

## Hip Fractures and Vitamin D: Helpful or Not?

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**Conflict-of-interest statement:** The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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Received: June 5, 2021

Revised: July 3, 2021

Accepted: July 6 2021

Published online: August 28, 2021

### ABSTRACT

**BACKGROUND:** Hip fractures have continued to be among the leading causes of excess morbidity and mortality rates among aging adults in all parts of the world for some time.

**QUESTIONS:** (1) Is the incidence and/or prevalence of hip fractures continuing to escalate given many efforts to improve bone and general health of older adults across the globe? (2) If so, will the use of vitamin D assist those at risk in some way?

**METHODS:** PUBMED was searched for related articles, especially those that were published between 2016-2021.

**RESULTS:** While hip fracture rates may have decreased in some locations over time, it is safe to say, they appear to remain highly important causes of disability in aging populations, which are increasing globally. Discordant findings on vitamin D persist however, although this substance seems helpful in some cases.

**CONCLUSION:** The body of research that examines vitamin D

relative to hip fractures is largely non-conclusive as regards a) the deterministic role of vitamin D deficiency; b) the role of vitamin D supplementation. More clarity in these areas is indicated in light of the anticipated global increase in hip fractures numbers by 2050 and their disabling consequences and incalculable costs.

**Key words:** Aging; Hip Fractures; Prevalence; Prevention; Vitamin D

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Marks R. Hip Fractures and Vitamin D: Helpful or Not? *International Journal of Orthopaedics* 2021; **8(4)**: 1518-1528 Available from: URL: <http://www.ghrnet.org/index.php/ijo/article/view/3205>

### INTRODUCTION

Many authors over the years have concluded that hip fractures, a highly common injury affecting many older adults, are strongly associated with significant morbidity and mortality rates<sup>[1-3]</sup>, plus marked deficits in function and life quality among survivors<sup>[2,4]</sup>, especially among men<sup>[5]</sup>. What is not agreed upon in this realm is whether this problem is increasing or decreasing. Moreover, if it is increasing, it remains unclear as to whether vitamin D is a factor explaining this. A third area of research focused on the actual outcomes of vitamin D supplementation, remains equally non uniform. Finally, whether surgeons should recommend vitamin D for fostering functional recovery or averting secondary hip fracture risk post-hip fracture surgery remains unclear.

At the same time, it appears that even if hip fracture rates have tended to decline in some countries in the recent past, globally, most countries are experiencing high rates of aging cohorts, as well as cohorts of higher ages than those previously studied. Thus, despite an apparent age-standardized incidence decline as regards hip fractures in several countries, it appears this may yet be outweighed by the extent of ageing across various populations, especially those with limited resources and populations living to higher ages. In this regard, predictions made recently do suggest that the global number of hip fractures can be expected to increase from 1.26 million in 1990 to 4.5 million by the year 2050<sup>[1]</sup>.

This enormous rise in hip fracture cases that is anticipated over time does not include the new numbers that might emerge following COVID-19 pandemic situations, where many elderly were isolated, sedentary, and located indoors for prolonged periods. This group

may also be less robust than groups assessed in prior years, and those sent home from hospital stays might be weaker, especially those who sustained a hip fracture during a lockdown period<sup>[6]</sup>. In any event, the anticipated total number of hip fractures predicted by 2050 clearly poses a significant global challenge to both healthcare systems and to older adults themselves according to Fernandez et al<sup>[7]</sup>, and is one that should not be ignored. The fact that a hip fracture injury can prove extremely devastating to an aging individual<sup>[8,9]</sup>, if they survive the trauma and surgery, surely stresses the need for implementing all possible strategies that have the potential to safely mitigate or minimize hip fracture risk, as well as the risk of suboptimal surgical outcomes, plus recurrent, second or third hip fractures.

Indeed, regardless of data source, and geography, the literature is quite consistent in identifying that hip fractures continue to have a substantial impact on older peoples' physical abilities, quality of life, and adaptability<sup>[4]</sup> that has not diminished substantively in this regard over time, even though many forms of prevention have been discussed and implemented. In fact, the direct costs associated with this condition appear to have remained considerable because the injury often requires a long period of hospitalization and subsequent rehabilitation due to the possible associated development or exacerbation of other health conditions such as depression, osteoarthritis, and cardiovascular problems that may predictably pose additional costs, especially social costs<sup>[1]</sup>.

