

Development and Application of a
Probabilistic/Mechanistic Model to
Investigate the Influence of Safety Flooring
on Population-Level Hip Fracture Risk

by

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public

Abstract

Hip fractures are a devastating injury in the older adult population. They are almost exclusively sustained during a fall-related event, with lateral falls resulting in an impact to the proximal femur most highly associated with fracture risk. The health consequences of hip fractures, as well as their large associated costs, have led to extensive research on this topic. Of particular interest is the prediction of hip fractures. While certain mechanical factors, such as impact force and bone strength, are directly related with fracture outcomes during a lateral fall to the hip, many clinical tools or models used to predict risk of hip fracture (such as FRAX) do not explicitly incorporate these mechanical aspects into their predictions. Furthermore, these models do not lend themselves well to population-level analysis, as they require variables that are specific to each assessed individual. A population-level model could provide insight into the population-level risk of fall-related hip fracture risk, as well as explore the effectiveness of population-level interventions in a virtual environment.

Accordingly, the primary goal of this thesis project was to develop a mechanistically based probabilistic model of population-level hip fracture risk for Canadian older adults. The model generated virtual individuals (VI), to whom certain physical characteristics were pseudo-randomly assigned. These physical characteristics were used as inputs into algorithms used to estimate impact force and bone strength. Factor of Risk (FOR) was calculated as the ratio between impact force and bone strength, and used as a metric of hip fracture risk. The model was pseudo-validated by replicating groups of VI representing the 4 samples reported in Dufour et al, 2012; the model estimated group mean FOR within 0.05 of those reported in the article. To estimate the population-level risk of fall-related hip fracture in the Canadian older adults, the model was run with a sample

of 100 000 VI; the model estimates were characterized as distributions of FOR for both males and females, with the mean (SD) FOR being 0.067 (0.34) for females and 0.422 (0.23) for males.

The secondary goal of this thesis project was to develop a safety flooring intervention module, and implement it into the probabilistic model in order to estimate the influence of a population wide safety flooring intervention on hip fracture risk. A mechanical testing experiment was conducted to investigate the effects of fall and faller-specific factors (impact velocity, effective mass, TSTT, and pelvic stiffness) on the force attenuation provided by a SmartCells™ safety floor. Regression analyses revealed significant main effects ($p < 0.05$) for fall factors, as well as several interaction effects. The results of the analysis were used to generate a predictive equation for safety flooring force attenuation.

The model was modified to include the predictive equation as a safety floor force attenuation module (or sub-model), calculating intervened net force (subtracting the predicted safety flooring force attenuation from the net force) and computing the Intervened Factor of Risk (IFOR) from the ratio of intervened net force and bone strength. The modified model was run with a sample of 100 000 VI, computing both FOR and IFOR for each VI, and found that the safety flooring intervention lead to a 0.0231 (34.6%) decrease in mean IFOR from FOR, and a 0.1215 (28.8%) decrease for males. These findings suggest that a safety floor intervention can lead to a marked reduction in fall-related hip fracture risk for Canadian older adults. This thesis presents insight into the use of probabilistic methods for estimating population-level hip fracture risk, as well as provide an interesting example of virtually testing the effectiveness of an intervention on population-level hip fracture risk.

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Chapter 1

Thesis Overview and Objectives

Fall-related injuries are a serious concern in the older adult population. While this is a broad category of injuries, a significant portion of fall-related injuries in older adults are fall-related hip fractures. In fact, out of the 256 011 documented fall-related injuries sustained by older adult Canadians (65 years or older) between the year 2009/2010, 7% were hip fractures (Canadian Community Health Survey, 2012). The gravity of this problem is further highlighted by the fact that in the year 2010/11, the 25 495 documented hip fractures in older adult Canadians made up over one third of all fall-related hospitalizations in Canada (Canadian Community Health Survey, 2012). While age itself is a risk factor for falling (Campbell et al., 1989), and by extension, fall-related injuries, age is also associated with other factors that influence hip fracture risk, such as reduced bone quality (Akdeniz et al., 2009; Fatayerji et al., 1999) and altered or impaired balance (Pavol et al., 2002; Rogers et al., 2001).

