

## Original Article

# Bisphosphonates: a cost benefit analysis patient

Sarah Cuschieri, Stephan Grech, Ray Gatt

**Abstract**

**Introduction:** Osteoporotic hip fractures are common in elderly. There is increased risk of sustaining other fractures that incur financial burden on the health system. Prescription of bisphosphonates after osteoporotic hip fracture surgery has been shown to reduce the overall incidence of re-fractures.

**Methods:** All osteoporotic hip fractures treated surgically in Mater Dei Hospital in the year 2011 were analysed in this observational retrospective study. The inclusion criteria were all primary osteoporotic hip fractures. The initiation, or not, of anti-osteoporotic treatment upon discharge from hospital was reviewed.

The mortality and re-fracture rate of this cohort was reviewed for a period of 3 years. The cost of hospitalization for hip fracture and re-fractures was calculated based on local health services costs and compared to the benefits of providing a free bisphosphonate medication to each patient.

**Results:** The osteoporotic hip fracture care pathway did not include initiation of anti-osteoporotic therapy after operations. A re-fracture rate of 11.7% over three years predominantly in female patients was observed. In the first year following hip fracture, an estimated direct medical health expenditure due to re-fractures was of €37,642.55 - €48,835.19.

**Conclusion:** Prescribing a bisphosphonate has been found to reduce both the re-fracture and mortality rates. In our study, a bisphosphonate prescription could have reduced the all cause mortality rate of 25.3% to 15.18% over the first year of hip fracture, as well as reduced the financial and social burden incurred due to a re-fracture.

**Keywords**

Osteoporosis; Prevention & control; Femoral fractures; Osteoporotic fractures; Diphosphonates; Cost of illness; Health care costs; Health expenditures

**Introduction**

In an aging population, bone mass is progressively lost in a physiological process, resulting in an increased risk of a fracture following minor trauma. The commonest osteoporotic fractures are at the neck of the femur (hip), vertebral body and forearm.<sup>1</sup>

The most important osteoporosis-related fractures from a public health perspective are hip fractures.<sup>2-3</sup> In 2000, there were 0.89 million osteoporotic hip fractures in Europe. An estimated 179,000 men and 611,000 women are expected to sustain a hip fracture each year in European countries.<sup>4-5</sup> Hip-fractures due to osteoporosis were related to the highest medical costs incurred on the health services.<sup>6</sup> An estimated 820 million pounds Sterling per year was attributed to osteoporotic hip fractures in the United Kingdom.<sup>7</sup>

Hip fractures are associated with a high mortality of 10-20% as well as morbidity.<sup>8-9</sup> It is common knowledge that these elderly patients often lose a substantial amount of their daily independence after a hip fracture with 25 - 50% of them requiring residential help or nursing homes.<sup>10-11</sup>

Patients run a cumulative risk for further osteoporotic fractures after suffering a hip fracture.<sup>12-13</sup> Therefore osteoporosis-targeting treatment should be prescribed to all patients with previous history of osteoporotic fractures as stated by both the national institute for health and care (NICE) and the Scottish intercollegiate guideline network (SIGN).<sup>14-15</sup>

Bisphosphonates are considered to be the gold standard first line treatment in established osteoporosis.<sup>16</sup> They are also recommended in treating patients who have suffered an osteoporotic hip fracture. Calcium and Vitamin D may also serve as good supplements in elderly with hip fractures since vitamin D deficiency contributes to loss of bone in advanced age.<sup>17</sup> This is more prevalent than one would suspect even in countries like Malta where natural sunlight is in abundance. Yet, starting patients on anti-osteoporotic treatment prior to discharge is not part of the standard management plan in Malta.

Physicians need to be on the look out for factors that may lead to secondary osteoporosis and therefore resulting into fractures including thyroid disease, alcoholism, steroid therapy and malignancy.<sup>20</sup> There

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have been mixed conclusions whether warfarin should also be considered as a predisposing factor to fractures.<sup>22-23</sup>

The aims of this study were to evaluate the current practice in Malta when it comes to prescribing anti-osteoporotic treatment following hip fracture surgery as well as:

- 1) Find the incidence of further osteoporotic fractures following a primary hip fracture;
- 2) Evaluate the costs involved in treating patients suffering an osteoporotic hip fracture.
- 3) Run a cost effectiveness comparison between the cost of prescribing anti-osteoporotic medication versus the cost of managing secondary fractures in the same patients suffering a primary osteoporotic hip fracture.

