

Antidepressant Drugs and Hip Fracture Associations 2018 - 2022

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Abstract

Introduction: Hip fractures, which commonly impact many older adults highly adversely, not only persist, but often lead to disabling hip joint osteoarthritis, premature death, second hip fractures, or reduced life quality, despite decades of research and an array of contemporary evidence based recommended preventive approaches. But are all hip fracture injuries other than pathological fractures inevitable?

Aims: This mini review aimed to specifically examine the current literature published in the English language concerning the most recent findings regarding the probable association of antidepressant medication usage and hip fracture risk among the burgeoning vulnerable older adult population.

Methods: An electronic scan and careful review of relevant peer reviewed published articles on this topic was conducted over the time period 1972 - 2022.

Results: A diverse set of non-uniform observations imply antidepressant usage may have the potential to independently or collectively heighten hip fracture risk in a fair number of vulnerable older adults suffering with depressive symptoms, but not all.

Conclusion: Until more conclusive research is forthcoming, efforts to prevent or minimize depression in at risk vulnerable older adults using alternate non-drug methods of mitigation, and/or extreme care in administering antidepressants, if essential, are strongly indicated.

Keywords: Antidepressants; Depression; Hip Fracture; Intervention; Prevention; Treatment

Introduction

As societies age and despite years of study, the incidence and prevalence of hip fracture injuries generally appears to persist with few exceptions [1]. A health condition where a host of risk factors, including falls has been put forth for many years, the possible contributory or cumulative role of antidepressants in this regard, while not novel, has been and continues to be studied [2]. Rashiq and Logan [3], however, who examined the role of drugs in influencing the risk of hip fractures found that with the exception of antibiotics, fracture risk was lower in those taking drugs. Other data show drugs reported to be related to falls that often predate hip fractures among the older adult include: cimetidine, psychotropic anxiolytic/hypnotic drugs, barbiturates (which may decrease bone quality), opioid analgesics, and antihypertensives [4], long-acting benzodiazepines, anticonvulsants and caffeine [5]. Tranquillizers, sedatives

and exposure to any of the three classes of antidepressants is also associated with a significant increase in the risk of falling and sustaining a hip fracture [6,7].

These aforementioned findings, while suggesting that unremitting depression and/or the persistence of depression-related mechanisms may drive the risk of incurring a hip fracture among those older adults being treated with antidepressants, remain challenging to separate from other possible confounding factors, however [8], such as poor health status, in general, and that could independently raise the risk for falls and a hip fracture regardless of any exposure to antidepressant drugs [2,9]. Others suggest, only some forms of antidepressant-related medications may prove harmful and not others, while others support the view that a role for antidepressants in hip fractures mechanisms cannot be ruled out [8,10-14] and may impact significantly upon post fracture costs [15]. Additionally, tricyclic antidepressants may increase the risk for hip fractures due to their detrimental cardiovascular side-effects, and/or their side-effects of sedation and confusion [16], as well as central nervous system depressant effects [13] linked to unintentional traumatic injury risk. Moreover, when studied it was found that first- and second-generation antipsychotics and antidepressants were associated with an increased risk of hip fracture in predominantly older adult populations [17].

Aims of Review

This mini review aimed to examine past as well as current observations and conclusions regarding whether there is any cause for concern in recommending antidepressants to vulnerable older adults, as far as hip fracture risk is concerned.

Relevance

The incidence of index hip fractures, while possibly declining in some spheres, may be rising when considered cumulatively and globally due to the rapid aging of most populations along with lengthier numbers of years of life with a projected 4.5 ~ 6 million cases in total by 2050 [18].

Given the untold human and social costs of this collective possibly preventable injury and in view of the high prevalence of hip fractures, the immense potential harm to the patient, cost to society, and lack of availability of efficacious preventive modalities-the frequent neglect of easy to perform risk factor-screening and underuse of non-injurious preventive interventions is quite alarming according to Shattner [19] and especially given the fact at least 23 percent of older adults who sustain a hip fracture are found to be depressed [20].

