Factors Associated with History of Hip Fracture in the Health and Retirement Study

By

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THESIS

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LIST OF ABBREVIATIONS

HRS	Health and Retirement Study
BMD	Bone Mineral Density
OR	Odds Ratio
MrOS	Osteoporotic Fractures in Men Study
DOES	Dubbo Osteoporosis Epidemiology Study
IADL	Instrumental Activities of Daily Living
ADL	Activities of Daily Living
BADLs	Basic Activities of Daily Living
BMI	Body Mass Index
WHO	World Health Organization
AHEAD	Assets and Health Dynamics Among the Oldest Old
CHS	Cardiovascular Health Study
IRB	Institutional Review Board
NEDICES	Neurological Disorders in Central Spain Study
DM	Diabetes Mellitus
H-EPESE	Hispanic Established Populations for the Epidemiologic Study of the Elderly

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ABSTRACT

Factors Associated with History of Hip Fracture in the Health and Retirement Study

Background: Amongst all osteoporotic fractures, hip fractures are the most devastating because they are associated with considerable disability, loss of independence, diminished quality of life, and reduced survival. Epidemiological associations have been observed between hip fracture and demographic, lifestyle, and physical function variables. This cross-sectional study was designed to 1) examine prevalence of self-reported history of hip fracture and 2) evaluate factors associated with self-reported history of hip fracture in United States community-dwelling older adults.

Methods: This is a cross-sectional analysis of Health and Retirement Study (HRS) participants who were 65 years or older in the 2004 wave who provided a response to "Have you fractured your hip since we talked (in the previous wave)?" The age-standardized prevalence of history of self-reported hip fracture was determined using 2000 US Census data as a reference population. Baseline characteristics of participants with a history of self-reported hip fracture and participants without a self-reported history of hip fracture were compared using the Student's t-tests for continuous variables and the chi-square test for categorical variables. Logistic regression models were constructed to identify the crude and age-adjusted odds ratios (ORs) of hip fracture. Multivariate models were built using manual backward selection. Variables included in the final models were gender, age, body mass index (BMI), index of Activities of Daily Living (ADLs), Nagi functional items, index of serious health conditions, education, alcohol consumption, and marital, smoking, and health status. An additional multivariable model included self-reported history of falls.

Results: There were 10,640 participants (4,534 men and 6,106 women), with a mean age of 75.4 years, included in analyses. At the 2004 baseline interview, 1.3% of participants (42 men and 142 women) reported a history of hip fracture in the previous two years. When participant characteristics were examined by hip fracture history, we found that those who reported a history of hip fracture were more likely to be female, 85 years or older, within the underweight and normal BMI ranges, to report a history of fall, have multiple chronic conditions, and report multiple functional limitations compared to those without a history of hip fracture. When all covariates were included in the multivariate model, history of a fall remained the factor most strongly associated with hip fracture (OR 6.35; 95% CI 3.89, 10.36). Women had 88% higher likelihood of having experienced a hip fracture than their male counterparts (OR 1.88; 95% CI 1.19, 2.95). Participants who were 85 years and older were twice as likely to have a history of hip fracture (OR 2.03; 95% CI 1.14, 3.62) than participants who were 65 to 75 years old. A reduced risk of reported hip fracture was observed in the higher BMI categories. Compared to their normal weight peers, overweight (OR 0.45; 95% CI 0.27, 0.77) and obese (OR 0.36; 95% CI 0.19, 0.70) participants were less likely to have experienced a hip fracture. Participants who had difficulty with 1-5 ADLs had a 73% higher likelihood of having experienced a hip fracture (OR 1.73; 95% CI 1.02, 2.93), while participants who had difficulty with 6 or more ADLs had a three-fold higher likelihood (OR 3.07; 95% CI 1.79, 5.26) of having experienced a hip fracture than participants with no difficulties with ADLs. When the history of a fall covariate was removed from the multivariate model, it strengthened the association between hip fracture history and gender, index of IADLs, Nagi functional items, and serious health conditions.

Conclusions: This study found hip fracture history was associated with female gender, advanced age, history of a fall, chronic health conditions and diminished physical functioning (as measured

by index of ADLs and Nagi functional limitations). From our results we suspect that chronic health conditions, Nagi functional limitations, and ADLs work as upstream mediators and may increase the likelihood of hip fracture through falls. As the mean lifespan of people increases and as more people reach advanced age, the numbers of hip fracture cases are likely to increase. Our results suggest that certain members of the population are at higher risk for hip fracture.

BACKGROUND

Hip fractures are associated with considerable disability, loss of independence, diminished quality of life, and reduced survival(1). Older adults have a 5- to 8-fold increased risk for all-cause mortality during the first 3 months after hip fracture(2). Though the excess mortality rate decreases during the next few years, it does not return to the pre-hip fracture rate(3). In addition, several studies have shown that having sustained a hip fracture is significantly associated with the risk of a subsequent fracture(4, 5). Many hip fractures require hospitalization and impose substantial economic burden upon those who incur the injury, their families, and the health-care system; the estimated per patient cost of hip fracture ranges from $19,335 to $66,000(6). Given the significant morbidity, mortality and health care costs associated with hip fractures, it is important to understand risk factors for hip fracture so that preventive measures may be developed.

Factors associated with hip fracture can be divided into three major categories: those that affect bone strength (e.g., gender(1, 7-9)), those related to falling (e.g., prior fall event(s) (10-12)), and those affecting both bone strength and falls (e.g., age(13-15), cigarette smoking(16-18), alcohol consumption(4, 13, 19, 20), Nagi functional limitations(21, 22), body mass index(1, 3, 6, 23-26), activities of daily living(22), and chronic conditions(5, 22, 27-29)). Often these risk factors interact and overlap. Hip fracture associations will be discussed in the following order: age, gender, body mass index (BMI), history of falls, alcohol and tobacco consumption, chronic health conditions, Nagi functional limitations, and activities of daily living (ADLs).

In both men and women, hip fracture rates increased with age(13, 14). People 85 and older are 10 to 15 times more likely to sustain hip fractures than are those aged 60 to 65(15). A plausible mechanism is that as a person ages their bone density, muscle mass, and vision decreases, and coupled with slower reaction time, these factors place them at risk for falls and subsequent hip fracture.

When age is controlled for in studies examining hip fracture relationships, it was consistently found that women tend to experience more hip fracture events than men(1, 7-9). Women lose bone density at a faster rate than men. In women, estrogen levels tend to drop during menopause and accelerate bone loss, which in turn increases the risk of hip fractures. The interaction of age and gender also influences the risk of hip fracture. The Dubbo Osteoporosis Epidemiology Study (DOES), a longitudinal population-based study of fracture incidence, revealed that the absolute number of fractures is increased with age in women(8). In men, however, the absolute number of hip fractures peaked at 80–84 years of age and then decreased

Relative to normal BMI, low BMI increases hip fracture risk. The well-established knowledge is that individuals with lower BMIs are more likely to experience a hip fracture than those with higher BMIs(1, 3, 23). In a meta-analysis, De Laet and colleagues found that when compared with a BMI in the overweight range, a BMI in the underweight range was associated with a nearly 2-fold increase in risk ratio (RR 1.95; 95% CI, 1.71–2.22) for hip fracture(6). Several mechanisms have been postulated on this association between BMI and hip fracture. One hypothesis suggests that being underweight is associated with loss of bone mineral density (BMD), which in turn increases the risk of hip fracture(24). A person with low BMI (low BMI reflects low muscle mass) and those with low muscle mass may be weaker and more prone to falls, which increase the chance of hip fracture(6). Furthermore, those with low BMI potentially have less soft tissue that may protect them from impact forces when they fall, resulting in a hip fracture(30).

Studies report conflicting results on the relationship between high BMI and hip fracture. A meta-analysis conducted by De Laet and colleagues found that, after adjusting for BMD, there was a small but significant protective effect of higher BMI on hip fracture in women but not in men(6, 25). However, in a large longitudinal study of osteoporosis in women, Compston and colleagues found no protective effect of higher BMI on hip fracture risk(26). In the Osteoporotic Fractures in Men Study (MrOS), Nielson and colleagues found that obese men were actually at significantly higher risk for hip fracture than normal weight men after statistical adjustment for BMD (30).

There is strong evidence for the relationship between hip fractures and falls, and it has been reported that more than 95% of hip fractures are caused by falling (10, 11). Hip fracture acts as both a consequence of and contributor to falls. Older adults are at a higher risk for falling and subsequently fracturing their hip as they tend to be slower to react and stop a fall (12). Alternatively, after suffering from a hip fracture, an individual is more likely to have unsteady footing which results in a fall.

The hip fracture and alcohol relationship is dependent on the frequency and quantity of which alcoholic beverages are consumed. In general, compared to abstainers, moderate alcohol consumers have a lower risk of hip fracture (4, 19, 20)and heavy alcohol consumers have a higher risk of hip fracture(13, 19). In the Cardiovascular Health Study (CHS), Mukamal and colleagues found that compared with long-term abstainers, the adjusted hazard ratios for hip fracture were 0.78 (95% CI 0.61-1.00) among moderate (defined as up to 14 drinks per week) alcohol consumers(20). Wilson and colleagues, using self-report data from 2 waves of the Asset and Health Dynamics Survey (AHEAD), found that, in comparison with no alcohol intake, moderate alcohol intake (defined as 2 drinks per day) was associated with a reduced likelihood of hip fracture (OR 0.2; 95% CI=0.05, 0.76)(4). Berg and colleagues found a J-shaped relationship between alcohol consumption and hip fracture risk; compared with abstainers, moderate drinkers (0.5 to 1 drink per day) had lower hip fracture risk (relative risk of 0.80; 95% CI 0.71-0.91) and heavier drinkers (2 or more drinks per day) had higher hip fracture risk (relative risk of 1.39; 95% CI 1.08-1.79) (19) . It is conceivable that the higher fracture risk is caused by an increased risk of falling or other types of trauma while intoxicated.

Tobacco smoking increases the risk of hip fracture. Compared to those who have never smoked tobacco, those who are current smokers have an increased risk of hip fracture; and compared to current smokers, former smokers have a slight decreased risk of hip fracture (16, 17, 31). The risk of hip fracture associated with smoking decreases with a longer duration of cessation (16, 18). Furthermore, when the quantity of tobacco smoking is examined, the risk of hip fracture increases with greater tobacco consumption (18). In an analysis of a population-based case-control study from Sweden, Baron and colleagues found that current smokers (compared with non-smokers) had a higher likelihood of hip fracture (age-adjusted OR, 1.66; 95% CI, 1.41-1.95) (16) . When Cornuz and colleagues explored the smoking-hip fracture relationship in female nurses, they found the risk of hip fracture declines in former smokers; however, the benefit was not observed until 10 years after cessation(18). Bauer and colleagues, using data from ambulatory non-black women age 65 years or older, found that smokers had lower bone mass when compared with nonsmokers; therefore, placing them at risk for hip fracture(32).

Chronic health conditions (such as stroke, diabetes, hypertension, and rheumatoid arthritis) increase the risk for hip fracture. Studies examining the relationship between diabetes and hip fracture have found that adults with type 2 diabetes have approximately 40–70% increased hip fracture risk compared to adults without diabetes(5). A possible explanation for this is that diabetes-related visual and neurologic impairments could affect an individual's risk for falling and subsequently put them at risk for a hip fracture(27). Additionally, stroke is a well-documented risk factor for hip fracture as there is an increased risk of fall following a stroke (especially because of hemiplegia), and stroke-related immobility induces sarcopenia and bone loss(22). Several studies have found that the patients have an increased risk of breaking a hip when of starting blood pressure medication(33, 34). It is proposed that side effects of antihypertensive treatment, which include dizziness and fainting, particularly upon standing, can lead to falls and subsequent hip fracture. Furthermore, in a population based case-control study, Copper and colleagues found hip fracture risk approximately doubled amongst patients with rheumatoid arthritis. Among rheumatoid arthritis patients, the increased risk of hip fracture appears to be attributable to the functional impairment associated with the disease(28).

Individuals who require greater assistance with everyday tasks or those with increased functional limitations are at an increased risk for hip fracture(21). Espino and colleagues examined the prevalence, incidence, and risk factors for hip fracture in community-dwelling, Mexican American older adults and found that women who had more initial impairment in their activities of daily living (ADLs) at baseline were at a greater risk for hip fracture. In addition, having more functional limitations may lead to problems of maintaining balance, which, in turn, may result in falls and hip fractures. ADL limitations may also affect one's participation in weight-bearing physical activity, which may result in decreased bone mass, thus increasing fracture risk. Furthermore, a study of older Japanese adults found that respondents with hip fracture reported more functional limitations, such as difficulty bending their knee (45% vs. 24%), and higher mean number of difficulty with IADLs (1.0 vs. 0.4) compared with those without(22). Not being able to bend the knee comfortably could result in instability of posture that may lead to falls(22).

In summary, factors that increase the risk of hip fracture include advanced age, female gender, fall history, current cigarette smoking status, heavy alcohol consumption, chronic health conditions, and functional limitations. The relationship between high BMI and hip fracture was inconsistently reported in the literature, whereas, low BMI was found to be inversely associated with hip fracture.

The magnitude of the impact of hip fracture on public health is likely to increase as the number and relative proportion of elderly people in the population continues to rise. It is estimated that about 20% of individuals who fracture their hip die within a year and, of the survivors, many never regain their pre-fracture level of physical function (28, 35). Due to how severely a hip fracture event can affect an older adult, it is imperative to examine all independent factors so that preventive-screening measures can be implemented. This study analyzes self-reported hip fracture prevalence in the 2004 wave of the Health and Retirement Study. Our study will contribute to the existing knowledge of hip fracture risk factors associated with self-reported hip fracture in a nationally representative sample of older adults in the United States.

METHODS

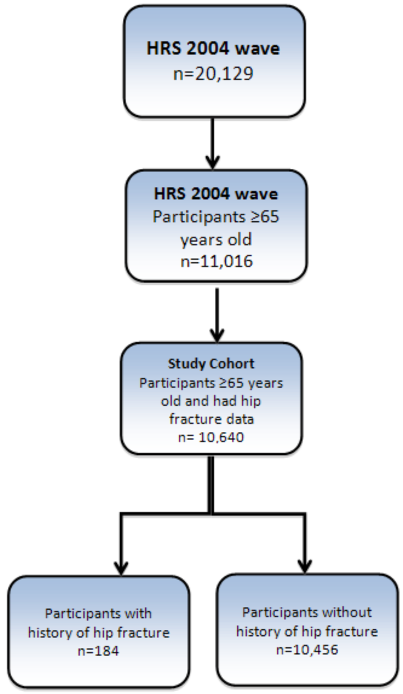
Study design and HRS population

The Health and Retirement Study (HRS) is a nationally representative, longitudinal survey designed to study health, economic, and family transitions of older adults. The study population consists of non-institutionalized adults living in the contiguous US, aged 50 years and older. The HRS is supported by the National Institute on Aging and is administered and conducted, every two years, by the Institute for Social Research at the University of Michigan. The full description of the HRS has been published elsewhere(36).

The HRS core survey is conducted with living respondents, which includes a survey of self-respondents, as well as proxy respondents (when a living respondent is not able to participate due to cognitive limitations, institutionalization, or for other reasons). Once an HRS respondent has died, an “exit” interview is conducted with a proxy respondent.