In addition, Abrahamsen et al<sup>[10]</sup> who examined osteoporotic medication usage from 2005-2015 in Denmark concluded the observed plateau in usage of osteoporosis treatment at a level was probably too low to make a meaningful impact on the societal hip fracture burden given its predicted age-specific increase in the future, thus other avenues of intervention must remain open to scrutiny. As well, Tsuda et al<sup>[11]</sup> found the use of the much discussed bone building pharmacologic product or bi-phosphonates did not significantly reduce fracture risk unless patients had a prior fracture. Their effect in patients without prior fracture, who constitute most cases, thus, remains unclear. Similarly, exercise, or nutrition or multi level preventive approaches have failed to be universally impactful, applied, or even practical.

### Specific aims

The specific aim of this present narrative review was to document whether hip fractures are likely to continue to be important disablers of the older adult in the future, and if so, whether vitamin D, a compound linked to bone health, muscle health, and overall well-being, is likely to be helpful in the context of both hip fracture prevention and rehabilitation. Since the available data are not clear on these points, we hoped to offer the reader an updated and comprehensive synthesis of what we know about the future of hip fracture injury rates, and whether vitamin D exposure can mitigate any aspect of the projected health burden, plus suggestions on how this data might be duly applied.

### Questions

The key questions posed in this present review were: (1) Is there a need to continue to pursue preventive strategies against hip fractures in the older population? (2) If so, is there a role for vitamin D, and in what respect?

### Significance

Hip fractures among the elderly pose a significant economic, social, and physical burden wherever they occur<sup>[1,12,13]</sup>. Moreover, as outlined by Haentjens et al<sup>[14]</sup>, even after initial hospitalization, hip fractures

continue to generate significant costs throughout the ensuing 12 months after discharge. Cost estimates based on data obtained prospectively from hip-fracture patients and matched controls also showed the costs associated with the treatment of hip-fractures to be about three times greater than those resulting from the treatments of age and residence-matched controls without a fracture. Thus it is clear that hip fracture prevention is a topic of immense import that clearly warrants attention, and in particular, warrants clarification as to whether vitamin D, of key import in the context of osteoporosis, a hip fracture determinant<sup>[15]</sup>, is of current relevance in this regard as discussed for some time with conflicting conclusions<sup>[16,17]</sup>.

## METHODS

To examine whether hip fractures remain a major health concern in a global context, and whether vitamin D is potentially of clinical relevance in the context of hip fractures prevention efforts, all pertinent articles listed on **PUBMED** that appeared to inform about hip fractures and/or vitamin D were sought and those of high relevance were examined specifically. A scan of the epidemiological data from different countries was also undertaken, and the nature of any predicted trend in coming decades was summarized as being either declining in nature or likely to increase. Then, regardless of trends, evidence to support a focus on hip fracture prevention was sought. As well, the specific role of vitamin D in influencing hip fracture risk, and its possible utility in preventive situations was examined. Finally, studies detailing the consequences of hip fracture surgery and the degree to which vitamin D applications may be warranted in this regard were undertaken.

Articles selected for independent assessment had to focus on vitamin D and hip fractures, or hip fractures and their outcomes as published between 2016-2021. Excluded were non-clinical studies, preprints, abstracts, and conference proceedings. The **PUBMED** data base was chosen to represent a majority of the works on the present topic published to date. Articles were screened for their relevance and data addressing the review questions were duly extracted, regardless of study approach. We accepted the fact many studies included in the data base were observational or of possible low quality, but that these might have some important clinical utility, nonetheless. Even when considering only prospective data, the diverse approaches and questions studied were deemed very challenging to aggregate, hence no definitive statistical analyses were conducted. In this regard, and among those articles that met criteria for discussing prevalence issues, we excluded those that did not provide future 2025-2050 projections. From those reports that met criteria, we elected to tabulate the key anticipated trends in upcoming decades, where available.

**Table 1** Table depicting search terms and their relative results concerning the current topic.

Key word	VARIABLE		
	Number of reports	Number in last 5 years	Number in past year [2020-2021]
Vitamin D	90584	23133	5564
Hip Fractures	40,500	9673	2477
Hip Fracture Prevalence	12819	3802	820
Hip Fracture Outcomes	13482	5170	1432
Vitamin D + Hip Fractures	1932	380	103

Note: 1) Commonly, these report numbers do not accurately reflect the topical information sought and are generally all overestimates as a result; 2) most systematic reviews rarely discuss contemporary or comparable data for example, ages, geographic regions, injury type, modes of assessment.