Methods

To achieve the review aims, a comprehensive search and subsequent examination of the present topic of interest was undertaken wherein the PUBMED electronic data base, as well as Google Scholar, Web of Science Consolidated, Scopus and PubMed Central were screened for salient articles. These data bases were selected due to their high volume of sound peer reviewed works. The search was not restricted in general, but searched for were all relevant peer reviewed full length articles especially those documented over the five years (2018 - 2022). The key words applied independently or simultaneously were: depression, hip fracture, antidepressants. All types of research as well as reviews were deemed acceptable. Excluded were abstracts, foreign language articles, many studies older than 15 years since publication, preprints, or articles on depression occurring after a hip fracture, or in parallel with dementia or a chronic health conditions such as kidney disease and those that discussed multiple themes, rather than hip fractures and the influence of antidepressants specifically.

After examining potential articles, those that were salient were selected and reviewed in detail. The diverse nature of the data and its very limited focus on any one issue precluded anything but a very limited descriptive report of some key observations. The facts as presented are also possibly limited by the nature of the research methods employed, a limited array of reports and inconsistent terminology

and varied cohorts studied. The term antidepressant was applied to collectively represent one or more prescriptive pharmacologic based interventions designed to alleviate symptoms of depression or prevent depression from reoccurring. No effort was made to identify the different classifications or types of antidepressant agent employed in the various study contexts, nor the duration for which these chemicals were applied, nor their dosage, which can all be quite diverse in nature. The term depression was used to encompass all forms of clinical depression, as well as depressive symptoms, which can range from mild to severe. The term hip fracture was applied to represent the different categories of this injury, rather than attempts to categorize and discriminate lesion site. This was owing to report limitations, and a failure of most studies to assess or conduct one or more sub-group analyses in any of the aforementioned spheres.

Results

General observations

As of September 20, 2022, the data examined and covering all years with no restrictions a PUBMED based search, which presumably houses the majority of all published studies, revealed only a comparatively small number of relevant studies as cited between 1972 and 2022, that is, 155 citations containing the key words: hip fracture and antidepressants. If compared to the broader topic of hip fracture with 43, 918 postings, and themes cited in related research, such as hip fracture and depression with 486 postings, cognitive hip fracture risk factors with 620 postings, and hip fractures and drugs with 1283 postings, this topic has arguably received quite limited attention to date in our view and was evident even when all the data bases cited above were carefully searched.

This is despite some evidence that there is a highly probable role for adverse drug reactions in the context of efforts to pinpoint significant hip fracture risk factors among the older adult population, in general and among those with depressive symptoms who may be using antidepressant medication, as well as those taking antidepressants for no psychiatric reasons. Indeed, evidence does show that that various antidepressant agents used alone or in combination, with other drugs whether for alleviating depressive symptoms or for other reasons, may well depress vital or timely central nervous system functions, as well as impairing sleep processes that may heighten hip fracture injury risk, even while their use implies neurotransmitters in the brain may be more balanced rather than not [13]. Additional noteworthy side effects are blurred vision, confusion, and dizziness, among other adverse general health concerns that could all be expected to heighten the risk for falling, the major antecedent of hip fractures [21] along with a probable increased risk of subsequent fractures in respect to usage of antidepressants, including past, as well as recent usage at one year following an incident osteoporotic fracture in adults 65 years of age or older [22].

However, despite quite a substantive body of cautionary data, and very little abatement of hip fracture worldwide prevalence and its disabling features, it seems very few intervention studies addressing depression and its possible prevention among vulnerable older adults at risk for hip fracture prevail, and that are approached through non pharmacologic modes of mitigation. The issue of the carry over effect of antidepressant usage post hip fracture, has not focused on the impact of past usage or continued antidepressant usage on possible prior or subsequent hip fractures, that remain quite common in hip fracture surgical cases [23].

