the overall –in general population-prevalence), or to avoid secondary effects (bisphosphonates indeed may provoke some secondary effects; e.g.: atypical femur fractures). This is one of the biases of RCT when conclusions are suggested to be inferred to general population: findings cannot be inferred to general population as

patients in RCT are selected according to inclusion/exclusion criteria; therefore prevalence of diseases in general population may be not affected whereas incidence found in these longitudinal cohort studies does. Some references on that are provided along the text: how pharmaceutical companies use this methodological bias. It is indeed a very important part of the philosophy of our paper. We also have read the papers suggested by the reviewer.

Reid IR. *Efficacy, effectiveness and side effects of medications used to prevent fractures.* J Intern Med. 2015 Jun;277(6):690-706. doi: 10.1111/joim.12339.

Reid says that “most trials provide little information regarding long-term efficacy or safety”, and that “a particular concern at present is the possibility that oral bisphosphonates might cause atypical femoral fractures”, that is why this author advice 'drug holidays' for avoiding atypical femoral fractures, as that is indeed a secondary effect. Moreover, none knows the appropriate duration of “drug holydays”.

Lozano-Calderon SA, Colman MW, Raskin KA, Hornicek FJ, Gebhardt M. *Use of bisphosphonates in orthopedic surgery: pearls and pitfalls.* Orthop Clin North Am. 2014 Jul;45(3):403-16. doi: 10.1016/j.ocl.2014.03.006.

These authors say that bisphosphonates have proved “to be cost-effective”. They recognize that “unexpected adverse effects have been reported recently...”.

Kling JM, Clarke BL, Sandhu NP. *Osteoporosis prevention, screening, and treatment: a review.* J Womens Health (Larchmt). 2014 Jul;23(7):563-72. doi: 10.1089/jwh.2013.4611. Epub 2014 Apr 25.

These authors also explore “current recommendations” where secondary effects are recognized and discussed.

To our knowledge, no paper has proven that being hip fracture a public health problem as the first sentence of our paper say, bisphosphonates or any other drug diminish the hip fracture prevalence of a determined *general* population (e.g.: the population of New York, Berlin, etc.), nor even with a before/after study. This is a key concept since public policies should be readdressed to what is epidemiologically useful (that has been discussed for long by the World Health Organization, by the way, in relation to AIDs prevention: sex abstention is indeed the only way to stop the disease but in terms of epidemiological prevention is not feasible). On the other hand, what we say is just that when a drug is launched the industry never say anything about those secondary effects detected years later, although clinical trials have been formerly performed. We do understand that this paper is certainly an editorial, and may provoke controversies.

Page 4-1: We agree with the reviewer, the fracture pattern in patients with osteoporosis is worse than in those patients without osteoporosis. We have added the suggested sentence: “Osteoporosis only helps to fracture a bone with less energy than non-osteoporotic bone”.

Page 4-2: We have change the sentence because the reviewer is right that with the former sentence a reference should be written. We have added “as discussed below” because discussion on that, start just in the next paragraph. Also along the text many other references - mainly by Cochrane reviews and particularly methodology by Gotzsche- are added.

Page 6-1: We have added references as requested.

Page 7-1: Thank you for the comment! The article is going to be published in Injury.

Page 8-1 and 8-2: We have changed the redaction and introduced a new sentence as requested.

Page 8-3: Thank you for the agreement.

Page 9-1: We have changed GDP to full “Gross Domestic Product”.

Page 9-2: References have been added as requested. We have readapted the sentence by introducing “national health services”; we also have changed incidence by prevalence which is more appropriate.

Page 10-1: All those references have been introduced

Page 10-2: We have included what the reviewer says.

Page 12-1: We have added: “However, so far, no an alternative standard has been published.”

Page 12-2: We have added: by pharmaceutical companies in order to strength the meaning of the sentence and the reference 50.

Page 13-1: We have added the sentence suggested by the reviewer.

Page 13-2: This sentence has been rewritten.

Page 14-1: Muscle mass has been added in the former sentence.

Page 14-2: Reference 45 has been reinforced by the number 28 and 31.

Page 15-1: We have included the idea of the reviewer (hip protectors kept in the wardrobe). This adds not so much to the discussion on the role of osteoporosis in hip fracture, but since we have been discussing about hip fracture prevention, we thought that we should mention it briefly, as have been discussing about vitamin D, bisphosphonates, etc.

Page 17-1: We have changed *liable* by *predisposed*. Now we think it is clearer.

Page 18-1: We have responded to the reviewer's question. We agree that this further clarifies the sentence.

Page 20-1: We have added a last sentence to further clarify what the reviewer points.

Proper explanation about the role making more severe fracture pattern by osteoporosis, has been made.

Thank you very much indeed for your immaculate correction!! We honestly believe the text has gained in clarity. We also want to apologize for any language mistake in this respond as translations are expensive and we send to native English only the actual paper. I hope you forgive us for that.