The HRS 2004 interview period was from March 2004 to February 2005 at which point a total of 20,129 participants were enrolled in the HRS 2004 wave(37). Of the 20,129 respondents, this cross-sectional analysis consisted of 10,640 participants who met the criteria for selection into the analytic cohort. Subjects in the analytic cohort had to be 65 years or older at the time the HRS 2004 wave was conducted and had to provide a response to “Have you fractured your hip since we talked in the previous wave?” Participants who did not answer this question were excluded from the study (refer to Figure 1). Participants included in the analytic cohort tend to be older, had more fall events, and were in poorer health (more chronic health conditions, functional limitations and difficulties with ADLs) than those not included in the analytic cohort ($p<0.001$).

Figure 1. Flowchart of Study Cohort formation



Weighting Methodology

Since the Health and Retirement Study uses complex sample designs involving stratification, multi-stage sampling, and unequal sampling rates, weights are needed in the analysis to compensate for unequal sampling and adjustments for non-response(38). HRS used oversampling to increase numbers of African Americans, Hispanics, and Floridian households. The complex sample design was taken into account via the application of survey weights for the 2004 study wave. Where applicable, survey weights were applied in examining baseline characteristics (counts were unweighted and the means and standard errors were weighted), bivariate analyses, and multiple logistic regression analyses.

Study Measures

History of hip fracture was the outcome variable of interest. History of hip fracture was examined as a dichotomous (yes/no) variable. Respondents were asked, "Have you fractured your hip since we talked in the previous wave?"

Exposure variables examined in this study include: age, gender, race, education, and marital status; alcohol consumption and smoking status; and index of Activities of Daily Living, Nagi functional items, BMI, self-reported health status, index of serious health conditions, and history of a fall.

Gender was dichotomized into male and female. Marital status was categorized as unmarried and married or partnered. Education was categorized into some high school or less, completed high school, and any college degree. Race was initially categorized as white, black, Hispanic, and other; however, due to an insufficient number of black, Hispanic, and other participants with a history of self-reported hip fracture (refer to Appendix I.), race was re-categorized as white and 'other' for use in analyses.

Alcohol consumption was categorized into abstainer, moderate drinker, and heavy drinker groups. Those who consumed 0 drinks were labeled as abstainers. Those who consumed 1-2 drinks per day were labeled as moderate drinkers, and those who consumed 3+ drinks per day were labeled as heavy drinkers. Cigarette smoking status was divided into never smoked, former smoker, and current smoker categories.

In the early 1960's Saad Nagi described the first model for the disablement process, which distinguished between 4 distinct phenomena: active pathology, impairment, functional limitations, and disability(39). At the level of the individual, Nagi used the term functional limitations to represent restrictions in the performance of the person (40). Functional limitations are the most direct way that disease and impairments contribute to functional disability because they involve tasks necessary for completion of important personal and social functions. In our study, the Index of Nagi functional items were used to assess the participants' ability to perform the following physical tasks: walking several blocks, walking one block, sitting for 2 hours, getting up from a chair after sitting long periods, climbing several flights of stairs without resting, stooping/kneeling/crouching, pulling/pushing large objects, lifting/carrying weights over 10lbs, and picking up a dime from a table. The index of Nagi functional items were additively measured (one point for each functional limitation) and ranged from no functional limitation (score of 0) to limited with all functional items (score of 9). The Nagi functional items were then categorized as no functional limitations, limitations with 1-4 items, and limitations with 5 or more items categories.

The most often used measure of functional ability, the Katz Activities of Daily Living Scale, was used to measure a set of basic, everyday tasks, performance of which is required for personal self-care and independent living (41). The Katz ADL scale, also referred to as the Basic Activities of Daily Living (BADLs), measure a person's ability to get dressed, walk without equipment, bathe, eat, use the toilet, and get in/out of bed without the assistance of others. Because BADLs do not measure the full range of activities necessary for independent living in the community, the Lawton Instrumental Activities of Daily Living (IADLs) (42) was used to partly fill the gap in disability classification. The IADLs capture a range of activities that are more complex than those needed for the BADLs, including preparing meals, shopping for groceries, making phone calls, taking medication, and managing money. Measures of functional disability typically contain items that reflect limitations in performing BADLs and IADLs, therefore, we combined the index of BADLs and IADLs together in the Activities of Daily Living (ADL) scale to better assess functional ability. The index of ADLs was additively measured (one point for difficulty with one ADL) and ranged from no difficulty with ADLs (score of 0) to difficulty with all ADLs (score of 11). The index of ADLs was categorized into no difficulty, difficulty with 1-5, and difficulty with 6 or more ADLs groups.

History of a fall was dichotomized as yes or no. BMI was categorized as underweight, normal, overweight, and obese categories. BMI was calculated by dividing weight (kg) by height-squared (m^2) and was classified based on the World Health Organization's International Classification of Adult BMIs(43). Age was grouped by 10-year increments: 65-74, 75-84, and ≥85 years. Self-reported health status was categorized as excellent/very good, good, fair, and poor. The index of serious health conditions quantified the number of chronic health conditions a participant had. Chronic health conditions include high blood pressure, arthritis, stroke, heart disease, cancer and diabetes. The index of serious health conditions was additively measured and ranged from no chronic conditions (score of 0) to have all the chronic conditions (score of 6). Due to insufficient sample size of hip fracture cases with 3-6 combined chronic conditions, the index of chronic conditions was divided into none, 1-2, and 3+ chronic condition categories. Refer to Appendix I for more information on how the covariates were constructed.

Demographic variables used in this study were extracted from the HRS 2010 Tracker file, while physical function and lifestyle variables were extracted from the HRS 2004 wave. Height and weight variables were extracted from HRS 1992, 1993, 1998, and 2004 waves as these data on these variables were collected at the participants' baseline interview. Refer to Appendix II for more information on how the analytic dataset was constructed.

Data Collection and Management

The HRS conducted most interviews by telephone, with the exception of face-to-face interviews when respondents who have health limitations that would make an hour-plus session on the telephone difficult or impossible or when there was no telephone in the household.

Meticulous attention was paid to the standardization of the questionnaire and training of the HRS interviewers. While HRS staff makes every effort to ensure the accuracy of the data and documentation, tasks related to cleaning and editing of HRS data files are the responsibility of those using the data. Refer to Appendices I and II for how covariates were extracted and coded.

To ensure privacy and confidentiality of all HRS participants, study participants' names, addresses, and contact information were maintained in a secure control file. It was a requirement that all personnel and affiliates with access to identifying information must sign a pledge of confidentiality. The survey data was only released to the research community after undergoing a rigorous process to remove or mask any identifying information. Furthermore, prior to release, the data files were subject to final review and approval by the HRS Data Release Protocol Committee(44). In order to obtain publicly available HRS data, researchers must complete the registration process (username and password assigned) and must login to download any data files.

The HRS was approved by the Behavioral Sciences Committee Institutional Review Board (IRB) at the University of Michigan and the National Institute on Aging. The IRB of Oregon Health and Science University exempted this project from review as the data used in this study was publicly available and contained no unique identifiers, thus ensuring respondent anonymity.

Statistical Analysis

To estimate the burden of hip fracture in the analytic cohort, the prevalence of self-reported hip fracture history was examined. Prevalence measures the proportion of a population found to have a condition at a designated time; period prevalence measures the proportion of a population found to have a condition at a period in time, whereas, point prevalence measures the proportion of a population found to have a condition at a point in time. Prevalence is estimated by comparing the number of people found to have the condition with the total number of people studied, and is often expressed as a percentage. Since we examined hip fracture in the 2004 HRS wave, which expands 2 years, the period prevalence was calculated.

A prevalence ratio (PR) indicates how large the prevalence of an event in one group of subjects with a certain characteristic is relative to another group of subjects lacking that certain characteristic; PRs measure the risk of the disease as a probability. Prevalence ratios can be used to examine hip fracture in women compared to men. Approximately 3.4 women to 1 man have a history of self-reported hip fracture in our analytic cohort {PRwomen (142/10640= 0.0133) to PRmen (42/10640=0.0039) is 0.013:0.004}.

It is also common to use odds ratios as an effect measure in cross-sectional studies. Odds measure the probability of incurring an event to the probability of non-events. Odds ratios (OR) measures the odds that an event will occur given a particular exposure compared to the odds of the event occurring in the absence of that exposure. Odds ratios can be used to examine hip fracture in women compared to men; women have more than two times higher odds of hip fracture compared to men (OR 2.59); {Women($0.023_{\text{probability of hip fracture}}$ / (1 – 0.023)} / {Men($0.009_{\text{probability of hip fracture}}$ / (1-0.009)} = 2.59.

The estimated unweighted prevalence ratio of hip fracture in women to men was 3.4; while, the estimated unweighted odds ratio of hip fracture in women to men was 2.5. Both effect measures conclude that women have an increased odds of hip fracture compared to men.

In cross-sectional studies, both prevalence ratio (PR) and odds ratio (OR) are commonly used to measure effect size. In our study we used ORs because Stata has a method for applying survey weights using logistic regression, whereas, Stata does not have a method of estimating PRs using survey weights.

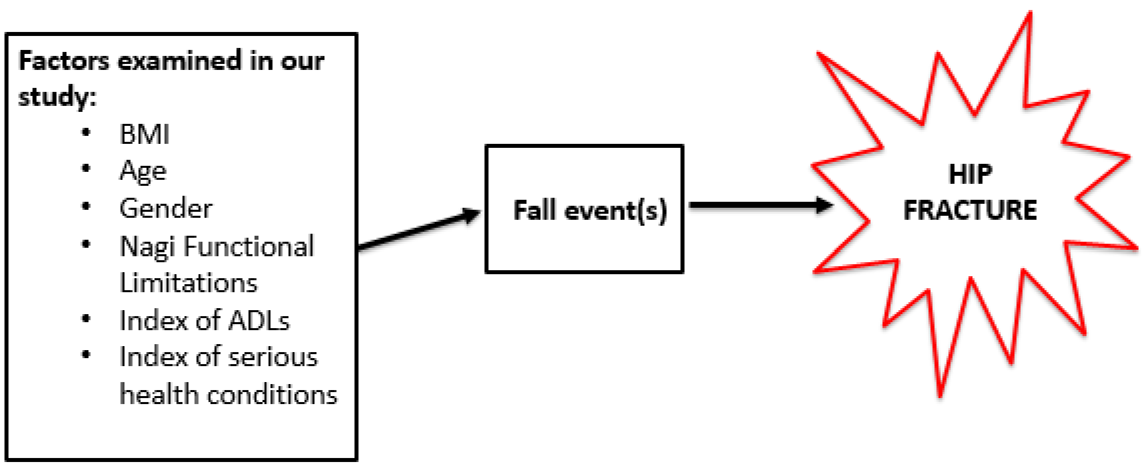
In addition, age-standardized prevalence of self-reported hip fracture history was examined because hip fracture is highly associated with old age. The 2000 US Census data was used as a reference population because it was the most recent and comparable census data available. Refer to Appendix III for more information on how age-standardized hip fracture prevalence was calculated.

Baseline characteristics of participants with a history of self-reported hip fracture and participants without a self-reported history of hip fracture were compared using the Student's t-tests for continuous variables and the chi-square test for categorical variables. Covariates tested for trend include: BMI, education, health status, smoking status, index of serious health conditions, index of ADLs, and index of Nagi functional items.

Participants included in the analytic cohort were compared to those not included in the cohort via the Student's t-tests for continuous variables and the chi-square test for categorical variables. Simple logistic regression models were constructed to identify the crude and age-adjusted odds ratios (ORs) for risk factors of hip fracture. Covariates were also tested for trend and include: BMI, education, health status, cigarette smoke, index of serious health conditions, index of ADLs, and index of Nagi functional items.

Since having experienced a fall lies on the pathway between several risk factors and hip fracture, the fall covariate was removed from the second multivariate model in order to assess potential associations with risk factors upstream of a fall event (Figure 2). Therefore, two multivariate models, (1) a model with history of a fall and (2) a model without history of a fall, were built using manual backward selection.

Figure 2. Fall as a suspected mediator of hip fracture



Manual backward selection was performed by adding all variables of interest (defined as variables with a p-value of ≤0.25 in bivariate analysis) into the first model. Variable with least significance was removed from each subsequent model until all remaining variables had a p-value of <0.05. The final models included: fall history (in model (1) only), gender, age, BMI, index of ADLs, Nagi functional items, and index of serious health conditions (in model (2) only). Refer to Appendix IV for more information on how the final multivariate models were built.

Weighted data were used for all parts of the statistical analysis. Stata 10.0 was used for all analyses (Stata Corporation, College Station, TX).

RESULTS

Analyses included 10,640 HRS participants (4,534 men and 6,106 women), with a mean age (SE) of 75.4 (0.07) years. At the 2004 baseline interview 1.3% of participants (42 men and 142 women) reported a history of hip fracture in the previous two years. The prevalence of hip fracture increased with age in women from 0.44% in participants aged 65-74 years to 0.73% in those aged 85 or above (Table 1). This trend, however, was not observed in men (0.23% and 0. 19% respectively).

Table 1. Prevalence of self-reported hip fracture history in the HRS 2004 analytic cohort

	Men			Women			Overall		
Age (years)	N = 4,534	Weighted prevalence (%[1])	Age-standardized prevalence (%[2])	N= 6,106	Weighted prevalence (%[1])	Age-standardized prevalence (%[2])	N = 10,640	Weighted Prevalence (%[1])	Age-standardized prevalence (%[2])
65-74	15	0.23	0.31	28	0.44	0.48	43	0.35	0.41
75-84	17	0.30	0.40	39	0.53	0.66	56	0.43	0.55
85 and over	10	0.19	0.25	75	0.73	0.97	85	0.50	0.73
Overall	42	0.71	1.00	142	1.70	2.10	184	1.30	1.70

1. Weighted prevalence calculated using survey weights.
2. Age-standardized prevalence calculated using 2000 US Census data as the reference population.

Overall, the weighted prevalence of hip fracture history was 1.7% in women and 0.71% in men. The age-standardized prevalence was 2.1% in women and 1.0% in men. Although women were older on average (0.73% of women vs. 0.19% of men were 85 years and over), the age difference did not explain the higher prevalence of hip fracture history in women.

When participant characteristics were examined by presence of hip fracture history (Table 2), we found that those who reported a history of hip fracture were more likely to be female, older age, within the underweight and normal BMI ranges, less educated, and not married/partnered compared to participants without a history of hip fracture. Additionally, participants with a hip fracture history were more likely to have experienced a fall in the previous two years compared to participants without a history of hip fracture. Furthermore, those with a reported history of hip fracture were more likely to report a lower health status, have chronic conditions, report functional limitations, and need help with daily tasks when compared to those without a history of hip fracture. Those with a history of hip fracture were more likely to be former cigarette smokers and less likely to drink alcoholic beverages than participants without a history of self-reported hip fracture. Race was the only variable examined that did not differ (p=0.67) between participants who had a history of hip fracture (91% in white, 9% in other) and those who did not (90% in white, 10% in other).