**Table 2** Summary of projections for hip fracture occurrences by 2050.

Authors	Geographic Location/Year	Key Anticipated Predictions for Hip Fracture Rates 2025-2050
Concin et al <sup>[21]</sup>	Austria, 2015	By 2050, case rates assessed in 2015 will have more than doubled, regardless of gender
Ramanau et al <sup>[22]</sup>	Belarus, 2015	The estimated number of hip fractures in persons older than 50 will increase substantially by 2050
Kirilova et al <sup>[23]</sup>	Bulgaria, 2015	In adults 50 years of age and above, hip fracture numbers of 9322 in 2015 will likely increase to 11,398 in 2050
Kebatse et al <sup>[24]</sup>	Botswana, 2020	The estimated number of hip fractures nationwide in persons over age 50+ for 2020 of 103 is predicted to increase to 372 in 2050
Diaz-Ledzma et al <sup>[25]</sup>	Chile	For 2030, hip fractures among the elderly population are projected to grow 27.5% to 9862 cases
Gong et al <sup>[26]</sup>	China	By 2050, the total number of hip fractures in people older than 65 years in China is predicted to be 1.3 million
Ong et al <sup>[27]</sup>	Global	By 2050, it is estimated six million hip fractures will occur annually and the majority will be in Asia
Cooper et al <sup>[28]</sup>	Global, 1990	Hip fracture numbers will increase from 1.66 million observed in 1990 to 6.26 million by 2050
Veronese and Maggi <sup>[1]</sup>	Global	Hip fracture numbers will increase from 1.26 million in 1990 to 4.5 million by 2050
Downey et al <sup>[29]</sup>	Ireland	The number of fragility hip fractures in adults >60 years is estimated to triple/quadruple by 2050
Barrios-Moyana et al <sup>[30]</sup>	Mexico, 2009	According to figures from 2009, 1/12 Mexican women and 1/20 men over age 65 will suffer a hip fracture when cases reach 110,055 patients in the year 2050
Lesnyak et al <sup>[31]</sup>	Kyrgyz Republic, 2015	An estimated 2752 hip fractures in 2015 will increase by 207% to 8435 in 2050
Issayeva et al <sup>[32]</sup>	Kazakhstan, 2015	2015 data estimates of 11,690 in 2015 are predicted to increase by 140% to 28,000 in 2050
Zakroyeva et al <sup>[33]</sup>	Moldova, 2015	The 2015 data reflecting 3911 hip fracture cases will increase by 60% to 6492 in 2050
Naureen et al <sup>[34]</sup>	Pakistan, 2015	An estimated 36,524 hip fractures in 2015 will increase by 214% to 114,820 in 2050
Kim et al <sup>[35]</sup>	South Korea, 2008	Hip fractures increases from 159.1/100,000 in 2008 to 181.5/100,000 in 2012, are estimated to increase by 1.4 times over the next 10 years
Wilk et al <sup>[36]</sup>	Poland	There will be an increase of a total crude rate of 467.2 (men 329.6; women 584.7) for the year 2050
Tuzun et al <sup>[37]</sup>	Turkey	The number of hip fractures is expected to increase to nearly 64,000 in 2035
Abeygunasekara et al <sup>[38]</sup>	Sri Lanka	According to the data, 3824 hip fractures would have occurred island-wide during the study period and will likely reach 12,068 in 2051
Leznyk et al <sup>[39]</sup>	Uzbekistan, 2015	Estimated numbers of hip fractures in persons 50+ years for 2015 of 16,764 are predicted to increase to 60,272 in 2050

Note: In general, most of these reports and others discuss hip fracture incidence and prevalence rates that are not necessarily current [eg., 20, 31-35, 40-45, 49].

In light of present space limitations, and the fact we sought to narrate data largely from 2016-2021, readers may want to examine those hip fracture trends that occurred between 2010-2019 by referring to the paper by Peng et al<sup>[18]</sup>. Those who wish to examine comparable hip fracture data covering the periods from 1980-2009 are referred to the detailed review by Marks<sup>[19]</sup>.

## RESULTS

### General findings

As of June 5, 2021, and highlighted in Table 1, it appears a considerable level of substantive and continuing interest in the context of efforts to better understand hip fractures, their occurrence, and modes of prevention and outcomes has prevailed since the 1960s. Among those that detail future hip fracture trends, most indicate a need for continued study (Table 2).