The large number of fall-related hip fractures in the older adult population of Canada comes with an equally large economic burden on the healthcare system, with an average annual cost of 26 527 dollars per fracture, and an estimated overall cost of 650 million dollars per year (Wiktorowicz et al., 2001). While there is a substantial societal burden, a significant burden is also placed on the injured individual, as the fracture itself is debilitating and severely impedes mobility. With restricted or impeded mobility, quality of life may also diminish. Furthermore, long term outcomes aren't favorable, with approximately 20% of older adult hip fracture cases leading to death (Ioannidis et al., 2009, Jiang et al., 2005).

Fortunately, these exact factors have also sparked interest for research in this area. By researching how these injuries occur as well as what puts a person at risk, we can better understand

why they happen and how to better prevent them. As this is a common goal for almost all other injuries, a large body of literature has already been established for this specific injury in the older adult population. The mechanics of hip impacts and proximal femur fractures are still being investigated, with past research finding that impact force and bone strength are two important factors that can influence whether or not a hip impact results in a hip fracture (Dufour et al., 2012). And yet, there are many other factors that can directly influence either of these two main factors; or both in some special cases. Factors such as bone mineral density (BMD) would directly affect bone strength, while BMD itself may be modulated by age, height, mass, or a host of other factors. Many of these contributing factors have been established as “risk factors”; the sum of the risk posed by these risk factors is directly associated with the ultimate risk for hip fracture. Using this concept as a framework, different models have been developed to assess hip fracture risk in individuals. An example of one of these models is FRAX (Fracture Risk Assessment Tool), which uses the presence or absence of certain risk factors to determine a level at which an individual is at risk of sustaining a hip fracture (Kanis et al., 2008).

While these models are useful and can help us take preventative measures before the fall, and ultimately hip fracture, occurs, they are limited by the fact that an individual’s medical history, as well as risk factor information, must be available. Even if this data is available, these models are also limited by scope, as they are restricted to an individual, case by case, basis; they do not provide any estimates of hip fracture risk at a population-level. Although there is clear value in individual risk assessment, population-level estimates on hip fracture risk could be a valuable tool for policy decision makers, helping to develop and enforce prevention methods in an attempt to reduce the rates of hip fracture.

An example of a model that addresses all of the previously mentioned limitations would be a stochastic or probabilistic model. With such a model, a fictional individual is generated, with characteristics (such as age, height, weight, sex) being randomly assigned based on population-derived distributions. Using these assigned characteristics as inputs, previously defined models for impact force and bone strength can be implemented within the model to predict if, for this specific ‘person’, a hip fracture would occur following a lateral fall to the hip. This process is repeated many times, with each iteration representing a randomly generated ‘person’. Accordingly, by incorporating population-specific data, a model of this type could theoretically generate population estimates for fracture rates or population-level fracture risk. While probabilistic models have been used to gain insights into cervical spine injuries (Thacker et al., 2001) or to explore subacromial space changes with muscle fatigue (Chopp-Hurley et al., 2016), such approaches have never been applied to hip fractures.

This model structure could lend itself well to predict the effectiveness or influence of an intervention on the population-level risk of fall-related hip fractures. One promising intervention for fall-related hip fractures, and other fall-related injuries, is safety flooring. This purpose designed engineering material is proposed to absorb, or dissipate, energy and attenuate forces during a fall-related impact. What makes safety flooring a particularly promising intervention is that it is a much more passive intervention compared to other hip fracture prevention methods like hip-protectors, which need to be worn by an individual to be effective. However, initial studies have demonstrated that the force attenuation provided by safety flooring is influenced by sex and anthropometrics (Bhan et al., 2014; Laing and Robinovitch, 2009). The development of a regression equation or an algorithm that could predict safety flooring force attenuation as a function of factors such as body mass, body mass index, and trochanteric soft tissue thickness,

would provide novel insights to support hip fracture prevention efforts. Furthermore, an algorithm of this type could then be included into a population probabilistic model to predict the influence of safety flooring on population-level hip fracture risk.

Therefore, the overall goal of my thesis was to first develop a mechanistic, probabilistic model to predict population-level hip fracture risk in the older adult population of Canada, and secondly to use this model to assess the influence of safety flooring on population-level hip fracture risk. My general hypotheses were that: 1) A mechanistic based probabilistic model of hip fracture risk could be developed successfully pseudo-validated against an existing dataset and 2) introducing a safety flooring intervention into the model would lead to a substantive reduction in the predicted risk of fall-related hip fractures in the older adult population of Canada.