Research observations

As outlined in 2022, a recent meta-analysis and systematic review of selected antidepressant studies relevant to hip fracture occurrences showed a fairly consistent risk of both hip and possibly vertebral fractures among those who used the drugs examined. Newer drugs were not examined, the role of multiple medications was not specifically examined and the possible evidence supporting a need for improved post operative preventive strategies against emergent depression in survivors was stressed, but not primary prevention [24]. The authors did suggest though that clinicians should clearly remain mindful in terms of administering these drugs, but no direct indications for exploring what other options might prevail, who should definitely not receive these drugs, and whether type of depression and user health and age is of relevance or not. It is also possible in a secondary analysis to omit capturing those who suffered premature

mortality post hip fracture that was linked to their depressed state, while failing to account for antidepressant exposure misclassification [25], survivor bias [24], cognitive impairment levels [26] and other possible confounding factors [27].

Other data show that one group in a well-established clinical center found no changes in the rates of usage of benzodiazepines and/or z-hypnotics usage over a 12 year period even though the risks attached to these drugs were quite well known at baseline. It thus appeared that although evidence based practice is often employed to discredit apparently potentially understudied useful health recommendations, the early research made no impact on the findings of this present study where all studied drugs and their concomitant use increased the risk for fractures. An ensuing set of recommendation pointed to the importance therefore of more careful usage and recommendations for potentially risky medications and their appropriateness for the elderly, along with more regular assessments to evaluate any untoward hip fracture risk. Unaddressed however, was the need to consider other forms of palliation or who should be prioritized in this regard [28].

To add to the confusing conclusions that yet prevail in this realm, a retrospective study of a Korean cohort of 15576 cases studied recently and published in 2022 concluded there is in fact no association between the uses of antidepressants and benzodiazepines after hip fracture and mortality risk in elderly patients who received psychiatric medication before hip fracture. However, the authors Yoo, *et al.* [29] found the use of these medications was associated with increased all-cause mortality risk in patients who had no history of psychiatric medication use before sustaining a hip fracture. Patients studied were those who had undergone surgical treatment for an index hip fracture and were over 65 years old and classified into Past, Current, and Non-users for each period according to their history of antidepressants or benzodiazepines drug usage. In the subgroup analysis where patients were classified by presence of past history for psychiatric medication. current uses of antidepressants or never-users, there was an increase in the adjusted hazard for death in the user groups compared to the non-users. Indeed, of 10 drugs commonly used by older adults, antidepressants reportedly do pose the greatest risk [30]. This further study conducted in Sweden by Leavy, *et al.* [30] was one that had examined a source population of a Swedish county, aged 50 years or higher (n = 117,494) and included all incident hip fractures during a one year period (n = 477). The outcome was hospitalization for hip fracture during the periods of 2009-2010. Exposures included: the prevalence of (1) inpatient diseases and (2) prescribed drugs dispensed in 2010 or the year prior to fracture. How these findings would compare in 2022 or in other venues remains unclear, however.

Zakarias, *et al.* [31] who investigated the association of benzodiazepines and antidepressants on the risk of hospitalization and hip fracture in patients with dementia found the risk of all-cause hospitalization during 180-days follow-up was significantly increased by 55% when antipsychotic usage was combined with benzodiazepine usage and compared to antipsychotic usage alone. While the association between the combination of antipsychotics and benzodiazepines with the risk of hip fracture did not reach statistical significance, it was concluded that the increased risk of all-cause hospitalization and hip fracture may indicate increased drug-related adverse events. Nyugen, *et al.* [13] further stress that there are many biologically plausible explanations as to why antidepressant or co-dispensed antidepressants can heighten hip fracture risk, including the fact they can impair psychomotor and cognitive function, and/or sleep status. Thus, even though not all researchers agree, it appears that when antidepressant drugs are indicated among older adults, careful and regular monitoring is needed to assess their responses to this type of treatment. Alongside more careful usage, insightful research to eliminate confounding factors such as the role of chance, reverse causation, and/or confounding by indication as discussed by Nyugen, *et al.* [13] is strongly indicated as well.