### Specific findings

#### Hip fracture trends and costs

The presently available research articles covering the time periods 2016-2021 strongly indicate that hip fractures will continue to pose an enormous challenge to health policy makers and others over the next few decades, despite some evidence of declining hip fracture incidence rates in some regions in recent years [eg., 20, 40, 45-49]. In particular, selected population trend estimates conducted largely prior to 2016, can be said to generally show that regardless of geographic location, or declining or low rates of hip fracture rates in the past, hip fractures will continue to increase in numbers up until at least 2050 in those regions studied. This seems especially evident in the case of men as well as those in the higher age groups that exhibit frailty or multiple coexisting diseases, health conditions thought to be

increasing among aging populations in their own right<sup>[21,50-52]</sup>.

Unsurprisingly, former ‘low risk’ countries such as China expect rising trends, especially in remote high altitude regions in the future<sup>[26]</sup>. Data may also be underestimates or inaccurate for countries that have taken concerted preventive measures and still tend to show benefits in research reports as of 2021, such as Taiwan until 2012<sup>[47]</sup>, and Japan up until 2017<sup>[45,52-53]</sup>, if current data sets fail to represent the changing nature of the aging population and its health status, in the face of anticipated widespread frailty increases, along with multi morbidities in the increasingly prevalent older age groups. The incidence rates applied to provide base line calculations in predictive models may also fail to depict more recent upward trends of relevance to fracture risk, such as increases in rates of osteoporosis, as well as how specific sub groups appear to be at higher risk than others<sup>[48]</sup>. In the Kyoto Prefecture for example. Asada et al<sup>[48]</sup> found the number of hip fractures to increase in the second half of their study period (2013-2017) compared to the first half (2008-2012), a finding similar to Lin et al<sup>[54]</sup> in Taiwan where there was a temporal trend of a 8.6% increase in the incidence of all types of hip fractures over the period of 2000-2010, yet, the incidence rate did not increase, with the exception of femoral neck fractures in men aged ≥ 75 and women aged ≥ 85.

Ha et al<sup>[55]</sup> who calculated projections of future hip fracture occurrences in Korea using the Poisson distribution and data from 2016 to 2025, implied the incidence of hip fractures in Korea will continue to increase, along with its socioeconomic burden, a conclusion echoed by Glinkowski et al<sup>[56]</sup> who collected data between 2008 and 2015 in Poland. Rapp et al<sup>[3]</sup> who conducted a thorough review of hip fracture incidence rates showed that while hip fracture rates tend to vary more than 100-fold between different countries, it appears not all have shown a decrease in hip fracture

**Table 3** Randomly selected research examples of possible relevant findings concerning vitamin D and hip fracture interactions showing possible areas of promise for future study, despite no effects of usage by some.