Table 2. Characteristics by Self-reported Hip Fracture History in the HRS 2004 Analytic Cohort (n=10640)

Characteristics	History of self-reported Hip Fracture (n=184, 1.3%[1])	No History self-reported Hip Fracture (n=10456, 98.7%[1])	P-value
Age (n, %)			
65 to 74	43 (27.5)	5533 (50.4)	
75 to 84	56 (33.4)	3513 (37.8)	<0.0001
≥85	85 (39.0)	1410 (11.8)	
Age (mean ± SE)			
	80.9± 0.81	75.3 ± 0.08	<0.0001
Gender (n, %)			
Male	42 (23.9)	4492 (43.0)	<0.0001
Female	142 (76.2)	5964 (57.0)	
Body Mass Index (n, %)			
Underweight	20 (10.4)	292 (2.6)	
Normal	114 (58.3)	3893 (38.4)	
Overweight	33 (20.6)	3960 (37.7)	<0.0001
Obese	17 (10.7)	3211 (21.3)	

BMI (mean ± SE)			
	23.6 ± 0.48	26.6 ± 0.06	<0.0001
Race (n, %)			
White	163 (91.0)	8862 (89.9)	0.6708
Other	21 (9.0)	1594 (10.1)	
Education (n, %)			
Some HS or less	75 (40.0)	3150 (27.1)	
Completed HS	58 (31.7)	3650 (36.0)	
2 yr. College Degree - Professional degree	51 (28.3)	3655 (36.8)	0.0085
Marital Status (n, %)			
Married or partnered	62 (40.7)	5945 (55.7)	0.0012
Unmarried	122 (59.3)	4511 (44.3)	
Self-reported health status in 2004 (n, %)			
Excellent/Very good	36 (17.6)	3576 (35.8)	
Good	45 (27.0)	3416 (33.5)	
Fair	51 (27.2)	2395 (21.5)	<0.0001
Poor	52 (28.2)	1060 (9.2)	
Fallen in the past two years? (n, %)			
Yes	147 (80.8)	3338 (31.6)	<0.0001
No	37 (19.2)	7097 (68.4)	
Do you smoke cigarettes? (n, %)			
Never smoked	89 (42.0)	4458 (42.8)	
Past smoker	44 (28.8)	1237 (12.0)	<0.0001
Current smoker	50 (29.2)	4705 (45.3)	
Do you ever drink alcoholic beverages? (n, %)			
Abstainer	142 (75.6)	6161 (65.4)	
Moderate Drinker	20 (15.9)	1613 (19.0)	0.02
Heavy Drinker	11 (8.46)	1265 (15.7)	
Index of serious conditions (mean ± SE)			
No chronic conditions	7 (2.0)	979 (10.4)	
1-2 chronic condition	97 (61.6)	5740 (61.3)	0.0031
3+ chronic conditions	57 (36.4)	2672 (28.3)	
Index of Activities of Daily Living (mean ± SE)			
No difficulty with ADLs	68 (46.3)	8396 (82.5)	
Difficulty with 1-5 ADLs	42 (26.4)	1322 (12.7)	<0.0001
Difficulty with 6+ ADLs	74 (27.3)	717 (4.8)	
Index of Nagi functional items (mean ± SE)			
No functional limitations	16 (9.8)	2547 (25.2)	
Functional limitations with 1-4 items	55 (34.8)	5197 (51.2)	<0.0001
Functional limitations with 5+ items	108 (55.3)	2635 (23.7)	

1. Weighted percentages
2. t-tests for difference in means and Pearson chi-square tests for differences in proportions and test for trend using testparm was calculated.

Logistic regression models were constructed to identify the crude and age-adjusted ORs for risk factors of hip fracture. Adjustment for age significantly attenuated the associations between history of hip fracture and history of a fall, gender, BMI, self-reported health status, index of serious health conditions, index of ADLs, Nagi functional items, and index of serious health conditions (Table 3). When adjusted for age, the association between hip fracture history and education, marital and smoking status, and alcohol consumption were no longer significant.

Table 3. Self-reported Hip Fracture History in HRS 2004 Analytic Cohort – Crude and Age-adjusted Odds Ratios						
Covariates	**Crude OR[1]**	**95% CI**	**P-value**	**Age-adjusted OR[2]**	**95% CI**	**P-value**
Fallen in the past two years?						
No	Referent			Referent		
Yes	9.10	(5.82, 14.22)	<0.001	7.61	(4.83, 12.00)	<0.001
Gender						
Male	Referent			Referent		
Female	2.41	(1.59, 3.65)	<0.001	2.16	(1.42, 3.27)	<0.001
Body Mass Index						
Underweight	2.66	(1.44, 4.91)	0.002	1.91	(1.01, 3.60)	0.05
Normal	Referent			Referent		
Overweight	0.36	(0.21, 0.60)	<0.001	0.43	(0.25, 0.71)	0.001
Obese	0.33	(0.18, 0.61)	<0.001	0.47	(0.25, 0.89)	0.020
Trend			<0.001			0.001
Self-reported health status in 2004						
Excellent/Very good	Referent			Referent		
Good	1.64	(0.96, 2.80)	0.071	1.47	(0.86, 2.52)	0.157
Fair	2.57	(1.51, 4.37)	0.001	2.13	(1.25, 3.65)	0.006
Poor	6.23	(3.60, 10.79)	<0.001	5.00	(2.83, 8.85)	<0.001
Trend			<0.001			0.001
Index of serious conditions						
No chronic conditions	Referent			Referent		
1-2 chronic condition	5.26	(1.86, 14.87)	0.002	4.38	(1.54, 12.44)	0.006
3+ chronic conditions	6.74	(2.35, 19.33)	<0.001	5.14	(1.79, 14.78)	0.002
Trend			0.002			0.010
Education						
Some HS or less	Referent			Referent		
Completed HS	0.60	(0.38, 0.94)	0.025	0.69	(0.44, 1.08)	0.104
2 yr College -Professional degree	0.52	(0.33, 0.81)	0.004	0.62	(0.40, 0.96)	0.034
Trend			0.0078			0.0723
Marital Status						
Unmarried	Referent			Referent		
Married or partnered	0.55	(0.38, 0.79)	0.001	0.81	(0.55, 1.02)	0.301
Do you smoke cigarettes?						
Never smoked	Referent			Referent		
Former smoker	2.45	(1.53, 3.91)	<0.001	1.45	(0.88, 2.42)	0.147
Current smoker	0.66	(0.43, 1.02)	0.059	1.04	(0.65, 1.67)	0.879
Trend			<0.001			0.350
Do you ever drink alcoholic beverages?						
Abstainer	Referent			Referent		
Moderate Drinker	0.73	(0.43, 1.23)	0.235	0.91	(0.54, 1.55)	0.740
Heavy Drinker	0.47	(0.24, 0.92)	0.027	0.56	(0.28, 1.10)	0.093
Trend			0.053			0.243
Index of Activities of Daily Living						
No difficulty with ADLs	Referent			Referent		
Difficulty with 1-5 ADLs	3.71	(2.30, 5.98)	<0.001	2.80	(1.65, 4.76)	<0.001
Difficulty with 5+ ADLs	10.05	(6.47, 15.61)	<0.001	6.34	(3.85, 10.44)	<0.001
Trend			<0.001			<0.001
Index of Nagi functional items						
No functional limitations	Referent			Referent		
Functional limitations with 1-4 items	1.74	(0.90, 3.38)	0.100	1.42	(0.73, 2.76)	0.305
Functional limitations with 5+ items	5.99	(3.13, 11.49)	<0.001	4.26	(2.15, 8.43)	<0.001
Trend			<0.001			<0.001

1. Bivariate model run with one covariate only.
2. Age-adjusted model run with continuous age variable and one covariate only.
3. Test for trend using testparm was calculated.

When all covariates were included in the multivariate logistic regression model (Table 4), fall history remained the factor most strongly associated with hip fracture (OR 6.35; 95% CI 3.89, 10.36). Women had 88% higher odds of having experienced a hip fracture than their male counterparts (OR 1.88; 95% CI 1.19, 2.95). Participants who were 85 years and older were twice as likely to have a history of hip fracture (OR 2.03; 95% CI 1.14, 3.62) than participants who were 65 to 74 years old. A protective effect was observed in the higher BMI categories. Compared to their normal weight peers, overweight (OR 0.45; 95% CI 0.27, 0.77) and obese (OR 0.36; 95% CI 0.19, 0.70) participants were less likely to have experienced a hip fracture. Participants who had difficulty with 1-5 ADLs had 73% higher odds of having experienced a hip fracture (OR 1.73; 95% CI 1.02, 2.93), while participants who had difficulty with 6 or more ADLs had three times the odds (OR 3.07; 95% CI 1.79, 5.26) of having experienced a hip fracture than participants with no difficulties with ADLs. Refer to Appendix V for more information on how this final model was built.

Table 4. Multivariate Models - odds ratios and p-values for self-reported hip fracture history						
	Age-Adjusted Bivariate Model[2]		Multivariate Model[1]		Multivariate Model without Falls[2]	
	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Fallen in the past 2 years?	7.61	(4.83, 12.00)	6.35	(3.89, 10.36)		
Gender	2.16	(1.42, 3.27)	1.88	(1.19, 2.95)	2.02	(1.23, 3.01)
Age						
65-74			Referent		Referent	
75-84			1.06	(0.62, 1.80)	1.08	(0.62, 1.87)
≥85			2.03	(1.14, 3.62)	2.03	(1.11, 3.74)
Trend				0.01		0.02
Body Mass Index						
Underweight	1.91	(1.01, 3.60)	1.53	(0.79, 2.98)	1.61	(0.81, 3.23)
Normal	Referent		Referent		Referent	
Overweight	0.43	(0.25, 0.71)	0.45	(0.27, 0.77)	0.41	(0.23, 0.73)
Obese	0.47	(0.25, 0.89)	0.36	(0.19, 0.70)	0.37	(0.18, 0.73)
Trend		<0.001		<0.001		<0.001
Index of Activities of Daily Living						
No difficulties with ADLs	Referent		Referent		Referent	
Difficulty with 1-5 ADLs	2.8	(1.65, 4.76)	1.73	(1.02, 2.93)	2.34	(1.36, 4.16)
Difficulty with 6+ ADLs	6.34	(3.85, 10.44)	3.07	(1.79, 5.26)	3.78	(2.05, 6.99)
Trend		<0.001		<0.001		<0.001
Nagi Functional Items						
No functional limitations	Referent		Referent		Referent	
Functional limitations with 1-4 items	1.42	(0.73, 2.76)	1.04	(0.51, 2.11)	1.27	(0.62, 2.59)
Functional limitations with 5+ items	4.26	(2.15, 8.43)	1.74	(0.82, 3.67)	2.75	(1.26, 5.98)
Trend		<0.001		0.05		0.03
Index of Serious Health Conditions						
No chronic conditions	Referent				Referent	
1-2 chronic conditions	4.38	(1.54, 12.44)			3.81	(1.32, 11.00)
3+ chronic conditions	5.14	(1.79, 14.78)			3.56	(1.17, 10.81)
Trend		0.01				0.05

1. Age-adjusted model run with continuous age variable and one covariate only
2. Multivariate Model includes all variables entered simultaneously. Built via Manual Backward Selection
3. Multivariate Model includes all variables entered simultaneously, excludes the fall variable. Built via Manual Backward Selection
4. Test for trend using testparm was calculated.

Because fall history lies on the pathway between several risk factors and hip fracture, the fall covariate was removed from the second multivariate model in order to assess potential associations with risk factors upstream from a fall. The removal of history of a fall from the multivariate model strengthened the association between history of hip fracture and gender, index of ADLs, and Nagi functional items (Table 4). In addition, the index of serious health conditions was significant and therefore included in this model; whereas it had been excluded based on p=0.08 in the multivariate model that included the history of a fall. Removal of the fall variable did not change the strength of association in the age categories. Refer to Appendix VI for more information on how this final model was built.

DISCUSSION

In this study of 10,640 community-dwelling older adults, we aimed to describe the prevalence of self-reported hip fracture history and to examine factors associated with self-reported hip fracture history in the analytic cohort. Because hip fracture complications can lead to chronic pain, disability, diminished quality of life, and premature death it is imperative that we make understanding risk factors a public health goal.

Prevalence. In our analytic cohort the prevalence of self-reported hip fracture history was found to be 1.3% overall, 0.71% in men and 1.7% in women. Similar studies reported slightly higher hip fracture prevalence. Guccione and colleagues reported an overall prevalence of 3.5% using data from the Framingham Study (49), Espino and colleagues observed the baseline prevalence of hip fracture to be 4% among Mexican American adults in the H-EPESE study(21), while, Bentler and colleagues, reported hip fracture prevalence of 8.98%, using data from the Survey on Assets and Health Dynamics Among the Oldest Old (AHEAD) (46) . We hypothesized three possible explanations for the lower hip fracture prevalence observed in our study: 1) decreased hip fracture incidence in the white US population in the 2000's 2) difference in hip fracture definition and 3) selection bias.

In recent studies, a significant decreasing trend ($p \leq 0.05$) in hip fracture incidence from 2000-2001 to 2008-2009 has been observed (47-49) ; therefore, we suspect that our lower hip fracture prevalence reflects the decline in hip fracture in white women and men in the US (the survey period for the HRS 2004 wave was from March 2004 to February 2005). This partially explains why hip fracture prevalence from the AHEAD, and Framingham studies, with baseline data collected from 1993 and 1983-85, respectively, are slightly higher than what was observed in our study. Though the H-EPESE study collected baseline hip fracture data during 1983 to 2000, we suspect the higher prevalence in the study is mainly due to the Mexican-American population in which hip fracture prevalence is examined. Typically, hip fracture rates among whites are said to be greater than those of non-white populations (16, 49, 50) and, as such, we would expect to see higher hip fracture prevalence in our study as the majority of our population identified themselves as white; however this was not the case. Using hospital admissions data from California, Zingmond and colleagues observed that hip fracture incidence doubled among Hispanics since 1983, while remaining unchanged or declining in other groups (47) . To further support our hypothesis, Zingmond and colleagues observed that, among non-Hispanic white women, the standardized annual incidence fell by 0.6% (4.0 fractures per 100,000) per year, while, the annual incidence among Hispanic women increased 4.9% (11.1 fractures per 100,000) per year.