Permissions from Mater Dei Hospital chief executive officer and data protection office were obtained. Ethical approval was granted in accordance to the Declaration of Helsinki from the University of Malta Research and Ethics Committee.

## Method

An observational retrospective study was performed analyzing all emergency osteoporotic hip fractures requiring surgery, presenting to Mater Dei Hospital, Malta, between January to December 2011. With the permission of the Chairman of the Department of Trauma and Orthopaedics as well as the Central Performance Unit (CPU), the operated hip fractures list was obtained. Mortality data was obtained from the Department of Health Information and Research.

The inclusion criteria for our study were patients over 60 years of age suffering a hip fracture following a low energy hip fracture. A low energy hip fracture was defined as a fracture suffered after minimal or low trauma. These were considered to be osteoporotic in nature.<sup>21</sup>

The exclusion criteria were those patients that were on long-term steroids, patients who consume large amounts of alcohol (over 3 units daily in males, over 2 units daily in females), had a history of malignancy, hypothyroidism or were on warfarin as well as those sustaining a high-energy trauma.

Using the 'Electronic Case Summary' software, which is a software used at Mater Dei Hospital on which discharge summaries are stored, each patient having undergone an osteoporotic hip surgery was analyzed as to the mechanism of injury and the management he/she was discharged on, with special attention to whether any anti-osteoporotic medication was prescribed. The picture archiving and communication system (PACS) was used to evaluate whether each patient re-presented to a state health care institution with another osteoporotic fracture over a period of 3 years following the primary hip fracture.

Data was stored in a spreadsheet and statistical analyses were performed using SPSS IBM v.11. An independent t-test evaluated the significance of age and gender in relation to hip fractures, while spearman's correlation co-efficient test was used to compare age and length of stay in hospital. The cost of hospitalization (including doctors, nurses, x-rays, bloods, electrocardiogram and physiotherapy) per night, major operation, intermediate operation costs and doctor consultation at outpatients at Mater Dei Hospital was obtained from the billing section of the hospital. Table 1 represents the itemized cost of each service.

**Table 1:** Represents the itemized cost per service

Service*	Cost
Hospitalisation**	€256.23/night
Intermediate Operation (Radial & humeral fractures)	€1048.22 / operation
Major Operation (Hip fracture)	€2329.37/ operation
Doctor consultation at outpatients	€36.94/visit

\* Cost based on 2014 prices.

\*\* Hospitalisation cost include in-patient doctors and nurses care, X-rays, Blood tests, ECG and Physiotherapy.

These costs were used to calculate the mean cost per patient who presented with a hip fracture as well as cost per re-fracture either requiring conservative management or an operation. The cost was calculated following the standard medical practice (as below) performed at the Department of Trauma and Orthopaedics, Mater Dei Hospital for each type of re-fracture.

The cost was calculated on the basis of an admission to hospital with a mean length of stay according to the type of fracture incurred and requiring an operation as follows; 11 days Hip fractures; one day Vertebral fractures; three days Humeral fracture; two days Radial fracture. The cost for radial and humeral re-fractures was calculated on the basis of either requiring an operation or just following a conservative management. Follow-up appointments were considered as follows: Conservative management of humeral and radial fractures requiring two follow-up appointments while one follow-up appointment after operative management. This is the standard protocol of follow up in our institution. Both humeral and radial fracture operations were considered as intermediate operations whilst hip fracture as major operations.

All costs excluded accident and emergency services and only considered direct medical costs.

## Results

In 2011, there were 370 admissions (280 females and 90 males) to Mater Dei Hospital, Malta, between the ages of 60 and 99 years that required an orthopaedic hip operation. Out of which, 89 were excluded due to the presence of risk factors predisposing them to fractures. The remaining 281 (226 females and 55 males) were considered to have sustained an osteoporotic hip fracture, with most fractures occurring in females between the age of 79 and 87 years ( $p=0.0001$ ).

The length of stay at hospital from day of admission to discharge ranged from three days to 51 days with a mean stay of 11 days. Figure 1 is a histogram that shows the length of stay of all patients with an osteoporotic hip fracture during the study period. The length of stay within hospital showed no co-relation with age ( $p=0.069$ ); or with age and gender (females  $p=0.212$ ; males  $p=0.793$ ). The calculated mean bed cost, hip

operation and follow-up (as discussed above) for an osteoporotic hip fracture was of €5,182.84.