Research groups	Findings and Conclusions
Aventi et al <sup>[81]</sup>	Vitamin D alone is unlikely to prevent fractures in the doses and formulations tested so far in older people. Supplements of vitamin D and calcium may prevent hip or any type of fracture.
Chutterpaul et al <sup>[82]</sup>	The high prevalence of vitamin D deficiency and/or insufficiency in the hip fracture cohort studied strongly implies a need for universal vitamin D supplementation in older adults, especially those at risk for osteoporotic fractures
Dadra et al <sup>[83]</sup>	The prevalence of vitamin D deficiency was found to be very high in patients with hip fragility (proximal femur) fractures in 75% cases studied
Dretkakis et al <sup>[84]</sup>	Older age, recurrent falls, and severe vitamin D deficiency were found to be associated with trochanteric fractures. Additionally, older age, female gender, and severe vitamin D deficiency were related to recurrent falls
Han et al <sup>[85]</sup>	Vitamin D deficiency and inadequacy were high in patients with low-energy hip fractures, with only 4.9% of patients having normal vitamin D levels
Jamal et al <sup>[86]</sup>	There is a significant association between the presence of a vitamin D deficiency and the severity of intertrochanteric fractures (p <0.05), in both genders
Niikuru et al <sup>[87]</sup>	Perennial vitamin D insufficiency was found to be prevalent in elderly Japanese hip fractures cases
Yao et al <sup>[88]</sup>	Daily supplementation with both vitamin D and calcium appears somewhat promising
Lai et al <sup>[89]</sup>	Neither higher nor lower dose vitamin D supplementation prevents hip fracture
Reid et al <sup>[90]</sup>	Widespread use of vitamin D for osteoporosis prevention in community-dwelling adults without specific risk factors for vitamin D deficiency seems inappropriate
Poole et al <sup>[91]</sup>	Using only a 1-year horizon, considering only reduction in hip fracture, prescribing 800 IU of vitamin D daily to all adults aged 65 and over, could reduce the number of incident hip fractures from 65,400 to 45,700, saving almost 1,700 associated deaths, whilst saving the United Kingdom taxpayers £22 million
Sim et al <sup>[92]</sup>	Preoperative severe vitamin D deficiency is an independent risk factor for poorer recovery of function and quality of life after hip fracture surgery.
Thorpe et al <sup>[93]</sup>	Without combined supplementation of both vitamin D and calcium, female vegans are at high risk of hip fracture
Wang et al <sup>[94]</sup>	Compared to low serum vitamin D levels, high serum vitamin D levels reduced the risk of hip fractures in patients aged 60 years or older, but not total fracture risk
Whiting et al <sup>[95]</sup>	In long term care homes, vitamin D had no observable effect on those hip fracture patients who used vitamin D. Models for mortality, stratified by sex, showed in women only, that vitamin D use resulted in a significant inverse association with time to death [HR (0.91(0.87-0.96)]; for men it was 0.94(0.88-1.01) . The impact of vitamin D supplementation in long term care contexts deserves further investigation
Weaver et al <sup>[96]</sup>	This meta-analysis of randomized controlled trails supported the use of calcium plus vitamin D supplements as an intervention for fracture risk reduction in both community-dwelling and institutionalized middle-aged to older adults
Zhao et al <sup>[97]</sup>	Levels of vitamin D were significantly associated with the severity of intertrochanteric, but not femoral neck, fractures
Zhang Et al <sup>[98]</sup>	Vitamin D deficiency precipitates and exacerbates osteoporosis among adults and causes the painful bone disease called osteomalacia. Osteoporosis is a systemic skeletal disease characterized by decreased bone strength and increased risk of fractures
Zhao et al <sup>[99]</sup>	The use of supplements that included calcium, vitamin D, or both compared with placebo or no treatment was not associated with a lower risk of fractures among community-dwelling older adults
Steingrimsdottir et al <sup>[100]</sup>	Results lend support to the overarching importance of maintaining serum vitamin D levels above 30 nmol/L
Yu et al <sup>[101]</sup>	Vitamin D deficiency is common in patients with brittle hip fractures, especially in women. With the increase of age, vitamin D continues to decrease and parathyroid hormone increases. The decrease of bone mineral density in patients with hip fractures is the result of a combination of age, gender, body mass, and vitamin D content
Neale et al <sup>[102]</sup>	Even in sunny Australia, vitamin D deficiency contributed to a considerable number of hospitalizations as a consequence of falls and for treatment of hip fracture in older
Conley et al <sup>[103]</sup>	To prevent secondary hip fractures, adequate dietary or supplemental vitamin D and calcium intake should be assured

rates over time even if they are considered high income locations such as Germany<sup>[3]</sup>. In addition, a recent study conducted in China by Zhang et al<sup>[42]</sup> showed that despite stable hip fracture incidence rates from 2012-2016, actual numbers of hip fracture injuries increased in parallel with the aging of the population. That is, the absolute number of hip fractures in those 55 years and older increased about 4-fold, and accordingly, the total costs for hospitalization showed a steep rise from US\$60 million to US\$380 million over the study period. As well, costs of hospitalization increased about 1.59-fold, from US\$4,300 in 2012 to US\$6,840 in 2016. These data may yet be underestimates because they did not necessarily account for the possible recurrence of the fracture at the initial injury site, or the development of a new fracture in the contra-lateral hip, that may occur in almost 10 percent of hip fracture survivors<sup>[57]</sup>. As well, regardless of case numbers, mortality rates post hip fracture remain high, especially for men<sup>[58]</sup>, and according to Hagen et al<sup>[47]</sup>, estimates of health lost to hip fractures will approximately double, from 32,850 DALYs in 2020 to 60,555 in 2040 in Norway, even though hip fracture incidence rates were found to be decreasing in the high incidence area of Oslo, Norway, among women<sup>[59]</sup>.