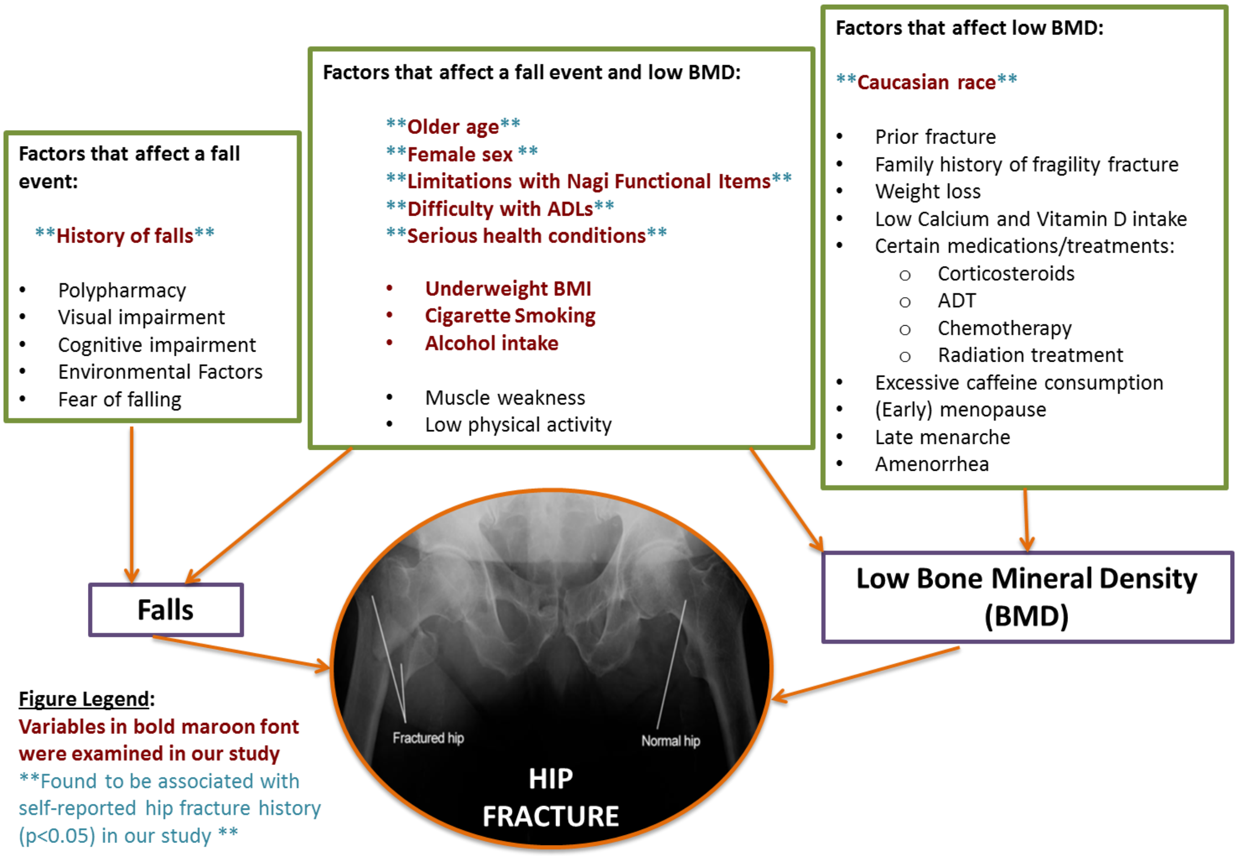
Furthermore, the difference in hip fracture definition amongst the studies may partially explain the lower hip fracture prevalence observed in our study. While we only examined hip fracture in the past two years, hip fracture was defined as “any prior hip fracture” in Framingham study and as “physician diagnosed hip fracture since the age of 50” in the H-EPESE study. In both the Framingham and H-EPESE studies how hip fracture is defined allowed for greater case ascertainment.

Lastly, the AHEAD study identified hip fracture cases via Medicare claims. Since hip fracture data was obtained via Medicare claims, the AHEAD study might have captured more hip fracture cases due to selection bias via the survivorship effect. Hip fracture prevalence could have been slightly underestimated in our study if the number of individuals who have had a hip fracture died prior to baseline interview and thus were excluded from the study. Though participants in the AHEAD cohort are older than participants in our study, we don't suspect the age difference between the two groups to explain the difference in prevalence rates, as the AHEAD participants are a subset of our study. Rather, we suspect the difference in prevalence is partially explained by selection bias and the decline in hip fracture incidence in the 2000's.

In a steady state, a relationship between prevalence, incidence, and duration exists and is quantified as: "Prevalence = Incidence x Duration." Based on this relationship, change in prevalence can be attributed to 1) change in incidence b) change in duration and/or c) change in both incidence and duration; where incidence is the measure of the number of new cases of a disease that develops in a population at risk during a specified time period and duration is defined as the length of time from diagnosis until recovery or until death. In our study, we suspect that death affects the prevalence of self-reported hip fracture. If participants with hip fracture were to have died prior to participating in the baseline survey, we would have observed lower prevalence of hip fracture, as these participants would not have been included in the study. This is a likely occurrence; a prior study has estimated that older adults have a 5- to 8-fold increased risk for all-cause mortality during the first 3 months after hip fracture (5.75 (95% CI, 4.94 to 6.67) in women and 7.95 (CI, 6.13 to 10.30) in men)(2).

<u>Risk Factors as Upstream Mediators.</u> When fall history was removed from the multivariate model, it strengthened the association between hip fracture history and gender, index of IADLs, Nagi functional items, and serious health conditions. Though not tested formally, but, in trend with our findings, we hypothesize that female sex, index of IADLs, Nagi functional items, and serious health conditions increase the likelihood of a fall, which in turn increases the likelihood of a hip fracture. In addition, though measures of BMD were not available, many of the risk factors for hip fracture may be mediated by low BMD. Multiple studies have demonstrated that osteoporotic fracture risk is inversely related to BMD (51-54). BMD accounts for the majority of bone strength and is the current gold standard for diagnosing osteoporosis, as well as for predicting fracture risk (55). Risk factors for low BMD include advanced age, low body weight, rheumatoid arthritis, previous bone fracture, the long-term use of corticosteroid drugs, and vitamin D deficiency (56).

Figure 3. Hypothesized mechanism of risk factors as upstream mediators



Several of our findings on characteristics of hip fracture were consistent with previous research, including higher hip fracture risk in women (3, 7, 21, 57, 58) , in those with advanced age (3, 57, 59) , in those who have experienced a fall (10, 60) , in those with more chronic health conditions (22, 27, 29, 61) and in those with diminished physical functioning (as measured by index of ADLs and Nagi functional limitations) (21, 22) . Contrary to what we expected, underweight BMI was not associated with hip fracture history in our study; however, individuals with overweight and obese BMI were found to be associated with hip fracture.

Gender. In our analytic cohort, women had 88% higher likelihood of having experienced a hip fracture than their male counterparts (OR 1.88; 95% CI 1.19, 2.95). When the history of a fall covariate was removed from the multivariate model, it strengthened the association between hip fracture history and gender. Due to this, we suspect that gender works upstream of a fall event to affect the likelihood of hip fracture. In a prospective study of community-dwelling elderly, Campbell and colleagues found a higher likelihood of experiencing a fall for women (OR 2.02; 95% CI 1.40-2.92) compared to men (OR 1.55; 95% CI 1.04-2.31) (62) . In addition, though we did not examine bone mineral density (BMD) in our study, the available literature supports an inverse relationship between hip fracture risk and BMD (52, 63-65) . Women lose BMD at a quicker rate than men do and, in women, bone loss significantly increases after menopause (51) . Low bone mass contributes to skeletal fragility and skeletal fragility can increase the risk of hip fracture. In summary, it is hypothesized that women are at higher risk for hip fracture than men because women tend to experience more frequent falls, have longer life spans, and have lower bone density after menopause (49, 66, 67) .

Age. In agreement with trends reported in the hip fracture literature, we found that the risk of hip fracture rose with increasing age. Those who reported a hip fracture history in our analytic cohort had a mean age of 81 years, which was slightly older than the mean age of the analytic cohort, of 75 years. Using similar survey data from the AHEAD study, Bentler and colleagues reported the mean age of hip fracture to be 85 years (46) . Furthermore, Johnell and colleagues found that the peak number of hip fractures occurred between the ages of 75-79 years in both men and women (68) .

Fall History. The factor most strongly associated with self-reported hip fracture history was history of a fall (OR 6.35; 95% CI 3.89, 10.36). Falls exponentially increase with age-related biological changes; visual impairments, slower reaction time, and neurological and musculoskeletal disabilities (69) . It is estimated that 30 to 60 percent of community-dwelling older adults fall each year(14). Approximately 90% of hip fractures occur from a simple fall from the standing position(11). In our cohort, 33% of the participants reported having experienced a fall, and 81% of those with a hip fracture history reported having fallen in the previous two years. This number is in agreement with studies in the elderly, in both men and women, though more commonly reported amongst women (12, 70) .

Index of serious health conditions. In our analytic cohort, compared to subjects with no chronic health conditions, history of hip fracture was more likely in participants with 1-2 (OR 3.81; 95% CI 1.32, 11.00) and 3 or more (OR 3.56; 95% CI 1.17, 10.81) chronic conditions. Using population-based survey data from the TromsØ study, Ahmed and colleagues examined individual chronic health conditions on hip fracture risk, as well as the chronic health conditions' combined effect on hip fracture. Similar to our findings, they found that the combined effect of chronic diseases (such as cancer, stroke, psychiatric disorders, asthma, hypo- and hyperthyroidism) increased the likelihood of hip fracture (57) . Certain chronic health conditions substantially increase the risk of falling, and, subsequently, the risk of hip fracture (71, 72) . Therefore, it was not surprising that once fall history was no longer controlled for in the multivariate model, index of serious health conditions was found to be associated with hip fracture. Of the serious health conditions examined in our study, type 2 Diabetes Mellitus (DM) is known to be associated with risk of hip fracture (5, 17, 70) . Strotmeyer and colleagues found that type 2 DM patients were at a 34% increased risk for hip fracture; it is proposed that complications of type 2 DM (such as neuropathy, vascular disease, and impaired vision) increase the risk of falling and thereby fracture(5). Furthermore, Schwartz and colleagues found that type 2 DM women, who on average have higher BMD, were at an increased risk for hip fracture (RR 1.41; 95% CI 1.17, 1.70) due to the use of thiazolidinediones (TZDs), an effective treatment for type 2 DM (73) . TZDs were found to promote more rapid bone loss via reduced bone formation and increased resorption (70) . In addition, stroke is a documented risk factor for hip fracture. Using nationwide population-based data from Taiwan, Kang and colleagues examined the frequency of stroke during a 1-year follow-up period after a hip fracture and found that the 1-year crude hazard of stroke among patients with hip fracture was 1.55 times (95% CI, 1.19 to 2.03; P=0.001) that of the non-hip fracture group (74) . Stroke survivors have an increased frequency of hip fracture due to balance and gait deficits (75) . In addition, the use of multiple medications for the management of disease has been shown to increase an individual's likelihood of falling (71, 72) . In a cohort of Spanish elderly adults, Fernandez-Ruiz and colleagues found a higher number of chronic medications were associated with hip fracture(3).

Functional limitations. To measure functional status limitations in our study we used index Nagi functional items (measure of an individual's difficulty with performing various physical tasks) and the index of ADLs (measure of an individual's ability to independently perform daily tasks related to self and home care). In our study, difficulty with ADLs was strongly associated with hip fracture; participants with a history of self-reported hip fracture were 2 times as likely to have difficulty with 1-5 ADLs (OR 2.34; 95% CI 1.36-4.16) and 3 times as likely to have difficulty with 6 or more ADLs (OR 3.78; 95% CI 2.05, 6.99). In addition, participants with a history of self-reported hip fracture were nearly 3 times as likely to have functional limitations with 5 or more Nagi items (OR 2.75; 95% CI 1.26-5.98). Our finding mirrors associations between hip fracture and physical limitations in older adults that have been reported in multiple other studies (28, 60, 67, 76-78) . In a population based study of osteoporotic fractures in women, Greendale and colleagues found that women who experienced a hip fracture were 3-4 times more likely to have problems bending, walking, and going down stairs, and 4-11 times more likely to have limitations in cooking and shopping (76) . Much like chronic health conditions, functional limitations may act as an upstream mediator that affects hip fracture risk through the risk of falls. Functional limitations such as difficulty bending the knee or stooping could result in instability of posture and may lead to falls. Gait or neuromuscular impairments may not only increase the risk of falling but also influence an individual's speed, coordination, and protective responses during a fall. Overall, when strength, endurance, muscle power, and function declines, one is unable to prevent a slip, trip, or stumble from becoming a fall (72) . In addition, studies indicate that lower physical activity, particularly weight-bearing activities, may contribute to decreased BMD and increase the risk for a hip fracture. In a study of healthy Moroccan women, Khazzani and colleagues found that low physical performance was associated with low BMD, a high risk of fall, and fracture history (60) . Physical activity produces a mechanical load on the bone through muscle contraction and surface impact, contributing to bone formation and remodeling, therefore, a lack of physical activity can then lead to a decrease in bone density (60) .

BMI. An increased odds of hip fracture was observed among underweight participants in the bivariate model (OR 2.33; 95% CI 1.44-4.91), however, it was not statistically significant in the final multivariate model (OR 1.53; 95% CI 0.79-2.98). As previously stated, the vast majority of the hip-fracture literature supports a strong association of underweight BMI with hip fracture (3, 79) . Though we cannot say with certainty that underweight BMI is associated with hip fracture in our analytic cohort, we can hypothesize that underweight is a likely risk factor for hip fracture. To support this hypothesis, we observed that the overweight and obese participants were at significantly decreased odds of hip fracture in the multivariate models.

We hypothesized two explanations for our statistically insignificant finding: 1) small sample size and 2) survivorship bias. The small sample of underweight participants was likely underpowered to detect a significantly higher likelihood of hip fracture with underweight BMI. Approximately 3% of our analytic cohort was in the underweight category, while the majority was of normal or overweight BMI. However, the proportion of adults 65 years or older in the US who are underweight is small (less than 5% from the National Health and Nutrition Examination Survey (NHANES)) (80) . Therefore, small sample size may only partially explain our insignificant finding. Furthermore, we hypothesized that those who were old and underweight with a hip fracture history were less likely to be alive and able to participate in HRS; thus, our result may be due to survivor bias. In a retrospective chart review of patients who underwent hip fracture surgery at the Mayo Clinic, Kirkland and colleagues found that advanced age, low BMI (<18.5), and high number of comorbidities were associated with 30-day mortality following hip fracture surgery (81) . Older adults with low BMI tend to have more co-morbidities (78) , which might preclude them from signing up for a study at a higher rate than other groups, even if they had survived to this point.

In our analytic cohort we found that overweight and obese BMIs were associated with a lower likelihood of hip fracture history (overweight OR: 0.41, 95% CI 0.23-0.73; obese OR: 0.37, 95% CI 0.18-0.73). In a meta-analysis of prospective cohort studies, Tang and colleagues evaluated the association between obesity and the risk of hip fracture in older adults. They found that obesity was a protective factor that significantly decreased the risk of hip fracture in adults (unadjusted RR: 0.66, 95% CI 0.56-0.78) (9) . In addition, Tang and colleagues found that this trend did not differ by gender; both obese men and women have a significantly decreased risk for developing hip fracture when compared to their normal weight peers (men: RR 0.54, 95% CI

0.48-0.60; women: RR 0.70, 95% CI 0.58-0.84) (9) . Obesity is proposed to be protective against hip fracture risk via an effect mediated predominately though high BMD. Individuals with a higher BMI have relatively higher BMD because an increased strain on the bones imposed by higher body mass may improve the structural integrity of the bones (82) . In addition, obesity is widely believed to be protective against fracture because of the effect of increased soft-tissue padding, which reduces impact forces during a fall, thereby reducing likelihood of fracture (9, 82) .

Strengths and Limitations

Our study involved several strengths. The HRS survey is a large, nationally representative sample of older adults, which allowed for the assessment of the rare hip fracture outcome. In addition, the HRS survey includes robust measures of demographic, health, socioeconomic factors that allowed us to comprehensively quantify ADLs and IADLs. HRS data are reliable and consistent as the data collection procedures in the HRS are well established and have been conducted every two years since 1992. HRS also surveys participants from midlife to the end of their lifespan; if a participant were to become institutionalized at any point during the survey, HRS will still include them in subsequent interviews. Similarly, if a participant were to pass away in an institutionalized setting, exit interviews were conducted via proxy interviews. Furthermore, because we used data from the HRS, our results are more likely than the results of hospital-based studies to be generalizable to the overall community-dwelling older adult population of the US. These factors all add strength to our study.