None of the patients who sustained an osteoporotic hip fracture were started on a bisphosphonate or a calcium supplement by the responsible caring team. The only few patients, three in total, on anti-osteoporotic supplements had already been on this treatment prior to suffering the initial hip fracture.

Over three years, 11.7% ( $n=33$ ) presented to a state health institute with a re-fracture with the majority being female ( $n=25$ ) and the most common fracture being a fracture to the contralateral hip. Figure 2 shows the re-fracture presentation per year over three years according to gender. Figure 3 represents the cumulative re-fractures over three years post-hip fracture, while Figure 4 shows the types of re-fractures sustained over three years.

The re-fracture rate over a year from the index hip fracture surgery was of 6% ( $n=17$ ). Table 2 represents the direct medical cost per re-fracture type and the cost sustained over the three years due to re-fractures in the population under study.

**Figure 1:** Histogram showing length of stay at hospital from admission to post-surgery discharge

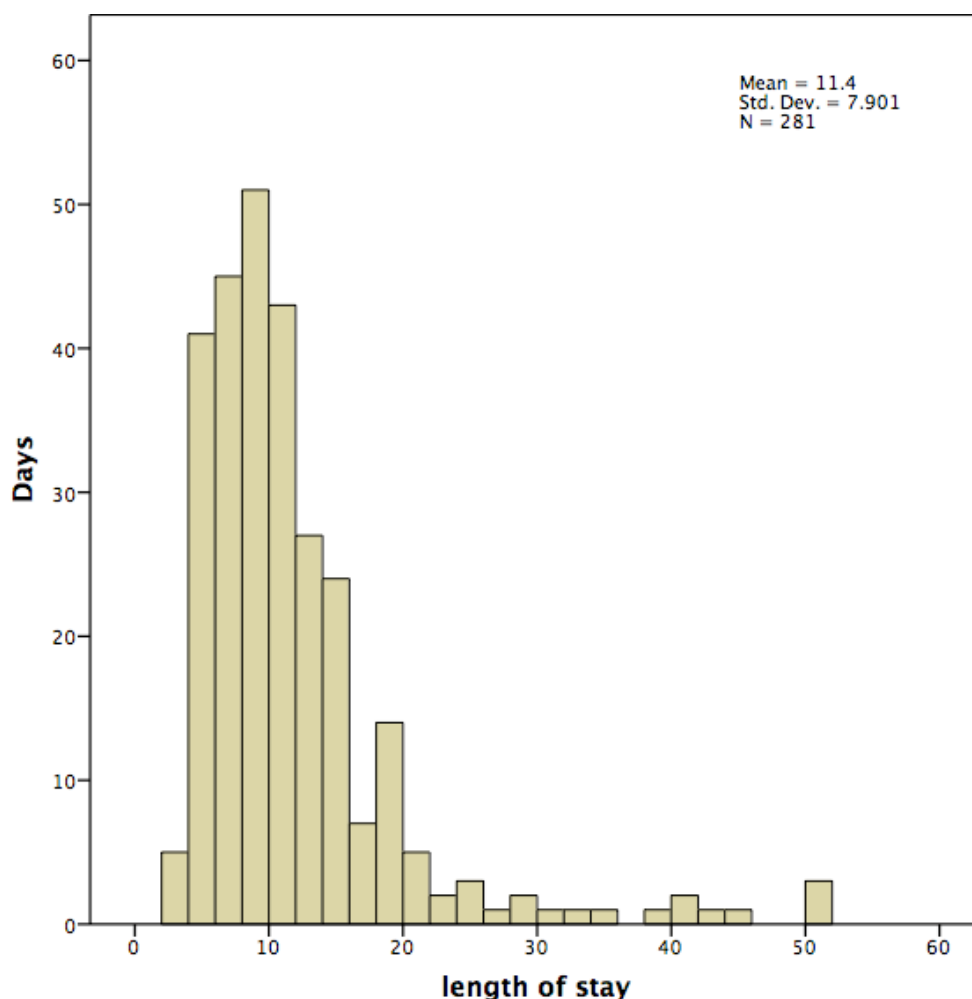


Figure 2: Presents the re-fractures per year over 3 years according to gender

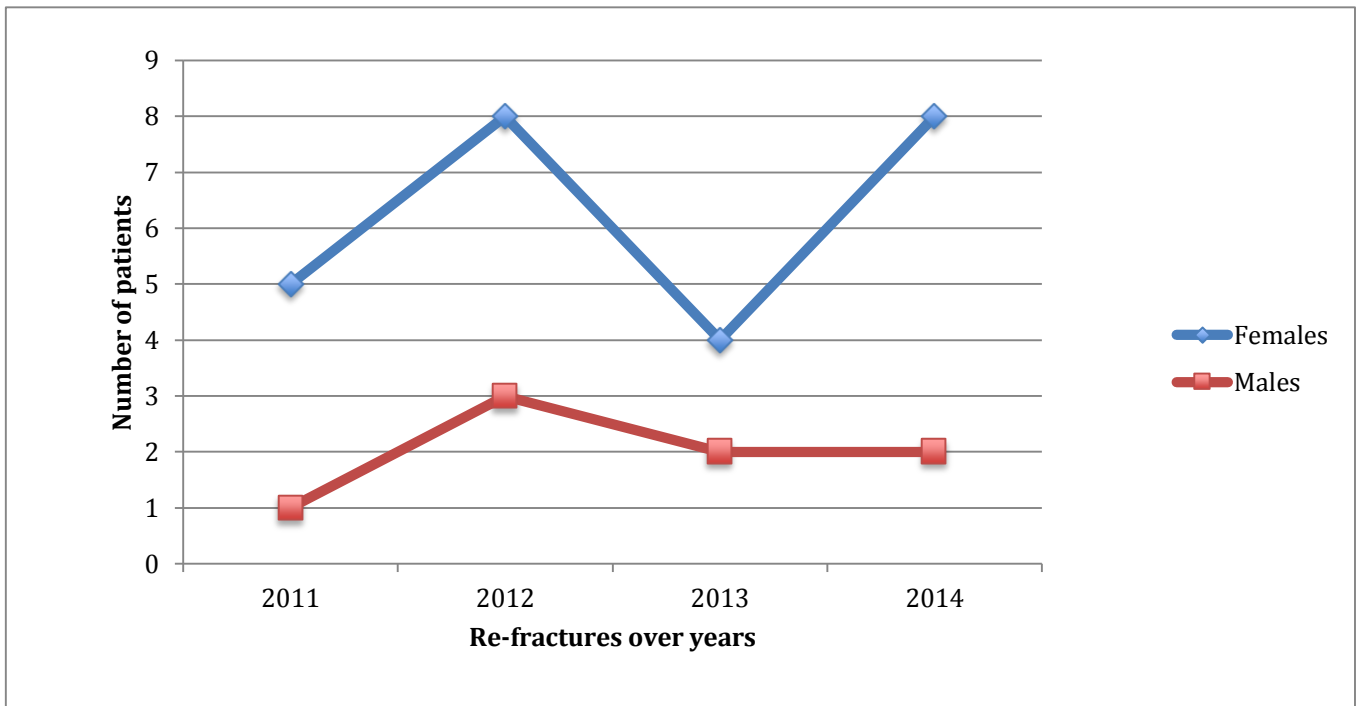
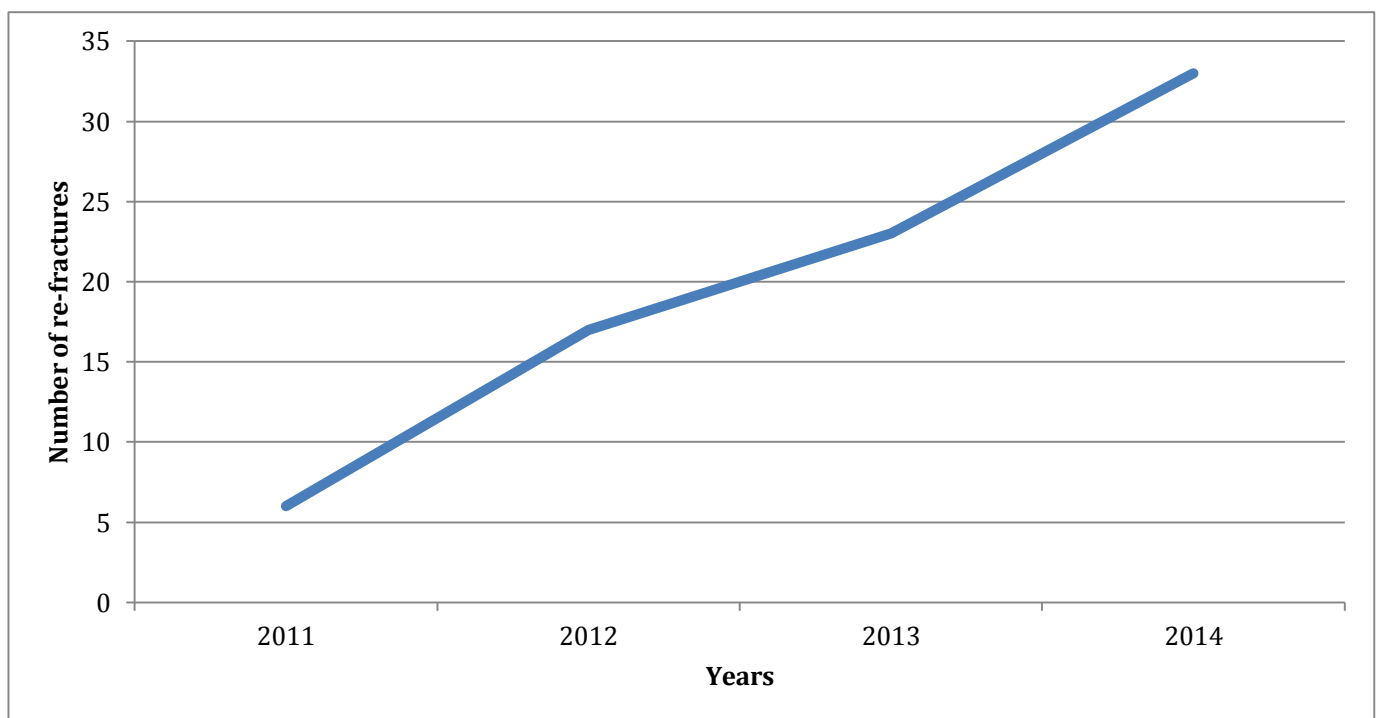
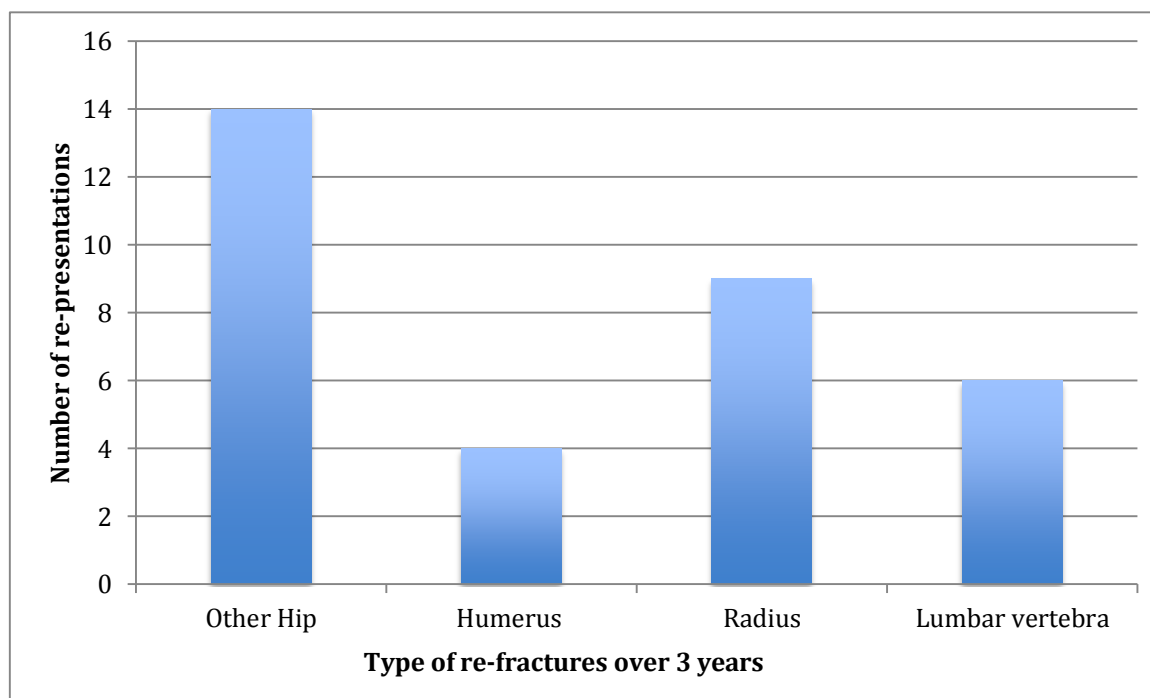