In short, in terms of the anticipated increases in coming decades of increasingly high hip fracture volumes and their dire consequences, as discussed by Von Friesendorff et al<sup>[60]</sup>, and when considering these injuries solely from a remaining lifetime perspective, it can be anticipated that post fracture all-cause and excess mortality rates will probably continue to be higher rather than lower, even after 20 years of follow-up if no comprehensive preventive programs are forthcoming in the immediate future. As well, Veronese and Maggi<sup>[1]</sup> too have noted hip fracture recovery to be commonly associated with highly negative health consequences, such as disability, depression, and cardiovascular diseases, as well as immense social costs, and these are expected to continue in the absence of dedicated preventive approaches and efforts. Moreover, as discussed by Dyer et al<sup>[4]</sup> the long-term outlook for hip fracture surgery survivors even those deemed initially independent in self-care pre-fracture, is bleak, and one where 20-60% of survivors will likely require assistance for various daily tasks for up to two years, especially in the older age groups and those with fragility fractures. Moreover, among those elderly living in residential care, which they may be forced to reside in post hip fracture, their level of function is likely to be lower than

those returning to and living in the community. As per Papadimitrou et al<sup>[61]</sup>, hip fracture injuries, which are found to increase in prevalence with age<sup>[62]</sup>, can also be expected to lead to a substantial loss of years of healthy life even in previously healthy older adults, in addition to producing substantive decrements in independence and mobility in the first year post fracture, along with an increase risk of depressive symptoms and a decrease in activity participation<sup>[63]</sup>.

In addition, high mortality rates within the first three to six months of their injury in surgical cases are common<sup>[64]</sup>, and may be even higher in non-operative cases, or in those receiving poorly integrated care<sup>[65-68]</sup>. Moreover, as well as a possible heightened risk for a second hip fracture<sup>[69]</sup>, those hip fractures cases with sarcopenia can be expected to have very poor functional outcomes<sup>[70]</sup>, as well as high levels of psychological distress<sup>[71]</sup>. Along with excess mortality rates in the first post surgical year<sup>[72]</sup>, hip fracture survivors may hence experience a highly reduced health-related life quality, and will be unlikely to return to their pre-fracture levels of performance without dedicated efforts to achieve this<sup>[73]</sup>.

### ***Hip fracture determinants and vitamin D***

In light of the high magnitude of excess disability and premature death rates associated with hip fractures, along with the failure of current modes of intervention to prevent this set of debilitating outcomes in most cases, it appears crucial to re examine whether the predicted 2050 predicted tsunami of death and distress due to this injury can be averted to some degree. These include, but are not limited to, a multitude of potentially remediable factors uncovered since the 1960s, including falls, low bone and muscle mass, chronic health conditions, impaired cognitions, low milk consumption, suboptimal exposure to sunlight, and vitamin D deficiency. Others include environmental and social factors, vision impairments, disability, neurological impairments, steroid usage, and medication effects<sup>[19,74-80]</sup>.

However, in the specific case of vitamin D, much conflict prevails, even though most hip fracture cases are found to be vitamin D deficient, and despite a strong rationale from basic research studies and others that vitamin D plays a key or important role in bone physiology and maintenance, muscle physiology, overall health status, and possibly in cognitive and falls associated situations. As well, many, although not all epidemiological studies suggest that vitamin D insufficiency is related to a number of other disorders frequently observed among elderly fallers who are prone towards hip fracture, such as type 2 diabetes, and cardiovascular disorders including hypertension. See Table 3 for representative summary data on this issue.

In short, as per Table 3, and discussed by Salaman et al<sup>[104]</sup> even though ample evidence supports the presence of vitamin D in maintaining calcium and bone metabolism, a risk factor of osteoporosis, falls and fracture in old age, its replacement seems to have differential effects or no effects as regards hip fracture risk, survival, or recovery.

### **Additional Findings**

In line with the selected findings outlined in Table 3, data collected by Dhanwahl et al<sup>[105]</sup> have shown almost 75% of admitted hip fracture cases currently can be expected to exhibit a vitamin D deficiency. An even higher rate of 96.7% of hip fracture cases were found to be vitamin D deficient however, in an Asian-Indian cohort with fragility hip fracture, and where the bone mineral density of these patients was also significantly lower than that of age and sex matched healthy controls<sup>[77]</sup>. This is important because as noted by

Zhao et al<sup>[106]</sup>, cases suffering from inter trochanteric hip fracture who exhibited with lower vitamin D levels were found to have more severe fractures than those with higher levels. They may also exhibit more evidence of post-operative delirium, more new hip fractures, and more medical readmissions, at 1 year<sup>[107]</sup>, unless action to counter this is forthcoming<sup>[108]</sup>.