Our study has a number of limitations. First is the potential for survivorship bias. In studies involving older adults, prevalence of hip fracture cases could be underestimated, since individuals who have had a hip fracture could have died prior to baseline interview and thus been excluded from the study. Time-to-event meta-analyses showed that older adults have a 5- to 8-fold increased risk for all-cause mortality during the first 3 months after hip fracture (5.75 (95% CI, 4.94 to 6.67) in women and 7.95 (CI, 6.13 to 10.30) in men)(2). Second, because this was a community-based survey, older adults in nursing homes and other institutional settings were excluded from the baseline interviews. It is well known that institutionalized older adults tend to have more functional limitations and comorbidities than their community dwelling peers (46) , therefore putting them at a greater risk for hip fracture. Cumming and colleagues found that patients residing in an institution prior to hip fracture have a significantly greater risk of sustaining a hip fracture than those residing at home (83) . However, it is important to note that, though institutionalized elderly were not included in the baseline HRS interviews, participants who later became institutionalized were included in subsequent interviews (36).

Third, all of our study measures can be considered cross-sectional data; thus, temporality cannot be established for certain risk factors. For instance, functional limitations can result in or be a consequence of hip fracture. Functional limitations, such as gait and balance deficits, could lead to neuromuscular impairments, which could increase a person's likelihood for falling and result in subsequent hip fracture. On the other hand, functional limitations can be a consequence of hip fracture. In a study of adults 50 years and older admitted to two large hospitals in Oslo for hip fracture, Osnes and colleagues examined the consequence of hip fracture with respect to changes in the ability to perform ADLs (84) . They found that 43% of the patients lost their pre-fracture ability to independently move around and more than a fourth of the patients (28%) lost their ability to cook their own dinner after sustaining hip fracture (84) .

Fourth, the relatively small sample size of hip fracture cases might have limited the power to detect some statistically relevant associations. This is most attributable to the fact that hip fracture if a very rare outcome to observe, even with a large cohort. Fifth, we lacked information on several other factors with known associations with hip fracture in the literature, including BMD, use of hormone replacement therapy, and use of corticosteroids. In a meta-analysis of prospective cohort studies in women, Marshall and colleagues concluded that BMD can predict osteoporotic fracture risk (54) , therefore, measure of BMD would have added value to our study. Lastly, a limitation of this study was that we used self-reported information for a few of our predictor variables (self-reported health status and index of serious health conditions) and for our main outcome of interest. As information was gained via a questionnaire, this information may have been susceptible to recall bias. However, the accuracy of self-reported conditions is generally considered to be high, particularly if illnesses are severe or result in hospitalization and prolonged disability (85) . Accordingly, previous studies have demonstrated an excellent agreement between self-reported hip fracture and a standardized diagnostic method based on the data abstracted from medical records(3).

Public Health Implications

The current study provides valuable information regarding the prevalence of and factors associated with hip fracture in a large cohort of community-dwelling older adults. It has been estimated that 1 in 3 women and 1 in 12 men will sustain a hip fracture in their lifetime (86) . Unless steps are taken to reduce the risk of hip fracture in older adults, the annual number of cases is estimated to increase to 512,000 by 2040 (83) . With a greater number of cases, increases in medical costs are sure to follow. According to data from the US Agency for Healthcare Research and Quality, approximately a third of all fracture patients receive a hip replacement and the estimated cost for treatment is approximately 10.3 to 15.2 billion dollars per year in the US (83, 87) . Furthermore, hip fractures impose a formidable burden of disability on the survivor (88) . Using a combination of different metrics to measure functional disability, four studies have found that only a third of hip fracture survivors regain their pre-fracture level of functioning (89) . In addition to a limited level of functioning, hip fracture survivors have a substantially increased risk of death that persists for at least 6 years post-fracture and this relative excess mortality is independent of comorbidity and known hip fracture risk factors (90) .

In summary, this study found hip fracture history was associated with female gender, high BMI, advanced age, history of a fall, chronic health conditions and diminished physical functioning (as measured by index of ADLs and Nagi functional limitations). From our results we suspect that chronic health conditions, Nagi functional limitations, and ADLs work as upstream mediators and may increase the likelihood of hip fracture through falls. The rate of falls and the likelihood of injury from falls increases with age, therefore, factors that influence the risk of falling should be studied further. Factors that increase an individual’s likelihood for falling include lower body weakness, difficulties with gait and balance, poor vision, chronic health conditions, adverse side effects of poly-pharmacy, pervious falls and advanced age (12, 78, 91, 92) .

Our results aim to help identify the at-risk population who may benefit from preventive measures. Measures to prevent falls and fractures should be studied in adults in advanced age, with prior history of a fall, with chronic conditions, and with diminished physical functioning.

APPENDICES

I. Table of Analytic Cohort Stratified by Race

Appendix I. Analytic cohort stratified by race

Race	History of self-reported Hip Fracture (n=184, 1.8%)	No History of self-reported Hip Fracture (n=10,456, 98.2%)	Analytic Cohort (n=10,640, %)
Black	17 (13.2)	1374 (98.8)	1391 (13.1)
Hispanic	15 (1.8)	800 (98.2)	815 (7.7)
White	150 (1.8)	8146 (98.2)	8296 (78.0)
Other	2 (1.4)	136 (98.6)	138 (1.3)

II. Table of Dependent and Independent Variables

Appendix II. List of dependent and independent variables

Specific Aim 1: To describe the prevalence of history of self-reported hip fracture in the HRS 2004 cohort.

Variable	Variable Type	HRS Wave	Description
Dependent Variable			
History of self-reported Hip Fracture	Categorical Yes = 1 No = 0	Extracted for HRS 2004 wave	Coded as "Broken Hip" in HRS codebook. Question asked: "Have you fractured your hip since we talked in (the previous wave)?" The previous wave is defined as two years ago. Participants responded in one of the following ways: yes, no, don't know, refused, or not ascertained. We categorized the response into yes and no. All "don't know, refused and not ascertained" responses were coded as missing.

Specific Aim 2: To examine factors associated with history of self-reported hip fracture in HRS 2004 cohort.

Variable	Variable Type	HRS Wave	Description
Dependent Variable			
History of self-reported Hip Fracture	Categorical • No • Yes	Extracted from HRS 2004 wave.	Coded as "Broken Hip" in HRS codebook. Question asked: "Have you fractured your hip since we talked in (the previous wave)?" The previous wave is defined as two years ago. Participants responded in one of the following ways: yes, no, don't know, refused, or not ascertained. We categorized the response into yes and no. All "don't know, refused and not ascertained" responses were coded as missing.
Independent Variable			
Body Mass Index (BMI)	Categorical • Underweight (<18.50) • Normal (18.50-24.99) • Overweight (25.00-29.99) • Obese (≥30.00)	Weight was extracted from HRS 2004 wave. Height was extracted from the 1992, 1993, 1998, and 2004 waves.	BMI variable is defined as the weight in kilograms divided by the square of the height in meters (kg/m2). Height was measured in inches and weight was measured in lbs. Inches and lbs. were later converted to kg and m2. BMI is classified into the following categories based on the World Health Organization's International Classification of

			Adult BMIs. Due to insufficient cell counts, obese I, II, III were collapsed to "Obese."
Age	Continuous	Extracted from HRS 2010 Tracker	Coded as "JAGE" in HRS 2010 Tracker for age at 2004 HRS interview. Age in years. The study cohort is comprised of participants who are 65 years or older only.
Age	Categorical • 65 to 74 • 75 to 84 • ≥85	Extracted from HRS 2010 Tracker	Coded as "JAGE" in HRS 2010 Tracker for age at 2004 HRS interview. Age in years. The study cohort is comprised of participants who are 65 years or older only.
Gender	Categorical • Male • Female	Extracted from HRS 2010 Tracker	Coded as "Gender" in HRS 2010 Tracker.
Race	Categorical • Black • Hispanic • White • Other For regression analyses: • White • Other	Extracted from HRS 2010 Tracker	Extracted "Race" and "Hispanic" variables from HRS 2010 Tracker to construct Race variable. "Race" variable defines race or ethnicity type. Participants responded in one of the following ways: not obtained, other, white/Caucasian, black or African American. "Hispanic" variable defines hispanicity type. Participants responded in one of the following ways: Hispanic type unknown, Mexican American, other Hispanic/not obtained. An overall Race variable was created using the "Race" and "Hispanic" variables. The race was categorized into: Black, White, Hispanic, and other. All "don't know, refused and not ascertained" responses were coded as missing. Due to insufficient number of Black and Hispanic participants with self-reported history of hip fracture, Black and Hispanic categories were further collapsed into one category, Other. "Other" is defined as: Black, Hispanic, Non-Hispanic, Non-Hispanic Black, and other.
Education	Categorical • Some high school or less • Completed high school • Any college degree	Extracted from HRS 2010 Tracker	Coded as "Degree" in HRS 2010 Tracker. Participants responded in one of the following ways: No degree, GED, High school diploma, 2 year college degree, 4 year college degree, Master degree, Professional degree, Degree unknown/some college. Education was initially categorized as: Some high school or less, completed high school, some college-post college degree. However, due to insufficient cell count, the education variable was collapsed to: Some high school or less competed high school, and any college degree.
Marital Status	Categorical • Unmarried • Married or partnered	Extracted from HRS 2010 Tracker	Participants were asked what their marital status was during the 2004 interview and their responses were: Married, Separated/Divorced, Widowed, Never Married, Marital Status Unknown. Married was coded as "Married or Partnered" Marital status unknown was coded as missing. Separated/divorced, widowed, and never married was coded as "Unmarried."
Health status	Categorical • Excellent/Very good • Good • Fair • Poor	Extracted from HRS 2004 wave	Participants were asked, "Would you say your health is excellent, very good, good, fair, or poor?" during the 2004 interview. They responded to one of the following: excellent, very good, good, fair, poor, don't know, or refused. "Don't know" and "refused" responses were coded as missing. Due to insufficient cell count, "Excellent" and "Very good"

			responses were collapsed to "Excellent/Very good." This is self-reported health status in 2004.
Fall	Categorical • No • Yes	Extracted from HRS 2004 wave	Participants were asked, "Have you fallen down in the last two years?" during the 2004 interview. Participant responses include: yes, no, don't know, or refused. "Don't know" and "Refused" were coded as missing. This is self-reported history of fall within the past two years.
Smoking status	Categorical • Never smoked • Past smoker • Current smoker	Extracted from the 2004 wave.	Participants were asked, "Have you ever smoked cigarettes?" By smoking HRS means more than 100 cigarettes smoked in a lifetime. If participants answered "yes" to that question, they were probed further and asked, "Do you smoke cigarettes now?" Participants responses include: yes, no, don't know, not ascertained, or refused. All "don't know, refused and not ascertained" responses were coded as missing. If participants answered "yes" to the first question, but "no" to the second, they were coded as a "past smoker." If participants answered "no" to the first question, they were coded as a "never smoker." If participants answered "yes" to both the first and second questions, they were coded as "current smoker."
Do you ever drink alcoholic beverages?	Categorical • Abstainer • Moderate drinker • Heavy drinker	Extracted from HRS 2004 wave	Participants were asked, "Do you ever drink alcoholic beverages such as beer, wine, or liquor?" Participants responses include: yes, no, don't know, not ascertained, or refused. If participant answered no, then they were coded as an "Abstainer." If participants answered "yes" to drinking alcoholic beverages, they were probed further and asked, "In the last 3 months, on the days that you drink, how many drinks do you have?" Participant's responses ranged from 1 to 50 drinks, don't know, not ascertained, or refused. All "don't know, refused and not ascertained" responses were coded as missing. Those who consumed 0 drinks were labeled as abstainers. Those who consumed 1-2 drinks per day were labeled as moderate drinkers. Those who consumed 3+ drinks per day were labeled as heavy drinkers.
Index of serious health conditions in 2004	Categorical • No chronic conditions • 1-2 chronic conditions • 3+ chronic conditions	Extracted from HRS 2004 wave	Participants were asked, "Has a doctor ever told you that you have ___?" This question was asked about high blood pressure, arthritis, stroke, heart disease, cancer, and diabetes. Participant responses include: yes, no, don't know, or refused. "Don't know" and "Refused" responses were coded as missing. Using the responses above, the index of serious health conditions variable was created by combining arthritis + high blood pressure + stroke + heart disease + cancer + diabetes. Index of serious conditions is an additive index with a range of 0 to 6, where yes=1 and no=0. Due to insufficient cell count, "1-2 chronic conditions" and "3+ chronic conditions" were collapsed.
Index of Activities of Daily Living (ADL)	Categorical • No difficulties with ADLs • Difficulty to with 1-5 ADLs • Difficulty with 6+ ADLs	Extracted from HRS 2004 wave	The Index of Activities of Daily Living is a measure of the ability to perform basic and instrumental tasks of daily living. This index is the combination of Basic Activities of Daily Living (BADLs) and Instrumental Activities of Daily Living (IADLs). Nagi functional items determine whether participants are routed to answer ADL questions. If participants report no problems doing any Nagi items then they are not asked ADL questions (assume no ADL difficulty). If participants report

			problem with 1 Nagi item and do not have difficulty dressing, then no more ADLs are asked (again, assuming no ADL difficulty). If participants reports problem with one Nagi item and reports difficulty dressing, then they are asked about other ADLs. Same applies for one or more Nagi functional limitations. For BADL items -- Participants were asked if they, "Have difficulty (getting dressed, walking without equipment, bathing, eating, using the toilet, and getting in/out of bed)?" Responses to this question include: yes, no, can't do, don't do, don't know, not ascertained, or refused. If participants answered "can't do" or "don't do" to previous question they were probed further and asked, "Does anyone help (you get dressed, walk across the room, you bathe, you eat, you use the toilet, you get in/out of bed)?" Responses to this question include: yes, no, don't do, don't know, or refused. For IADL items -- Participants were asked if they, "Have difficulty (preparing meals, grocery shopping, making phone calls, taking medication, managing your money)?" Responses to this question include: yes, no, can't do, don't do, don't know, not ascertained, or refused. If participants answered "can't do" or "don't do" to previous question they were probed further and asked, "Is it because of a health or memory problem you have difficulty (preparing meals, grocery shopping, making phone calls, taking medication, managing your money)?" Responses to this question include: yes, no, don't do, don't know, or refused. All "yes" responses to the second question were coded as 1 and all "no" responses coded as 0. All "don't know, refused and not ascertained" responses were coded as missing. Index of BADLs = BADLdress04 + BADLwalk04 + BADLbath04 + BADLeat04 + BADLtoilet04 +BADLbed04 Index of IADLs = IADLmeals04 + IADLgroc04 + IADLphone04 + IADLmeds04 + IADLmoney04. Index of ADLs = Index of BADLs + Index of IADLs The index is additive with a range of 0 to 11, where yes=1 and no=0.
Index of Nagi functional items	Categorical • No functional limitations • Functional limitations with 1-4 items • Functional limitations with 5+ items	Extracted from HRS 2004 wave	The Index of Nagi functional items are a measure of functional limitations. Participants were asked if they, "Because of a health problem, do you have any difficulty with (reach/extend arms above shoulder level, walking several blocks, walking one block, sitting for 2 hours, getting up from a chair after sitting long periods, climbing several flights of stairs without resting, stooping/kneeling/crouching, pulling/pushing large objects, lifting/carrying weights over 10lbs, and picking up a dime from a table)? Responses to this question include: yes, no, don't do, can't do, or refused. All "don't know, refused and not ascertained" responses were coded as missing. All "yes" and "can't do" were coded as "yes" to having a functional limitation. All "no" and "don't do" were coded as no because you are assuming that just because you don't do the activity doesn't mean you have difficulty with it. Index of Nagi functional items = blocks + sit + chair + stairs + stoop + reach + push + weights + dime. The index is additive with a range of 0 to 9, where yes=1 and no=0.