Figure 3: Cumulative re-fracture rate over 3 years



**Figure 4:** Different type of secondary fracture after the index hip fracture**Table 2:** Represents the direct medical cost per fracture management and the total cost incurred per fracture over the 3 years due to re-fractures

Type of fracture	Cost per fracture in Euro	N	Direct medical cost incurred due to fractures over 3 years in Euro
Hip fracture	5,182.84	14	72,559.76
Vertebral fracture	291.17	6	1,747.02
Humeral fracture (Conservative)	69.88	4*	279.52
Humeral fracture (Operative)	1,851.85	4*	7,407.40
Distal radius fracture (Conservative)	69.88	9*	628.92
Distal radius fracture (Operative)	1,595.62	9*	14,360.58

\* Cost for both conservative and operative management was calculated but in actual fact only one of the management plans was followed for these patients.

## Discussion

Low-energy trauma causing a fracture in a major bone is a sign of bone fragility. Osteoporotic hip fractures are the most severe and serious results of osteoporosis.<sup>22</sup> The determining factors for osteoporotic fractures are a combination of bone strength and risk of falls.<sup>23</sup>

Our study evaluated low-energy traumatic hip fractures within the adult population of 60 years and over presenting to the only general hospital in the island.

Although private clinics are available, hip fractures are generally referred to Mater Dei hospital for management. Therefore this study can be considered as a population-based study over a period of one year. Since no patients were started on bisphosphonates post-osteoporotic hip fracture surgery, it was impossible to present a case-control study for possible re-fracture outcomes.

The majority of the patients presenting with an

osteoporotic hip fracture were female, which follows the findings of Couris CM et al. who stated that women aged 60 to 85 years, have increased risk of hip fractures.<sup>24</sup> Those elderly patients with a previous history of an osteoporotic hip fracture are at higher risk to develop other fractures later on. These elderly patients have a 2.5-fold increased risk of suffering vertebral fractures and 2.3-fold risk for further hip fractures.<sup>25</sup> This could be seen in our study where 11.7% (n=33) of the adult population under study experienced a re-fracture with 14 patients sustaining a fracture of the other hip, followed by nine patients exhibiting a distal radius fracture. Females showed a higher incidence of re-fractures when compared to males.

Once a hip fracture has been sustained, the quality of life decreases and the mortality increases by about 20%.<sup>26</sup> A hip fracture does not only have a negative impact on the quality of life of the patient but also on his/her family and society. It also implies an economic burden on the national health system (NHS), which in Malta amounts to a mean direct cost of €5,182.84 per osteoporotic hip fracture when there is a hospital stay of 11 days. Sustaining a re-fracture will further increase the negative impact on the patient as well as medical costs incurred by the NHS. A hip fracture has direct consequences on the patient himself apart from carrying a direct financial burden on the national health system. The study aimed to evaluate the direct costs incurred from the moment of hospitalization up to discharge from acute care. It is virtually impossible to calculate all the indirect costs including days off work (both by patients and relatives), rehabilitation costs, possible surgery related complications requiring further hospital readmissions, household alterations in order to render them more fall proof etc. All these hidden costs increase the overall expenditure dramatically.

Within a year the re-fracture rate was of 6% of the total population under study, with direct mean medical costs estimations ranging between €37,642.55 to €48,835.19, depending whether a conservative or an operative management plan was followed. In actual fact the total costs would be much greater due to indirect costs as well emergency services and rehabilitation, which were excluded. The estimated cost is based on whether the distal radial fractures and the vertebral fractures followed a conservative care pathway or a surgical pathway, in which case the cost would vary as discussed above. Only the financial aspect was taken into consideration. It is immediately obvious, that several patients and their relatives undergo a physically and psychologically painful experience. In fact, 24% (n=8) of the patients in the study, died after their re-fracture, within a three-year follow up period. Three patients passed away within three months of the second fracture.