Brännström, *et al.* [32] who investigated the association between antidepressant drug treatment and hip fracture starting one year before the initiation of treatment using a nationwide cohort of 204 072 individuals listed in the Prescribed Drugs Register of Sweden's National Board of Health and Welfare and who were aged 65 years or older who were prescribed antidepressants between July 1, 2006 and December 31, 2011 found antidepressant users sustained more than twice as many hip fractures than did nonusers. in the year before and year after the initiation of therapy (2.8% vs 1.1% and 3.5% vs 1.3%, respectively). In adjusted analyses, the odds ratios were highest for the associations between antidepressant use and hip fracture 16 to 30 days before the prescription was filled, rather than when these were actually used. It was verified in separate analyses of age groups, and of men and women and of individual antidepressant types that

the highest odds ratios were seen 16 to 30 days before treatment initiation, and that no clear dose-response relationship was evidenced. The authors concluded that their findings raise questions about the association between antidepressant usage and hip fracture risk that should be studied further.

In another comparable study, Gorgas, *et al.* [33] who strove to describe the association between exposure to different antidepressant drugs and a subsequent hip fracture among an older Mediterranean population of non-traumatic hip fracture cases aged 50 - 95 years admitted to the emergency room during 2010, results of 134 cases and 544 controls showed that the adjusted odds ratio for hip fracture associated with exposure to any antidepressants was 2.42. For those categorized as receiving selective serotonin reuptake inhibitors it was 3.52. For non-selective monoamine reuptake inhibitors the odds ratio was 1.07 and for other antidepressants it was 0.82. Sertraline with an odds ratio of 3.88 was the only active drug with a significant adjusted risk. When only exposures greater than six months duration were considered, significant risks were found to prevail as regards the use of selective serotonin inhibitors known as SSRIs. It was concluded there is a significantly elevated hip fracture risk in those taking SSRIs serotonin inhibitors, but not other types of antidepressants.

A meta-analysis of 23 studies conducted by Wu, *et al.* [34] and where hazard ratios were used as the outcome, the aggregated data of nine studies of a total of 309,862 cases revealed depression alone was associated with a 26% increase in fracture risk. The seven studies that reported risk ratios as the outcome for 64,975 cases specifically suggested that depression was associated with a 39% increase in fracture risk. Among eight studies that reported hip bone mineral density as an outcome (sample size, 15,442), the researchers found that depression was indeed associated with a reduced mean annual bone loss rate of 0.35%. This increased risk of fracture and bone loss associated with depression was consistent in all meta-analysis, as well as those having modified inclusion criteria and when performing different subgroup analyses. Unfortunately, despite finding no significant publication bias in the reviewed reports, the role of antidepressants per se was not examined. Tamblyn, *et al.* [35] who applied a common protocol to cohorts of older antidepressant users in multiple jurisdictions to estimate fracture risk associated with different antidepressant classes, drugs, doses, and potential treatment indications found an increased fracture risk in some, but not all jurisdictions. The authors concluded however, that even though antidepressants are used to alleviate non-depressive symptoms in some cases, such as pain, fracture risk in all classes is higher when prescribed for depression than for chronic pain. In another report, McArthur, *et al.* [36] found that among the key risk factors unique to non-hip fractures as compared with hip fractures was having a history of psychotropic medication usage.