III. Formation of analytic dataset from HRS data files

Due to the fact that certain variables, i.e. height, were only collected at the participants' baseline interview, to form the analytic dataset, various HRS data files had to be extracted, appended, and merged. Steps taken to create the analytic dataset are:

1) Called relevant variables from HRS Cross wave Tracker 2010 file, HRS 2004 core and exit, HRS 1992 core, HRS 1993 core, and HRS 1998.
2) Merged HRS 2004 core and exits together to create HRS2004Master.dta
3) Merged HRS2004Master with HRS Crosswave Tracker 2010 file to create tempMaster.dta
4) Height was collected from participants' baseline interview and appended to create MasterHeight.dta
5) Merge updated tempMaster.dta with MasterHeight.dta to create AnalyticDataset.dta

IV. Age-standardized history of hip fracture prevalence using 2000 US Census Data

Age-standardized history of self-reported hip fracture prevalence in HRS 2004 Analytic Cohort using 2000 US Census Data						
Age	**Hip Fracture Cases**	**N**	**Crude Hip Fracture Prevalence**	**US 2000 Standard Population**	**Age Distribution of Standard Population**	**Age-standardized Prevalence**
65 to 69	25	2904	0.0086	9652663	0.2730	0.0024
70 to 74	18	2629	0.0068	8953973	0.2532	0.0017
75 to 79	24	1959	0.0123	7487310	0.2118	0.0026
80 to 84	32	1554	0.0206	4988791	0.1411	0.0029
≥85	85	1410	0.0603	4276211	0.1209	0.0073
Total	184	10456	0.0176	35358948	1.0000	0.0169

Age-standardized history of self-reported hip fracture prevalence in Women using 2000 US Census Data						
Age	Hip Fracture Cases	N	Crude Hip Fracture Prevalence	US 2000 Standard Population	Age Distribution of Standard Population	Age-standardized Prevalence
65 to 69	14	1564	0.0090	9652663	0.2730	0.0024
70 to 74	14	1464	0.0096	8953973	0.2532	0.0024
75 to 79	13	1075	0.0121	7487310	0.2118	0.0026
80 to 84	26	928	0.0280	4988791	0.1411	0.0040
≥85	75	933	0.0804	4276211	0.1209	0.0097
Total	142	5964	0.0238	35358948	1.0000	0.0211

Age-standardized history of self-reported hip fracture prevalence in Men using 2000 US Census Data						
Age	Hip Fracture Cases	N	Crude Hip Fracture Prevalence	US 2000 Standard Population	Age Distribution of Standard Population	Age-standardized Prevalence
65 to 69	11	1340	0.0082	9652663	0.2730	0.0022
70 to 74	4	1165	0.0034	8953973	0.2532	0.0009
75 to 79	11	884	0.0124	7487310	0.2118	0.0026
80 to 84	6	626	0.0096	4988791	0.1411	0.0014
≥85	10	477	0.0210	4276211	0.1209	0.0025
Total	42	4492	0.0093	35358948	1.0000	0.0096

V. <u>Model (1) Backward Manual Selection Model with Fall variable</u>

STATA does not allow for automated model selection processes such as backwards, forwards, stepwise processes or best subset selection using weighted data. Hence, backward manual selection was performed by adding all variables of interest (defined as variables with a p-value of ≤0.25 in bivariate analysis) into the first model. Variable with least significance was removed from each subsequent model until all remaining variables had a p-value of <0.05.

Model (1) Backward Manual Selection Model with Fall variable

Characteristic	**Model1 OR (95% CI)**	**Model2 OR (95% CI)**	**Model3 OR (95% CI)**	**Model4 OR (95% CI)**	**Model5 OR (95% CI)**	**Model6 OR (95% CI)**	**Model7 OR (95% CI)**
Fallen in the past 2 years?	7.51 (4.31, 13.07)	7.49 (4.30,13.04)	7.46 (4.27, 13.04)	7.52 (4.31, 13.13)	7.59 (4.36, 13.21)	6.91 (4.07, 11.71)	6.35 (3.89, 10.36)
Gender	2.12 (1.18, 3.83)	2.11 (1.17, 3.83)	2.00 (1.17, 3.41)	1.96 (1.19, 3.22)	1.87 (1.20, 3.22)	1.96 (1.20, 3.22)	1.88 (1.19, 2.95)
Age							
65 to 74	Referent	Referent	Referent	Referent	Referent	Referent	Referent
75 to 84	0.93 (0.47, 1.85)	0.93 (0.47, 1.85)	0.90 (0.47, 1.72)	1.00 (0.57, 1.75)	0.98 (0.56, 1.74)	1.03 (0.59, 1.78)	1.06 (0.62, 1.80)
85 and over	1.65 (0.70, 3.86)	1.66 (0.71, 3.89)	1.56 (0.72, 3.37)	1.88 (1.01, 3.48)	1.78 (0.96, 3.33)	1.85 (1.01, 3.38)	2.03 (1.14, 3.62)
Trend	(0.10)	(0.09)	(0.09)	(0.11)	(0.06)	(0.05)	(0.01)
Body Mass Index							
Underweight	1.37 (0.60, 3.11)	1.36 (0.60, 3.11)	1.37 (0.60, 3.12)	1.34 (0.58, 3.05)	1.39 (0.62, 3.13)	1.65 (0.80, 3.38)	1.53 (0.79, 2.98)
Normal	Referent	Referent	Referent	Referent	Referent	Referent	Referent
Overweight	0.44 (0.25, 0.77)	0.44 (0.25, 0.77)	0.44 (0.25, 0.77)	0.44 (0.25, 0.79)	0.44 (0.25, 0.80)	0.41 (0.23, 0.74)	0.45 (0.27, 0.77)
Obese	0.36 (0.18, 0.74)	0.37 (0.18, 0.76)	0.37 (0.18, 0.76)	0.36 (0.17, 0.75)	0.37 (0.18, 0.76)	0.38 (0.19, 0.77)	0.36 (0.19, 0.70)
Trend	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)
Index of Activities of Daily Living							
No difficulty with ADLs	Referent	Referent	Referent	Referent	Referent	Referent	Referent
Difficulty with 1-5 ADLs	1.64 (0.92, 2.94)	1.67 (0.93, 2.94)	1.65 (0.93, 2.30)	1.67 (0.93, 2.97)	1.87 (1.04, 3.34)	1.97 (1.13, 3.45)	1.73 (1.02, 2.93)
Difficulty with 6+ ADLs	2.49 (1.32, 4.82)	2.55 (1.33, 4.89)	2.57 (1.34, 4.92)	2.52 (1.32, 4.83)	2.98 (1.61, 5.49)	2.83 (1.55, 5.17)	3.07 (1.79, 5.26)
Trend	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.00)	(0.00)
Nagi functional items							
No functional limitations	Referent	Referent	Referent	Referent	Referent	Referent	Referent
Functional limitations with 1-4 items	0.76 (0.34, 1.69)	0.77 (0.35, 1.70)	0.77 (0.35, 1.69)	0.77 (0.35, 1.69)	0.80 (0.37, 1.70)	0.93 (0.44, 1.94)	1.04 (0.51, 2.11)
Functional limitations with 5+ items	1.43 (0.60, 3.42)	1.43 (0.60, 3.42)	1.43 (0.60, 3.42)	1.44 (0.61, 3.42)	1.62 (0.70, 3.75)	1.70 (0.77, 3.78)	1.74 (0.82, 3.67)
Trend	(0.04)	(0.05)	(0.05)	(0.04)	(0.02)	(0.04)	(0.05)
Index of Serious Health Conditions							~
No chronic conditions	Referent	Referent	Referent	Referent	Referent	Referent	

1-2 chronic conditions	3.16 (1.06, 9.45)	3.15 (1.05, 9.40)	3.14 (1.05, 9.38)	3.20 (1.07, 9.52)	3.25 (1.11, 9.59)	3.33 (1.14, 9.74)
3+ chronic conditions	2.30 (0.72, 7.36)	2.29 (0.72, 7.33)	2.26 (0.71, 7.20)	2.28 (0.72, 7.21)	2.48 (0.80, 7.70)	2.84 (0.92, 8.72)
Trend	(0.07)	(0.07)	(0.06)	(0.06)	(0.06)	(0.08)
Drink alcoholic beverages?						
Abstainer	Referent	Referent	Referent	Referent	Referent	~
Moderate Drinker	1.52 (0.80, 2.86)	1.47 (0.80, 2.70)	1.49 (0.81, 2.73)	1.52 (0.83, 2.77)	1.47 (0.81, 2.66)	
Heavy Drinker	0.77 (0.33, 1.80)	0.74 (0.33, 1.67)	0.76 (0.34, 1.68)	0.79 (0.37, 1.66)	0.74 (0.35, 1.57)	
Trend	(0.26)	(0.27)	(0.27)	(0.27)	(0.27)	
Self-reported Health Status						
Excellent/Very good	Referent	Referent	Referent	Referent	~	
Good	0.98 (0.53, 1.82)	0.99 (0.54, 1.84)	0.98 (0.53, 1.82)	1.00 (0.54, 1.85)		
Fair	1.13 (0.57, 2.20)	1.14 (0.59, 2.23)	1.14 (0.58, 2.22)	1.16 (0.60, 2.23)		
Poor	1.72 (0.80, 3.7)	1.77 (0.85, 3.70)	1.78 (0.86, 3.69)	1.82 (0.87, 3.82)		
Trend	(0.44)	(0.38)	(0.35)	(0.34)		
Smoke cigarettes?						
Former smoked	Referent	Referent	Referent	~		
Past smoker	1.48 (0.76, 2.89)	1.47 (0.75, 2.88)	1.47 (0.75, 2.87)			
Current smoker	0.96 (0.53, 1.74)	0.96 (0.53, 1.74)	0.94 (0.53, 1.68)			
Trend	(0.49)	(0.51)	(0.49)			
Marital Status	1.21 (0.70, 2.08)	1.18 (0.69, 2.02)	~			
Level of Education		~				
Some HS or less	Referent					
Completed HS	0.87 (0.51, 1.50)					
Any college degree	0.84 (0.46, 1.55)					
Trend	(0.84)					

VI. Model (2) Backward Manual Selection Model without Fall variable

Model (2) Backward Manual Selection Model without Fall variable

Characteristic	Model1 OR (95% CI)	Model2 OR (95% CI)	Model3 OR (95% CI)	Model4 OR (95% CI)	Model5 OR (95% CI)	Model6 OR (95% CI)
Gender	2.07 (1.15, 3.72)	2.27 (1.28, 4.05)	2.28 (1.27, 4.07)	2.22 (1.30, 3.78)	2.12 (1.30, 3.46)	2.02 (1.23, 3.01)
Age						
65 to 74	Referent	Referent	Referent	Referent	Referent	Referent
75 to 84	0.94 (0.48, 1.83)	1.01 (0.53, 1.92)	1.01 (0.53, 1.92)	1.00 (0.54, 1.85)	1.10 (0.64, 1.88)	1.08 (0.62, 1.87)
85 and over	1.66 (0.71, 3.90)	1.81 (0.80, 4.09)	1.82 (0.81, 4.09)	1.77 (0.83, 3.77)	2.15 (1.18, 3.92)	2.03 (1.11, 3.74)
Trend	(0.11)	(0.08)	(0.08)	(0.09)	(0.01)	(0.02)

Body Mass Index						
Underweight	1.38 (0.62, 3.08)	1.49 (0.73, 3.07)	1.49 (0.72, 3.07)	1.49 (0.72, 3.07)	1.47 (0.73, 3.03)	1.61 (0.81, 3.23)
Normal	Referent	Referent	Referent	Referent	Referent	Referent
Overweight	0.44 (0.25, 0.78)	0.41 (0.23,. 0.72)	0.41 (0.23, 0.72)	0.41 (0.23, 0.72)	0.41 (0.23, 0.73)	0.41 (0.23, 0.73)
Obese	0.35 (0.18, 0.71)	0.37 (0.18, 0.73)	0.37 (0.18, 0.73)	0.37 (0.18, 0.73)	0.36 (0.18, 0.72)	0.37 (0.18, 0.73)
Trend	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)
Index of Activities of Daily Living						
No difficulty with ADLs	Referent	Referent	Referent	Referent	Referent	Referent
Difficulty with 1-5 ADLs	1.93 (1.08, 3.44)	2.01 (1.14, 3.53)	2.01 (1.14, 3.56)	2.01 (1.14, 3.56)	2.04 (1.16, 3.61)	2.34 (1.36, 4.16)
Difficulty with 6+ ADLs	3.33 (1.73, 6.40)	3.05 (1.59, 5.86)	3.07 (1.60, 5.89)	3.07 (1.60, 5.89)	3.03 (1.57, 5.83)	3.78 (2.05, 6.99)
Trend	(0.00)	(0.00)	(0.03)	(0.03)	(0.03)	(0.00)
Nagi functional items						
No functional limitations	Referent	Referent	Referent	Referent	Referent	Referent
Functional limitations with 1-4 items	1.10 (0.52, 2.34)	1.19 (0.57, 2.47)	1.19 (0.57, 2.47)	1.19 (0.57, 2.47)	1.18 (0.57, 2.45)	1.27 (0.62, 2.59)
Functional limitations with 5+ items	2.36 (1.01, 5.54)	2.23 (0.98, 5.03)	2.23 (0.99, 5.01)	2.23 (0.99, 5.02)	2.24 (1.00, 5.04)	2.75 (1.26, 5.98)
Trend	(0.01)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)
Index of Serious Health Conditions						
No chronic conditions	Referent	Referent	Referent	Referent	Referent	Referent
1-2 chronic conditions	3.51 (1.20, 10.34)	3.63 (1.24, 10.58)	3.62 (1.24, 10.55)	3.61 (1.24, 10.54)	3.71 (1.27, 10.80)	3.81 (1.32, 11.00)
3+ chronic conditions	2.78 (0.89, 8.72)	3.12 (1.01, 9.63)	3.12 (1.01, 9.62)	3.10 (1.01, 9.53)	3.17 (1.04, 9.71)	3.56 (1.17, 10.81)
Trend	(0.06)	(0.06)	(0.06)	(0.06)	(0.05)	(0.05)
Self-reported Health Status						
Excellent/Very good	Referent	Referent	Referent	Referent	Referent	
Good	0.98 (0.53, 1.84)	1.12 (0.62, 2.03)	1.12 (0.62, 2.04)	1.12 (0.62, 2.03)	1.13 (0.62, 2.04)	
Fair	1.24 (0.64, 2.41)	1.33 (0.70, 2.52)	1.34 (0.71, 2.51)	1.33 (0.71, 2.51)	1.35 (0.73, 2.51)	
Poor	1.84 (0.84, 4.01)	2.30 (1.01, 4.75)	2.32 (1.13, 4.76)	2.31 (1.12, 4.76)	2.31 (1.12, 4.76)	
Trend	(0.37)	(0.26)	(0.11)	(0.12)	(0.12)	
Smoke cigarettes?					~	
Never smoked	Referent	Referent	Referent	Referent		
Former smoker	1.54 (0.78, 3.03)	1.16 (0.86, 3.05)	1.60 (0.86, 2.98)	1.60 (0.87, 2.97)		
Current smoker	0.93 (0.52, 1.66)	0.99 (0.57, 1.74)	0.99 (0.57, 1.73)	0.99 (0.57, 1.70)		
Trend	(0.38)	(0.38)	(0.32)	(0.31)		
Drink alcoholic beverages?						
Abstainer	Referent	Referent	~			
Moderate Drinker	1.47 (0.77, 2.83)	1.43 (0.77, 2.66)				
Heavy Drinker	0.86 (0.37, 1.98)	0.83 (0.38, 1.83)				
Trend	(0.38)	(0.39)				
Marital Status	1.14 (0.67, 1.95)	1.12 (0.66, 1.89)				