The total all-cause mortality rate after one year of

the index osteoporotic hip fracture was of 25.3%, with two of these patients having a re-fracture and dying within the first year. Therefore it is important to try to prevent such re-fractures from occurring by securing a number of measures. One simple way is prescribing anti-osteoporotic treatment. The aim of starting therapy is to prevent the re-fracture rate as well as improve the quality of life. Unfortunately a large amount of patients with hip fractures are not prescribed any anti-osteoporotic treatment.<sup>22</sup> This is the case in Mater Dei Hospital, Malta, where none of the osteoporotic hip fracture patients post-surgery were prescribed anti-osteoporotic treatment. Unfortunately there has not been any change in the management plan to date and no preventive policies or funding for osteoporotic drugs been implemented. It is hoped that this study will stimulate policy makers to implement this widely accepted international preventive management.

A study conducted in Belgium showed that only 6% of patients with hip fractures were discharged with anti-osteoporotic medication.<sup>5</sup> The same situation was found in the United States, where only 6.6% of the patients with hip fractures were prescribed calcium and vitamin D supplements and 7.3% were prescribed anti-osteoporotic agents.<sup>27</sup> This lack of anti-osteoporotic therapy prescription among the orthopedic community can be described as ‘Clinical inertia’ that is defined as “failure of healthcare providers to initiated or change treatment when the health status of the patient indicates such action is necessary”.<sup>28</sup> This clinical inertia is having a negative impact both directly and indirectly to the economic situation in the country leading to a financial burden on the health and social services.

Different types of bisphosphonates have shown to decrease the incidence of hip fractures in women who are osteoporotic as well as increase bone density in the femoral neck and lumbar spine.<sup>29, 30</sup> Bisphosphonates both orally and intravenously have shown a reduction in mortality rate after an osteoporotic hip fracture. It was reported that oral bisphosphonates could lead to a relative reduction of 60% death per year.<sup>31, 32</sup> Although one must keep in mind the complications that may arise from their usage such as necrosis of the jaw and upper gastrointestinal side effects.<sup>33</sup>

Bisphosphonates for osteoporotic fractures are not part of the free medication scheme entitlement in Malta, so if prescribed by the orthopaedic team, the patient will have to incur the cost. Considering alendronic acid monthly tablets at retail price from a pharmacy in Malta for a year supply would cost €117.12 per individual. If this was provided as part of the discharge requirements and entitlement to every patient leaving the NHS after sustaining an osteoporotic hip fracture during the study period (n = 281), the cost would have amounted to €49,770.72 per year. At retail price this would have cost the NHS €935.53 more than the re-

fracture management direct medical expense incurred. It is important to consider that the wholesale price of this drug to the NHS would be much cheaper. Also one needs to consider the fact that the indirect costs and rehabilitation costs were not included, so one can still suggest that providing a bisphosphonate to every patient sustaining an osteoporotic hip fracture is more economical and socially beneficial. Keeping in mind that following the osteoporotic hip fracture there was an all-cause mortality rate of 25.3%, prescribing of a bisphosphonate might have reduced this percentage by 60%<sup>31-32</sup>, where 43 patients would have survived the first year post-hip fracture out of the 71 patients that died. The cost effectiveness of bisphosphonates is a well-established fact with multiple repeated studies published in the literature. The effectiveness takes between six to twelve months to be evident on bone mineral density measurement, and is effective up to ten years post continuous treatment.<sup>34-36</sup>

### Study limitation

Our study investigated only patients that presented to the state health care institutes, where the national PACS is only available, so re-fractures presenting to private clinics or hospitals have been excluded in the study. The mechanism of injury, risk factors and treatment on discharge of each patient were based on case summaries that were written by doctors working in the orthopaedic department, therefore information could have been subject to human errors. The medical costs quoted are calculated according to the local NHS expenses at 2014 and does not represent the cost for different hospitals. All other anti-fragility hip fractures measures were not evaluated in this study as it is complex to put a cost to all these. They include steps taken to make homes safer such as attention to carpets and loose furniture.

### Conclusion

Osteoporotic hip fractures are a common occurrence in the elderly population. These increase the overall morbidity and mortality in this sub population. Withstanding evidence based medicine; orthopaedic surgeons even nowadays still fail to prescribe anti-osteoporotic treatment post surgical fixation of an osteoporotic hip fracture. There should be an increased drive through the Mater Dei policy makers, to institute anti-osteoporotic treatment. Prevention is better than cure; prescribing a bisphosphonate post-surgery may be more beneficial both to the patient and to the national health services with a decrease incidence of osteoporotic fractures and related morbidity and cost to the health services.

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