Iaboni and Maust [37] note furthermore that in the case of benzodiazepines for alleviating mental distress, and where the primary concern for older adults has been their increased risk of falls-related injuries, all benzodiazepines, even those that are short-acting appear to heighten an unanticipated falls risk. Macri, *et al.* [38] support this view based on the observation that those adults who started taking antidepressants had a significantly increased risk of falls and fall-related injuries among long-term care residents that tended to prevail regardless of patient subgroup and antidepressant class. The parallel observation that the presence of depression appears to impact an increased risk for falls [39], plus low bone mineral density at common fracture sites, which can be exacerbated by antidepressant medication [23], clearly speaks to a possible further need to prevent, rather than mitigate, depression via potentially risky medications in vulnerable older adults [40]. This may be very important to consider given that plasma analysis has shown the use of antidepressants and benzodiazepines - a specific class of psychoactive depressant drugs - when assayed among hip fracture cases is observed to be present more prevalently than respective prescription frequencies that occur in the general older population. Moreover, this association may be underestimated due to a lack of consistency between recorded and actual use of psychotropic fall-risk drugs at the time of hospital admission of the hip fracture patient. Thus, the risk of using antidepressants may not be acknowledged or accurately evaluated in all cases [41], and hence its associated relevance is underestimated, even though Cheng, *et al.* [2] found the use of antidepressants to have no adverse effect on hip fracture risk in their Taiwanese population, where depression alone was strongly implicated. Other data reveal that for all examined antidepressants, the odds were higher for other fractures than for hip-pelvis fractures [42], even though their actions may contribute to excess falls risk consequent to their sedative and orthostatic hypotension properties [43].

But what the causes of depression are among the older vulnerable adult, what explains the mechanism of depression associated hip fractures in the presence as well as the absence of antidepressant drugs, and whether depression as examined in most reports refers to symptomatic, severe, or mild depression, a diagnosis that was validated clinically uniformly was uncertain at best. In addition, in many instances actual medication adherence and dosages, exposure misclassification, as well as unknown medication variations, the importance of identifying the longevity of using antidepressants, extent of falls risk or prior falls, and other factors remains challenging to unravel, and needs to be carefully studied as pointed out almost 20 years ago [44]. Subjects studied in the few currently available reports that show negligible antidepressant effects on hip fracture risk may be confounded if indeed subjects studied were receiving multi component therapies including counseling or were non adherent prescription drug users. Subjects studied to date have also been largely those who survived their hip fracture injury and surgery, and were treated in major centers, and may thus have been healthier and had better outcome options than those who had already died post hip fracture, but were antidepressant users, but who were not treated in an advanced care setting.

Another area of concern not yet addressed is how post COVID symptoms such as cognitive dysfunction and fatigue will impact overall health, bone health, feelings of depression and antidepressant needs. In the meantime, Mazza, *et al.* [45] imply that based on current insights on inflammation in psychiatry and the present observation of worse inflammation leading to worse depression, it appears reasonable to recommend periodic assessments of any ensuing psychopathology among COVID-19 survivors and how to treat this, while avoiding hip fracture injury risk that might be heightened by poorly considered antidepressant medication usage. According to Ettman, *et al.* [46] post-COVID-19 plans should account for the probable increase in mental illness to come, particularly among at-risk populations, and added to this are probable injuries due to a combination of pharmacologic interventions.

In sum, many conflicting conclusions, gaps in the research, design issues, and challenges in separating current medication practices and modes of delivery from those embedded in the past literature preclude any definitive conclusion as to whether there is a heightened risk of sustaining one or more hip fractures among antidepressant users, and if so, in what respect. Caution is advised however, by multiple authors as regards the unrestricted usage of antidepressants among older adults, and against assumptions that the evidence base is sufficient to guide safe practices.

Discussion

In addition to age, a variety of age-related physiological changes, and other factors such as low levels of physical activity participation, poor nutrition practices and some forms of medication may impact two crucial determinants of hip fracture, namely, femoral bone strength and the propensity to falls. As well, the decline in muscle function with aging, along with cognitive, visual and neural reflex response declines that may be impacted by medications such as antidepressants, is likely to impact the propensity of older adults towards hip fracture injuries, which remain highly devastating injuries with a high premature mortality rate despite years of study. In this regard, medications to combat one or more health associated issues that commonly predominate in older adults, where administered in high risk older adults, may well explain why hip fracture incidence rates remain substantive, despite much research and considerable advancements in medical, surgical and preventive approaches among those with a depressive history.