Level of Education		
Some HS or less	Referent	~
Completed HS	0.86 (0.50, 1.50)	
Any college degree	0.86 (0.47, 1.56)	
Trend	(0.84)	

VII. Characteristics of Participants in Analytic Cohort vs. Not in Analytic Cohort

Appendix VI. Characteristics of Participants in Analytic Cohort vs. Not in Analytic Cohort

Characteristics	**Analytic Cohort (N=10,640)**	**Not in Analytic Cohort (N=9,489)**	**P-value**
Age (mean ± SE)	75.4 ± 0.07	57.5 ±0.06	<0.001
Gender			
Male	42.60%	42.70%	
Female	57.40%	57.30%	0.88
Body Mass Index			
Underweight	2.90%	0.90%	
Normal	37.70%	27.20%	
Overweight	37.50%	38.20%	
Obese	21.80%	33.60%	<0.001
BMI (mean ± SE)	26.7 ± 0.05	28.6 ± 0.07	<0.001
Race			
White	78.00%	70.80%	
Black	13.10%	15.90%	
Hispanic	7.70%	11.00%	
Other	1.30%	2.30%	<0.001
Education			
Some HS or less	30.30%	17.90%	
Completed HS	34.90%	31.20%	
Any college degree	34.80%	51.00%	<0.001
Marital Status			
Married or partnered	56.50%	70.10%	
Unmarried	43.50%	29.90%	<0.001
Self-reported health status in 2004			
Excellent/Very good	34.00%	45.40%	
Good	32.60%	29.60%	
Fair	23.00%	17.30%	

Poor	10.50%	7.70%	<0.001
Fall History			
Yes	32.80%	0%	
No	67.20%	100%	<0.001
Cigarette smoke			
Never smoker	43.00%	40.10%	
Former smoker	12.10%	0.17%	
Current smoker	44.90%	59.70%	<0.001
Drink Alcohol			
Abstainer	68.40%	51.30%	
Moderate drinker	17.70%	33.60%	
Heavy drinker	13.90%	15.20%	<0.001
Index of serious health conditions			
No chronic conditions	10.30%	29.60%	
1-2 chronic conditions	61.10%	57.90%	
3+ chronic conditions	28.60%	12.60%	<0.001
Index of Activities of Daily Living			
No difficulty with ADLs	79.70%	90.80%	
Difficulty with 1-5 ADLs	12.80%	7.70%	
Difficulty with 6+ ADLs	7.50%	1.50%	<0.001
Index of Nagi Functional Items			
No functional limitations	24.30%	41.20%	
Functional limitations with 1-4 items	49.70%	41.40%	
Functional limitations with 5+ items	26.00%	17.40%	<0.001

1. Participants included in the analytic cohort were compared to those not included in the cohort via the Student’s t-tests for continuous variables and the chi-square test for categorical variables.

VIII. <u>Mechanism by which risk factors affect hip fracture</u>

Risk Factors	Fall (↑ fall = ↑ Hip Fracture)	Bone Mineral Density (BMD) (↓ BMD = ↑ Hip Fracture)
Age	The incidence of falls increases with age. (62, 72, 93) A plausible mechanism is that as a person ages their bone density, muscle mass, and vision decreases, and coupled with slower reaction time, these factors places them at risk for falls and subsequent hip fracture(72).	As a person ages, BMD decreases. Warming and colleagues found, in women, minimal premenopausal bone loss only at the hip, postmenopausal bone loss at the distal forearm and hip (which lasts throughout postmenopausal life) and bone loss at the lumbar spine (that is only found in the first decade after menopause). In men <50 years of age Warming and colleagues found continuous bone loss throughout life at the hip and an accelerated bone loss in old age at the distal forearm (89).
Gender	For the younger old, fall rates for men and women are similar, but among the older old, women fall more often than men, and are far more likely to incur fractures when they fall (72)	Women loose BMD at a faster rate than men do. A woman's bone density declines by about 30% between the ages of 50 and 80. During the first 5 years after menopause, the decline is accelerated at some 2% annually (1). Low bone mass contributes to skeletal fragility and skeletal fragility is the principal cause of age-related osteoporotic fractures. The risk of breaking a hip doubles for each standard deviation reduction bone mineral density.
Body Mass Index	Person with low BMI might be frailer which could increase chances of fall. A low body mass index suggesting malnutrition is associated with an increased risk of falling. (12, 78) . Himes et al found obese adults were more likely to fall; however, because they have more soft tissue padding, they were less likely to have an injury due to the fall (20).	Underweight is associated with loss of BMD, which in turn increases the risk of hip fracture. Overweight/Obese is associated with increase in BMD, which helps lower the risk of hip fracture.
Race		Compared to Blacks and Hispanics, Whites typically have lower BMD. Asians have lower BMD than Whites on average.
Marital Status	Individuals who are living alone may not have readily available assistance for housekeeping and maintenance tasks that involve climbing, lifting, or moving heaving objects and this may place them at higher risk for falls. In a systematic review of literature on risk factors for falls, Bloch and colleagues found that (in a subgroup of patients older than	

	80) being married protected people from falling (OR 0.68; 95% CI 0.53, 0.87) (94, 95) . A meta-analysis of cohort studies was conducted by Manzoli and colleagues to produce an overall estimate of the excess mortality associated with being unmarried in elderly individuals and showed that marriage had a protective influence that remained significant, although the effect size was reduced (RR = 0.94; 0.92-0.95)(90).	
Self-reported health status	Those with chronic disease are more likely to report worse health, and those with more chronic disease are affected by fall.	Those with chronic disease are more likely to report worse health, and some chronic disease affect BMD (see index of serious health conditions section).
Cigarette smoke	Smoking may influence the fracture risk through other mechanisms unrelated to osteoporosis, such as poorer balance and physical performance due to neurovascular deleterious effects of smoking (96, 97) .	Smokers have lower BMD than non-smokers. Meta-analyses have shown that cigarette smoking is associated with reduced BMD and increased risk of fracture (91,92). The risk of fracture was increased with a smoking history and current smoking, but was higher for current smokers. Smoking may indirectly affect bone strength through decreases intestinal calcium absorption, increased metabolism or decreased production of estrogen and through hypercorticolism (24.)
Alcohol consumption	The relationship between alcohol use and falls appears to depend on the amount of alcohol consumed. In a study of 6000 men aged 65 years and older, light drinkers (less than 14 drinks per week) had a decreased risk of two or more falls in one year compared to abstainers (RR 0.77, 95% CI 0.65-0.92). However, men with problem drinking had a higher risk of two or more falls than those without problem drinking (RR 1.59, 95% CI 1.30-1.94) (98) . Too much alcohol consumed can lead to impaired balance and to falls.	Chronic alcohol consumption is widely considered a risk factor for low bone density – mostly in men. Though, moderate alcohol consumption can have a protective effect; moderate drinking = increased BMD (72).
Index of Serious Health Conditions (Chronic health conditions include = high blood pressure, arthritis, stroke, heart disease, cancer, and diabetes)	Diabetes-related visual and neurologic impairments could affect an individual's risk for falling and subsequently putting them at risk for a hip fracture (5, 99) . Stroke-related hemiplegia can lead to falling[65]. Chronic comorbidity and presence of polypharmacy have been documented as risk factors for falls (75, 94). The prevalence of falling increases with rising chronic disease burden. Thyroid dysfunction leading to excess circulating thyroid hormone, diabetes and arthritis	Stroke-related immobility induces sarcopenia and bone loss (67). Cancer treatments including hormone therapy and androgen deprivation therapy can decrease BMD (especially cancers that target the bone - myeloma). Myelomas are treated with corticosteroids and corticosteroids decrease muscle mass, lower muscle mass = lower BMD. Although the higher weight of many type 2 diabetic patients is likely the main contributor to of their overall higher BMD, at an equivalent body size to a non-diabetic older adult, type 2 diabetic

	leading to loss of peripheral sensation also increases risk of falling (72).	patients are more likely to fracture(5).
Index of Activities of Daily Living (ADLs) (Measures difficulty with = getting dressed + walking across the room + bathing + eating + using the toilet + getting in/out of bed + prepping meals + shopping for groceries + using the phone+ taking medications + managing money.)	In a systematic review of literature on risk factors for falls, Bloch and colleagues found that loss of autonomy is a major risk factor for falls: difficulties in at least one activity of daily living (OR 2.26; 95% CI 2.09, 2.45) or instrumental activities of daily living (OR 2.10; 95% CI 1.68,2.64) double the risk of falling (94) .	
Index of Nagi function items **(**Measures functional limitations with = blocks + sit + chair + stairs + stoop + reach + push + weights + dime.**)**	The decline in strength and endurance after the age of 30 (10% loss per decade) and muscle power (30% loss per decade) result in physical functioning dropping below the threshold where activities of daily living become difficult and then impossible to carry out – this can occur in early old age for those who have been sedentary most of their lives. When strength, endurance, muscle power and hence function declines sufficiently, one is unable to prevent a slip, trip or stumble becoming a fall (72, 78) . Gait or balance problems or functional limitations involving the lower limb can lead to falling (i.e. difficulty bending knee or stooping could result in instability of posture and may lead to falls)(72). Neuromuscular impairment – may not only increase the risk of falling but also influence an individual's speed, coordination, and protective responses during a fall (75). Poor physical performance, such as walking speed, lower extremity performance, and balance, increases the likelihood of falling (59).	If unable to participate in weight-bearing activities (pulling/pushing large objects. Lifting/carrying weights over 10lbs) could lead to lower BMD. Weight bearing exercises increases BMD. Activity produces a mechanical load on the bone through muscle contraction and surface impact, which contributes to bone formation and remodeling. It is considered that a lack of physical activity reduces mechanical load on bones, which can then lead to a decrease in bone density (59). Vitamin D deficiency is particularly common in older people in residential care facilities and may lead to abnormal gait, muscle weakness, osteomalacia and osteoporosis(72).

REFERENCES

1. Benetou V, Orfanos P, Benetos IS, et al. Anthropometry, physical activity and hip fractures in the elderly. Injury. 2011;42(2):188-93. (doi: 10.1016/j.injury.2010.08.022 [doi]).

2. Haentjens P, Magaziner J, Colon-Emeric CS, et al. Meta-analysis: excess mortality after hip fracture among older women and men. Ann Intern Med. 2010;152(6):380-90. (doi: 10.7326/0003-4819-152-6-201003160-00008 [doi]).

3. Fernandez-Ruiz M, Guerra-Vales JM, Trincado R, et al. Hip fracture in three elderly populations of central Spain: data from the NEDICES study. Intern Emerg Med. 2014;9(1):33-41. (doi: 10.1007/s11739-011-0728-y [doi]).

4. Wilson RT, Chase GA, Chrischilles EA, et al. Hip fracture risk among community-dwelling elderly people in the United States: a prospective study of physical, cognitive, and socioeconomic indicators. Am J Public Health. 2006;96(7):1210-8. (doi: AJPH.2005.077479 [pii]).

5. Strotmeyer ES, Kamineni A, Cauley JA, et al. Potential explanatory factors for higher incident hip fracture risk in older diabetic adults. Curr Gerontol Geriatr Res. 2011;2011:979270. (doi: 10.1155/2011/979270 [doi]).

6. De Laet C, Kanis JA, Oden A, et al. Body mass index as a predictor of fracture risk: a meta-analysis. Osteoporos Int. 2005;16(11):1330-8. (doi: 10.1007/s00198-005-1863-y [doi]).

7. Chevalley T, Guilley E, Herrmann FR, et al. Incidence of hip fracture over a 10-year period (1991-2000): reversal of a secular trend. Bone. 2007;40(5):1284-9. (doi: S8756-3282(06)00948-3 [pii]).

8. Chang KP, Center JR, Nguyen TV, et al. Incidence of hip and other osteoporotic fractures in elderly men and women: Dubbo Osteoporosis Epidemiology Study. J Bone Miner Res. 2004;19(4):532-6. (doi: 10.1359/JBMR.040109 [doi]).

9. Tang X, Liu G, Kang J, et al. Obesity and risk of hip fracture in adults: a meta-analysis of prospective cohort studies. PLoS One. 2013;8(4):e55077. (doi: 10.1371/journal.pone.0055077 [doi]).

10. Dargent-Molina P, Favier F, Grandjean H, et al. Fall-related factors and risk of hip fracture: the EPIDOS prospective study. Lancet. 1996;348(9021):145-9. (doi: S0140673696014407 [pii]).

11. Parkkari J, Kannus P, Palvanen M, et al. Majority of hip fractures occur as a result of a fall and impact on the greater trochanter of the femur: a prospective controlled hip fracture study with 206 consecutive patients. Calcif Tissue Int. 1999;65(3):183-7. (doi: CTI486 [pii]).

12. Himes CL, Reynolds SL. Effect of obesity on falls, injury, and disability. J Am Geriatr Soc. 2012;60(1):124-9. (doi: 10.1111/j.1532-5415.2011.03767.x [doi]).

13. Karagas MR, Lu-Yao GL, Barrett JA, et al. Heterogeneity of hip fracture: age, race, sex, and geographic patterns of femoral neck and trochanteric fractures among the US elderly. Am J Epidemiol. 1996;143(7):677-82.

14. Samelson EJ, Zhang Y, Kiel DP, et al. Effect of birth cohort on risk of hip fracture: age-specific incidence rates in the Framingham Study. Am J Public Health. 2002;92(5):858-62.

15. Scott JC. Osteoporosis and hip fractures. Rheum Dis Clin North Am. 1990;16(3):717-40.

16. Baron JA, Farahmand BY, Weiderpass E, et al. Cigarette smoking, alcohol consumption, and risk of hip fracture in women. Arch Intern Med. 2001;161(7):983-8. (doi: ioi00617 [pii]).

17. Hoidrup S, Prescott E, Sorensen TI, et al. Tobacco smoking and risk of hip fracture in men and women. Int J Epidemiol. 2000;29(2):253-9.

18. Cornuz J, Feskanich D, Willett WC, et al. Smoking, smoking cessation, and risk of hip fracture in women. Am J Med. 1999;106(3):311-4. (doi: S0002934399000224 [pii]).

19. Berg KM, Kunins HV, Jackson JL, et al. Association between alcohol consumption and both osteoporotic fracture and bone density. Am J Med. 2008;121(5):406-18. (doi: 10.1016/j.amjmed.2007.12.012 [doi]).

20. Mukamal KJ, Chung H, Jenny NS, et al. Alcohol consumption and risk of coronary heart disease in older adults: the Cardiovascular Health Study. J Am Geriatr Soc. 2006;54(1):30-7. (doi: JGS561 [pii]).

21. Espino DV, Palmer RF, Miles TP, et al. Prevalence, incidence, and risk factors associated with hip fractures in community-dwelling older Mexican Americans: results of the Hispanic EPESE study. Establish Population for the Epidemiologic Study for the Elderly. J Am Geriatr Soc. 2000;48(10):1252-60.