Although supplementation of vitamin D is not currently advocated for all hip fracture cases, Jaruswan et al<sup>[109]</sup> have concluded that in treatment settings where baseline serum vitamin D level can't be evaluated in older adults with fragility hip fracture, high-dose vitamin D2 of approximately 60,000 IU/week for 12 weeks, with a subsequent switch to a maintenance dose is likely to prove beneficial because this regimen can effectively restore serum vitamin D to optimal levels in 82.8% of patients without causing symptomatic hypercalcemia.

Mak et al<sup>[110]</sup> who conducted a randomized, double-blind, placebo-controlled trial of 218 adults, aged 65-years or older, requiring hip fracture surgery who were assigned to receive a single loading-dose of vitamin D (250,000 IU vitamin-D3, termed the REVITAHIP - Replenishment of Vitamin D in Hip Fracture strategy) or placebo, and who both received daily vitamin-D (800 IU) and calcium (500 mg) supplements for 26-weeks, did find falls related benefits in the active group at week 4. As well, a higher percentage of the active group reported 'no pain or consistent discomfort', and trended for higher life quality scores at week-26.

Sprague et al<sup>[111]</sup> who used data from a large hip fracture trial to determine the proportion of patients who used vitamin D after hip fracture surgery and whether supplementation was associated with improved health-related quality of life and reduced reoperation rates found that despite guidelines recommending vitamin D supplementation, a low proportion of elderly patients with hip fracture were using vitamin D consistently, suggesting a need for additional strategies to promote compliance if this is indicated. The authors of this study also found vitamin D usage to be associated with significant improvements in health-related quality of life after sustaining a hip fracture. It also appears that vitamin D supplements may be more helpful than not in selected cases with fragility fractures who may have a severe vitamin D deficiency, and a high risk of significantly poorer baseline and 6-month outcomes<sup>[92,108]</sup> post hip fracture surgery than those with adequate vitamin D levels. As well, higher one year and four year survival rates may be evidenced if vitamin D supplementation is coupled with exercise<sup>[115]</sup>.

## **DISCUSSION**

This review examined whether hip fractures remain a noteworthy cause of excess morbidity and mortality among older adults, and if so, if there is a need to prevent the injury and its consequences. It also examined the possible role of vitamin D in this regard. Using data published primarily between 2016 and 2021, it seems most nations can clearly anticipate increases, rather than decreases in hip fractures case rates by 2050, regardless of geographic location or prior successes in reducing hip fracture rates. At the same time, many aging adults will be likely to be in poor health with deficient vitamin D levels and at high risk for fracturing a hip, a potentially devastating event<sup>[79]</sup>.

Yet, although a strong case can be made for vitamin D, a steroid hormone involved in bone physiology and a substance possibly implicated in the hip fracture risk cycle, this area of research remains unproven and conflicting reports prevail. Indeed, despite the urgency of this issue, a very limited numbers of research projects from limited

geographical locations prevail, some using retrospective data or observational approaches.

Further, very few clinical controlled studies prevail, and many suffer from low quality or questionable efforts to aggregate dissimilar data sets. As such, and in light of the very modest successes of past preventive approaches, and a trend to more rather than less favourable role for vitamin D in hip fracture prevention efforts, more should clearly be done in the future, especially in the less developed world<sup>[39,42,113]</sup> to examine vitamin D and its presence in the serum and how this might be harnessed to play an important preventive role in the context of hip fracture risk, and recovery, as outlined by Chevalley et al<sup>[114]</sup>.

At the same time, and according to Bischoff-Ferrari<sup>[115]</sup> given that about two-thirds of hip fracture cases may show signs of a vitamin D insufficiency, and a recent review indicated its possible benefits in averting hip fractures due to falls<sup>[116]</sup>, as well as in improving health and extra-skeletal health status<sup>[117]</sup>, in the event the older adult is deficient in vitamin D, it seems this possible avenue of mitigation and causality should not be ignored or need to await future study. Accordingly, and notwithstanding the lack of any robust evidence to validate universal supplementation of vitamin D among the older at risk population, in addition to encouraging the use of sound safety measures against falls<sup>[78]</sup>, appropriate routine screening measures to determine the prevailing level of serum vitamin D in vulnerable older adults, along with timely follow up procedures by practitioners may not only help to identify those at risk elderly people who should clearly be targeted, but may alleviate much distress and pain, and may even save lives.