In a search for more practical approaches to avert preventable hip fractures, this mini review elected to focus on whether a variety of commonly used antidepressant medications, often employed by older adults, is a noteworthy under represented risk factor for hip fractures in those older than 65 years of age worthy of more focused attention. Yet, despite over 50 years of research in this realm, even though the weight of the evidence points to possible mediating or moderating hip fracture risk, it remains impossible to definitely attribute all hip fractures among those who use antidepressants to this factor and their weight must remain unclear in this respect as discussed by De Filippis, *et al* [26]. Indeed even if a fair number of past observations imply a role for higher than expected relative risk rates of antidepressants in certain hip fracture cases, not all data are current, and most do not include all available antidepressants that are variously

employed. As put forth by Iaboni and Maust [37], even though each of these new antidepressant drug classes have offered significant treatment benefits-typically because of fewer adverse effects-the recognized risks for each has steadily grown the longer the newer class is used. The mediating role of overall health status, total numbers of medications used, age and other factors, the sample studied, and mode of inquiry among other factors [47], are not sufficiently well articulated in this regard however, and need to be carefully studied.

Nonetheless, it seems safe to say that a sizeable number of current researchers do agree that regardless of a possible fracture risk, caution is advised when antidepressant remedies are recommended among older adults at risk for falling and possible hip fractures. The impact of antidepressant medication may also be underestimated if indeed its influence is more immediate rather than delayed [48] and may be overlooked if other fall risk-increasing drugs such as opioids, dopaminergic agents, anxiolytics and hypnotics/sedatives are being taken without due caution [26,49].

Bruun., *et al.* [50] confirm the prevalence of antidepressant usage may indeed be deemed to be quite high among a fair percentage of older hip fracture patients compared with the general population, especially in the context of frailty, comorbidity, and polypharmacy. Other data reveal that the use of multiple medications, including antidepressants could interact to induce falls as well as cognitive lapses [50]. Accordingly Brännström., *et al.* [32] do show fully twice as many hip fractures tend to occur among those older adults who have used antidepressants compared to nonusers in the year before (2.8% vs. 1.1%) and the year after (3.5% vs. 1.3%) initiation of treatment that cannot be readily ignored even though the adjusted analyses showed the odds ratios for association between antidepressant use and hip fracture was highest 16 to 30 days before the prescription was filled.

Yang., *et al.* [51] propose that older adults do thus need to be made aware of the possible risks of employing benzodiazepines alongside antidepressants, and other medications that may heighten their fracture risk, especially following benzodiazepines initiation. Those older adults who are suffering unremitting depression, osteoporosis and/or other comorbid illnesses might be preferentially targeted in this regard.

In addition, to reduce any possible changes of falling, periodic screenings and evaluations may prove helpful, as may any opportunity to uncover the prevailing source of any persistent depressive state and its potential for mitigation by non-pharmacologic strategies. Educating caregivers accordingly, along with efforts to encourage the creation of a safe supportive environment that reduces the presence of excess fears, distress, and anxiety, and one that promotes healthy living from a young age, is also clearly warranted. Torvinen., *et al.* [52] also advocate for periodic screening and re evaluations based on their findings that antidepressants as a class of drugs did tend to increase the risk of fracturing a hip among those older adults living in the community, an association that persisted even after adjusting for use of other medications known to increase falls and hip fracture risk. It was consequently suggested that vulnerable adults who are reliant on antidepressants should have their antidepressant prescriptions reviewed regularly as to whether they still need that drug, or that dose of the drug, or another. Moreover, whether their antidepressant burden was reduced over time was important to assess.