22. Yamashita T, Noe DA, Bailer AJ. Risk factors of falls in community-dwelling older adults: logistic regression tree analysis. Gerontologist. 2012;52(6):822-32. (doi: 10.1093/geront/gns043 [doi]).

23. Prieto-Alhambra D, Premaor MO, Fina Aviles F, et al. The association between fracture and obesity is site-dependent: a population-based study in postmenopausal women. J Bone Miner Res. 2012;27(2):294-300. (doi: 10.1002/jbmr.1466 [doi]).

24. Alfaro-Acha A, Ostir GV, Markides KS, et al. Cognitive status, body mass index, and hip fracture in older Hispanic adults. J Am Geriatr Soc. 2006;54(8):1251-5. (doi: JGS820 [pii]).

25. Nielson CM, Srikanth P, Orwoll ES. Obesity and fracture in men and women: an epidemiologic perspective. J Bone Miner Res. 2012;27(1):1-10. (doi: 10.1002/jbmr.1486 [doi]).

26. Compston JE, Flahive J, Hosmer DW, et al. Relationship of weight, height, and body mass index with fracture risk at different sites in postmenopausal women: the Global Longitudinal study of Osteoporosis in Women (GLOW). J Bone Miner Res. 2014;29(2):487-93. (doi: 10.1002/jbmr.2051 [doi]).

27. Sennerby U, Melhus H, Gedeborg R, et al. Cardiovascular diseases and risk of hip fracture. JAMA. 2009;302(15):1666-73. (doi: 10.1001/jama.2009.1463 [doi]).

28. Cooper C, Atkinson EJ, Jacobsen SJ, et al. Population-based study of survival after osteoporotic fractures. Am J Epidemiol. 1993;137(9):1001-5.

29. Cooper C, Coupland C, Mitchell M. Rheumatoid arthritis, corticosteroid therapy and hip fracture. Ann Rheum Dis. 1995;54(1):49-52.

30. Nielson CM, Marshall LM, Adams AL, et al. BMI and fracture risk in older men: the osteoporotic fractures in men study (MrOS). J Bone Miner Res. 2011;26(3):496-502. (doi: 10.1002/jbmr.235 [doi]).

31. Law MR, Hackshaw AK. A meta-analysis of cigarette smoking, bone mineral density and risk of hip fracture: recognition of a major effect. BMJ. 1997;315(7112):841-6.

32. Bauer DC, Browner WS, Cauley JA, et al. Factors associated with appendicular bone mass in older women. The Study of Osteoporotic Fractures Research Group. Ann Intern Med. 1993;118(9):657-65.

33. Butt DA, Mamdani M, Austin PC, et al. The risk of hip fracture after initiating antihypertensive drugs in the elderly. Arch Intern Med. 2012;172(22):1739-44. (doi: 10.1001/2013.jamainternmed.469 [doi]).

34. Tinetti ME, Han L, Lee DS, et al. Antihypertensive medications and serious fall injuries in a nationally representative sample of older adults. JAMA Intern Med. 2014;174(4):588-95. (doi: 10.1001/jamainternmed.2013.14764 [doi]).

35. Jacobsen SJ, Goldberg J, Miles TP, et al. Race and sex differences in mortality following fracture of the hip. Am J Public Health. 1992;82(8):1147-50.

36. Herringa SG., Connor J. *Technical description of the Health and Retirement Study sample design.* : National Institute of Health, 2010.

37. Health and Retirement Study 2004 Core Final, Version 1.0: Data Description and Usage. , 2006.

38. Ofstedal M, Weir D, Chen K, et al. *Updates to HRS Sample Weights*. : National Institute on Aging. National Institutes of Health., 2011.

39. Snyder AR, Parsons JT, Valovich McLeod TC, et al. Using disablement models and clinical outcomes assessment to enable evidence-based athletic training practice, part I: disablement models. J Athl Train. 2008;43(4):428-36. (doi: 10.4085/1062-6050-43.4.428 [doi]).

40. Jette AM. Toward a common language for function, disability, and health. Phys Ther. 2006;86(5):726-34.

41. Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. J Am Geriatr Soc. 1983;31(12):721-7.

42. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist. 1969;9(3):179-86.

43. World Health Organization's Global Database on Body Mass Index. *BMI Classification.* , 2012.

44. Karp F. Growing old in America: The Health and Retirement Study. : National Institute on Aging, National Institutes of Health, and U.S. Department of Health and Human Services., 2013.

45. Thompson ML, Myers JE, Kriebel D. Prevalence odds ratio or prevalence ratio in the analysis of cross sectional data: what is to be done? Occup Environ Med. 1998;55:272–277.

46. Bentler SE, Liu L, Obrizan M, et al. The aftermath of hip fracture: discharge placement, functional status change, and mortality. Am J Epidemiol. 2009;170(10):1290-9. (doi: 10.1093/aje/kwp266 [doi]).

47. Zingmond D, Melton LJ,3rd, Silverman S. Increasing hip fracture incidence in California Hispanics, 1983 to 2000. Osteoporosis International and other metabolic bone diseases. 2004;15(8):603-610.

48. Wright NC, Saag KG, Curtis JR, et al. Recent trends in hip fracture rates by race/ethnicity among older US adults. J Bone Miner Res. 2012;27(11):2325-32. (doi: 10.1002/jbmr.1684 [doi]).

49. Melton LJ,3rd, Therneau TM, Larson DR. Long-term trends in hip fracture prevalence: the influence of hip fracture incidence and survival. Osteoporos Int. 1998;8(1):68-74.

50. Wolinsky FD, Fitzgerald JF, Stump TE. The effect of hip fracture on mortality, hospitalization, and functional status: a prospective study. Am J Public Health. 1997;87(3):398-403.

51. Ahlborg HG, Johnell O, Turner CH, et al. Bone loss and bone size after menopause. N Engl J Med. 2003;349(4):327-34. (doi: 10.1056/NEJMoa022464 [doi]).

52. Cummings SR, Black DM, Nevitt MC, et al. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. Lancet. 1993;341(8837):72-5.

53. Kroger H, Tuppurainen M, Honkanen R, et al. Bone mineral density and risk factors for osteoporosis--a population-based study of 1600 perimenopausal women. Calcif Tissue Int. 1994;55(1):1-7.

54. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ. 1996;312(7041):1254-9.

55. Segal E, Zinman C, Raz B, et al. Current criteria for hip fracture risk assessment--are we missing something? Isr Med Assoc J. 2007;9(1):35-8.

56. American Academy of Family Physicians. Bone-density tests: When you need them and when you don't. Choosing Wiesly: an initiative of the ABIM Foundation, 2012.

57. Ahmed LA, Schirmer H, Berntsen GK, et al. Self-reported diseases and the risk of non-vertebral fractures: the Tromso study. Osteoporos Int. 2006;17(1):46-53. (doi: 10.1007/s00198-005-1892-6 [doi]).

58. Fang J, Freeman R, Jeganathan R, et al. Variations in hip fracture hospitalization rates among different race/ethnicity groups in New York City. Ethn Dis. 2004;14(2):280-4.

59. Lonnroos E, Kautiainen H, Karppi P, et al. Increased incidence of hip fractures. A population based-study in Finland. Bone. 2006;39(3):623-7. (doi: S8756-3282(06)00369-3 [pii]).

60. Khazzani H, Allali F, Bennani L, et al. The relationship between physical performance measures, bone mineral density, falls, and the risk of peripheral fracture: a cross-sectional analysis. BMC Public Health. 2009;9:297,2458-9-297. (doi: 10.1186/1471-2458-9-297 [doi]).

61. El-Khoury F, Cassou B, Charles MA, et al. The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systematic review and meta-analysis of randomised controlled trials. BMJ. 2013;347:f6234. (doi: 10.1136/bmj.f6234 [doi]).

62. Campbell AJ, Spears GF, Borrie MJ. Examination by logistic regression modelling of the variables which increase the relative risk of elderly women falling compared to elderly men. J Clin Epidemiol. 1990;43(12):1415-20.

63. De Laet CE, van Hout BA, Burger H, et al. Bone density and risk of hip fracture in men and women: cross sectional analysis. BMJ. 1997;315(7102):221-5.

64. Duan Y, Parfitt A, Seeman E. Vertebral bone mass, size, and volumetric density in women with spinal fractures. J Bone Miner Res. 1999;14(10):1796-802. (doi: jbm558 [pii]).

65. Greenspan SL, Myers ER, Maitland LA, et al. Fall severity and bone mineral density as risk factors for hip fracture in ambulatory elderly. JAMA. 1994;271(2):128-33.

66. Cummings SR, Rubin SM, Black D. The future of hip fractures in the United States. Numbers, costs, and potential effects of postmenopausal estrogen. Clin Orthop Relat Res. 1990;(252)(252):163-6.

67. Grisso JA, Kelsey JL, O'Brien LA, et al. Risk factors for hip fracture in men. Hip Fracture Study Group. Am J Epidemiol. 1997;145(9):786-93.

68. Johnell O, Kanis JA. An estimate of the worldwide prevalence, mortality and disability associated with hip fracture. Osteoporos Int. 2004;15(11):897-902. (doi: 10.1007/s00198-004-1627-0 [doi]).

69. Hayes WC, Myers ER, Morris JN, et al. Impact near the hip dominates fracture risk in elderly nursing home residents who fall. Calcif Tissue Int. 1993;52(3):192-8.

70. Schwartz AV, Nevitt MC, Brown BW,Jr, et al. Increased falling as a risk factor for fracture among older women: the study of osteoporotic fractures. Am J Epidemiol. 2005;161(2):180-5. (doi: 161/2/180 [pii]).

71. Marks R, Allegrante JP, Ronald MacKenzie C, et al. Hip fractures among the elderly: causes, consequences and control. Ageing Res Rev. 2003;2(1):57-93. (doi: S1568163702000454 [pii]).

72. Todd C, Skelton D. *What are the main risk factors for falls among older people and what are the most effective interventions to prevent these falls?* . Copenhagen: World Health Organization, 2014.

73. Schwartz AV, Sellmeyer DE, Ensrud KE, et al. Older women with diabetes have an increased risk of fracture: a prospective study. J Clin Endocrinol Metab. 2001;86(1):32-8. (doi: 10.1210/jcem.86.1.7139 [doi]).

74. Kang JH, Chung SD, Xirasagar S, et al. Increased risk of stroke in the year after a hip fracture: a population-based follow-up study. Stroke. 2011;42(2):336-41. (doi: 10.1161/STROKEAHA.110.595538 [doi]).

75. Aizen E. Falls in patients with stroke. Harefuah. 2014;153(3-4):195,8, 237.

76. Greendale GA, Barrett-Connor E, Ingles S, et al. Late physical and functional effects of osteoporotic fracture in women: the Rancho Bernardo Study. J Am Geriatr Soc. 1995;43(9):955-61.

77. Guccione AA, Felson DT, Anderson JJ, et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. Am J Public Health. 1994;84(3):351-8.

78. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med. 1988;319(26):1701-7. (doi: 10.1056/NEJM198812293192604 [doi]).

79. Lau EM, Suriwongpaisal P, Lee JK, et al. Risk factors for hip fracture in Asian men and women: the Asian osteoporosis study. J Bone Miner Res. 2001;16(3):572-80. (doi: 10.1359/jbmr.2001.16.3.572 [doi]).

80. McDowell MA, Fryar CD, Hirsch R, et al. Anthropometric reference data for children and adults: U.S. population, 1999-2002. Adv Data. 2005;(361)(361):1-5.

81. Kirkland LL, Kashiwagi DT, Burton MC, et al. The Charlson Comorbidity Index Score as a predictor of 30-day mortality after hip fracture surgery. Am J Med Qual. 2011;26(6):461-7. (doi: 10.1177/1062860611402188 [doi]).

82. Shapses SA, Sukumar D. Bone metabolism in obesity and weight loss. Annu Rev Nutr. 2012;32:287-309. (doi: 10.1146/annurev.nutr.012809.104655 [doi]).

83. Cumming RG. Nursing home residence and risk of hip fracture. Am J Epidemiol. 1996;143(12):1191-4.

84. Osnes EK, Lofthus CM, Meyer HE, et al. Consequences of hip fracture on activities of daily life and residential needs. Osteoporos Int. 2004;15(7):567-74. (doi: 10.1007/s00198-003-1583-0 [doi]).

85. Simpson CF, Boyd CM, Carlson MC, et al. Agreement between self-report of disease diagnoses and medical record validation in disabled older women: factors that modify agreement. J Am Geriatr Soc. 2004;52(1):123-7. (doi: 52021 [pii]).

86. Chami G, Jeys L, Freudmann M, et al. Are osteoporotic fractures being adequately investigated? A questionnaire of GP & orthopaedic surgeons. BMC Fam Pract. 2006;7:7. (doi: 1471-2296-7-7 [pii]).

87. Huddleston JM, Whitford KJ. Medical care of elderly patients with hip fractures. Mayo Clin Proc. 2001;76(3):295-8. (doi: S0025-6196(11)62891-7 [pii]).

88. Craik RL. Disability following hip fracture. Phys Ther. 1994;74(5):387-98.

89. US Congress, Office of Technology Assessment. Hip fracture outcomes in people age 50 and over. Washington, DC: US Government Printing Office, 1994.

90. Farahmand BY, Michaelsson K, Ahlbom A, et al. Survival after hip fracture. Osteoporos Int. 2005;16(12):1583-90. (doi: 10.1007/s00198-005-2024-z [doi]).

91. Rubenstein LZ, Josephson KR. The epidemiology of falls and syncope. Clin Geriatr Med. 2002;18(2):141-58.

92. Shumway-Cook A, Ciol MA, Gruber W, et al. Incidence of and risk factors for falls following hip fracture in community-dwelling older adults. Phys Ther. 2005;85(7):648-55.

93. Robbins AS, Rubenstein LZ, Josephson KR, et al. Predictors of falls among elderly people. Results of two population-based studies. Arch Intern Med. 1989;149(7):1628-33.

94. Bloch F, Thibaud M, Dugue B, et al. Episodes of falling among elderly people: a systematic review and meta-analysis of social and demographic pre-disposing characteristics. Clinics (Sao Paulo). 2010;65(9):895-903. (doi: S1807-59322010000900013 [pii]).

95. Manzoli L, Villari P, M Pirone G, et al. Marital status and mortality in the elderly: a systematic review and meta-analysis. Soc Sci Med. 2007;64(1):77-94. (doi: S0277-9536(06)00442-4 [pii]).

96. Ward KD, Klesges RC. A meta-analysis of the effects of cigarette smoking on bone mineral density. Calcif Tissue Int. 2001;68(5):259-70.

97. Kanis JA, Johnell O, Oden A, et al. Smoking and fracture risk: a meta-analysis. Osteoporos Int. 2005;16(2):155-62. (doi: 10.1007/s00198-004-1640-3 [doi]).

98. Cawthon PM, Harrison SL, Barrett-Connor E, et al. Alcohol intake and its relationship with bone mineral density, falls, and fracture risk in older men. J Am Geriatr Soc. 2006;54(11):1649-57. (doi: JGS912 [pii]).

99. Pit SW, Byles JE, Henry DA, et al. A Quality Use of Medicines program for general practitioners and older people: a cluster randomised controlled trial. Med J Aust. 2007;187(1):23-30. (doi: pit10990_fm [pii]).