In particular, as discussed by Downey et al<sup>[29]</sup>, since the number of fragility hip fractures in adults 60 years of age or older is estimated to triple or quadruple by 2050, with an estimated global cost of hip fractures in the year 2050 of \$130 billion<sup>[118]</sup>, the possible favorable role of vitamin D supplements in mitigating this to some degree, as indicated, must surely warrant widespread consideration. Indeed, since it is also estimated that the prevalence of contra-lateral hip fractures are expected to increase as well by 2050, more emphasis on all preventive possibilities against both primary as well as secondary hip fractures is not just a theoretical ideal, but one that is possibly an absolute requirement to have any chance of staving off the extent of the anticipated associated hip fracture injury burden in the future, including the presence and persistence of postoperative pain associated with osteoporotic hip fractures<sup>[8]</sup> and further surgeries for secondary hip fractures<sup>[103]</sup>.

To resolve the discrepancies in the literature, as well as limitations of these due to lack of comparability and low quality evidence, key issues that might be valuable to address in a more consistent fashion in future efforts to garner a better understanding of these issues are: the nature of the methods of measuring and classifying vitamin D, the nature of the injury, pre-existing health status, and follow-up periods and procedures, the demographic features and geographical location of the sample studied, the duration of the follow-up periods, where published-plus attention to seasonal variations in vitamin D levels and activities<sup>[119]</sup>. In addition, careful consideration of the individual's level of outdoor exposure, nutrient intake and access, falls history, and extent of frailty warrants careful attention in intervention studies. A specific focus on examining and differentiating between the causes and outcomes of the two main types of hip fractures, namely cervical and intertrochanteric fractures, especially in the context of vitamin D and its potential role in preventing and treating hip fractures also appears highly desirable. Nyugen and Lui<sup>[118]</sup> further imply that to enable more effective implementation and outcomes of hip fracture

prevention strategies, it is imperative to develop an optimal model of care for older patients with hip fracture, especially in rapidly aging nations. Unfortunately, although a substantive number of authors identify high predicted magnitudes of hip fractures in 2050 among older adults, very few authors spelled out the implications of these associated dire prognostic conclusions, and only a very few mentioned any strategy or need to intervene on this future possible epidemic<sup>[eg 3,26]</sup>.

However in light of the undisputed and severe individual and economic consequences of hip fractures, and their adverse influence on health care utilization, premature mortality, independence and life quality, it seems reasonable to consider all possible efforts to offset this burden and to do this by extending available research concerning the most salient risk factors underlying this condition that can be subjected to practical and widespread measurement and remediation. There is also a need to investigate whether it is possible to improve upon current rehabilitation strategies for restoring functional recovery post-hip fracture surgery, particularly for preventing second hip fractures and third hip fractures and certain types of articular degeneration, and extensive disability. Based on a considerable volume of supportive literature and biological rationale, vitamin D may be one factor worthy of consideration due to its possible impact on: (1) Bone mineral content/bone metabolism; (2) Balance/walking speed; (3) Effectiveness of protective reflexes; (4) Chronic pain; (5) Muscle strength/mobility; (6) The risk of falls and falling; (7) Extra skeletal health status; (8) Cognitive health status.

Ideas provided by researchers that may be especially worthy of consideration in efforts to minimize anticipated hip fracture 2050 rates of occurrence and their consequences include the need for: (1) Prompt action to counteract predicted global hip fracture increases<sup>[21,27]</sup>; (2) More effective falls and other practical prevention and safety approaches<sup>[78,118]</sup>; (3) More intense efforts to offset vitamin D deficiencies, bone fragility, and frailty<sup>[102-103,120-122]</sup>.

## CONCLUDING REMARKS

Despite an obvious pressing need for timely efforts to avert hip fractures and their debilitating costly outcomes among the elderly, current efforts to offset this projected hip fracture health burden are unlikely to prove uniformly successful. In particular, the possible role of vitamin D deficiencies, and their well established adverse health ramifications as this pertains to hip fracture risk, remains a contested issue. As well, the utility of vitamin D supplementation for purposes of primary and secondary hip fracture risk preventive, while promising, remains in question. To minimize the magnitude of the anticipated growing hip fracture burden, although seldom discussed in the current literature, sufficient data supports the importance of continuing to carefully examine vitamin D and its possible linkages as regards mitigating or influencing hip fracture risk and recovery in a timely and comprehensive manner, and efforts to examine this premise are hence strongly encouraged.

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