In the interim, considerable evidence also shows antidepressants may not be safe to recommend for all older adults with depressive symptoms. In addition, their use in the non-depressed older adult may be overlooked as impacting hip fracture risk, for example if being used for the treatment of chronic pain and behavioral and psychological symptoms of dementia, including insomnia, anxiety and agitation. In addition, Walkerly., *et al.* [53] warn that peripheral serotonin applications and their probable negative effects on bone may outweigh the benefits caused by any antidepressant enhancement of central serotonin neurotransmission, hence must be recommended with all due caution.

In short, despite their limitations, and a need for continued research, a fair proportion of available current research findings do tend to suggest that unremitting depression and the persistence of depression-related mechanisms in remitted depression may heighten the risk of fracturing a hip among antidepressant-treated older adults, even if other factors are implicated [8]. However, since this association

is not uniformly supported by others in all cases, readers and clinicians who are evaluating the findings of prevailing studies that relate exposures to antidepressants to hip fracture occurrences must clearly consider how the investigators addressed confounding factors, and draw conclusions not merely on the findings, but also on multiple issues related to their research designs.

At the same time, as per Mortensson, *et al.* [54] there are indeed several medications quite strongly associated with sustaining a fragility hip fracture, hence, medical interventions for the older adult should take into account their possible adverse impacts on bone status and this possible attribute in fostering fracture risk. Conservative approaches including exercise for alleviating depression among older adults that might be helpful and that are not truly represented in the literature need to be studied in well controlled comparative studies, along with cognitive behavioral and counseling approaches, plus sleep therapy [55]. More emphasis on identifying minimal doses that can be used safely to alleviate depression are indicated, as well as comprehensive efforts to catalyze changes in the care of older vulnerable adults, including the promotion of healthy behaviors and lifestyles, the provision of careful periodic bone, mental health and general health assessments and follow up, evaluations of any advocated antidepressant treatment approaches, multidisciplinary and holistic planning approaches, plus closer provider-older adult partnerships focused on falls prevention, sleep hygiene, and good nutrition, appear warranted as well [56].

Alternately, if no further progress is forthcoming in this regard, it seems fair to say, a modest proportion of older adults who are using antidepressants may incur preventable hip fracture injuries, and a life of extreme suffering if they survive. To this end, even if this current issue is a highly complex one, it does seem plausible to suggest that more insightful dedicated collaborative attention by primary care providers, psychiatrists, cardiologists, and nurses, alongside pharmacists and social workers may be expected to make a sound contribution here if they so desire. Indeed, all are urged to work collectively with their older at risk clients and families, policy makers, and retirement and other health organizations to mitigate or avert the onset or perpetuation of depressive symptoms where possible among those 65 years of age or older, and advise them thoughtfully on the use of antidepressant drugs and their multiple side effects that may alleviate depression, but may still prove highly injurious [21,57]. To reduce the projected hip fracture burden, what the roots of the issue are-as regards depression in older adults, and how this prioritizes a role for antidepressants in the face of a probable falls, frailty, multiple comorbid health conditions, and fracture risk [58-60], as well as the possible effective counter role of dedicated efforts to empower and educate vulnerable older adults should arguably be more formidably addressed in carefully construed research designs sooner rather than later and to rule out current multiple confounders, discrepancies, and competing conclusions.

Conclusion

This mini review, while not all inclusive, appears to support the view that:

1. Older adults at risk for depression are not receiving basic interventions that may be risk free and long lasting, and safer for purposes of overall cognitive health and bone health.
2. Reliance on one or more forms of antidepressants, is likely to increase social as well as individual costs, even if care is taken to avert their known impacts on hip fracture injuries.
3. Efforts to broaden and expand upon the scope of understandings regarding the mechanisms of depression in older vulnerable adults and how to mitigate this safely and effectively are urgently needed.

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