This thesis project was structured as three separate studies, each addressing different questions while still contributing to the overall goals of this thesis project. The first study, titled “Predicting Population-level Hip Fracture Risk: A Novel Probabilistic Modelling Approach Incorporating Factor of Risk Principles” (Chapter 3), involved the development, pseudo-validation, and application of a probabilistic, mechanistic model to predict the population-level hip fracture risk for Canadian older adults. The second study, titled “Safety flooring – Investigations of Biomechanical Effectiveness and Effects on Population-level Hip Fracture Risk” (Chapter 4), involved the mechanical testing (simulated lateral hip impacts using a surrogate human pelvis) of a safety flooring sample to quantify the influence of fall and faller-specific factors on the force attenuation provided by the safety flooring. Additionally, the results of this study were used to develop a regression equation that predicts safety flooring force attenuation in the event of a fall to the hip. The third and final study, titled “The Effect of a Simulated Safety Flooring Intervention on the Population-level Hip Fracture Risk for Canadian Older Adults” (Chapter 5),

combined the model developed in the first study with the regression equation developed in the second study to estimate the influence of a safety flooring intervention on the population-level risk. Furthermore, this study further evaluated the reliability of the model. Additional details of these studies are presented in their respective Chapters.

Chapter 2

Literature Review

2.1 Fall-Related Hip Fractures in Older Adults

The term ‘hip fracture’ is a general category of fractures in the proximal femur. Common sites include the femoral neck and intracapsular fractures, but can also include locations such as intertrochanteric fractures (fractures including the greater or lesser trochanter) or subtrochanteric fractures (fractures occurring just below the trochanters) (OrthoInfo, American Academy of Orthopaedic Surgeons, 2009). Just like other bone fractures, hip fractures are the result of an external load greater than the bone strength being applied to the bone. As these fractures occur within a bone involved in the loadbearing structures for stance and ambulation, mobility can become severely hindered and assistive devices such as wheelchairs are often required. While this severely hindered mobility is a deleterious outcome, what makes hip fractures such a serious concern in the older adult population is the fact that 20% of cases will lead to death in the first year of the injury (Ioannidis et al., 2009; Jiang et al., 2005). In the following sub sections, both the prevalence and the associated risk factors for hip fractures will be discussed.

2.1.1 Prevalence in the Older Adult Population of Canada

Hip fractures are a common fall-related injury in the older adult populations both in Canada and the rest of the world. As previously mentioned, they account for 7% of all fall-related injuries in the older adult population of Canada, yet account for over one third of all fall-related hospitalizations (Canadian Community Health Survey, 2012). While hip fractures can occur at any stage in life and can be due to more than just falls, the majority of hip fractures, approximately 95%, occur in older adults as a result of falls (Stevens and Olson, 2000; Wolinsky et al., 2009). In fact, a study by Jean et al regarding age-related trends in hip fracture rates in Canada between 1985

and 2005, found that the incidence rates for hip fractures do not deviate much between the age of 0 and 60 years, but increase exponentially as age increases beyond 60 years (Figure 2.1) (Jean et al., 2013). As can be seen from Figure 1, the rates of hip fracture increase exponentially for older adults, and the rates are much higher for females. In fact, Hopkin et al. found that 72.6% of the hip fractures reported in 2007/8 were sustained by females (Hopkins et al., 2012). This study quantified the lifetime risk of hip fractures (life table method, unadjusted) for both sexes, which were 12.1% for females and 4.6% for Canadian men; these estimates, done in 2008, were lower than the original estimates done in 1989, which were 14% and 5.2% for females and males, respectively (Kanis et al., 2002). And while Jean et al. also found a 31.8% decrease in age-adjusted hip fracture rates for females, and a 25.0% decrease for males (per 100 000 person-years, from 1985 to 2005), there were still 25 495 documented hip fracture hospitalizations for older adults in the year 2010/2011, which made up over one third of the 78 330 fall-related hospitalizations (Canadian Community Health Survey, 2012). These numbers show that, while not the most common fall-related injury, hip fractures pose a disproportionality large burden on the Canadian Health Care system.

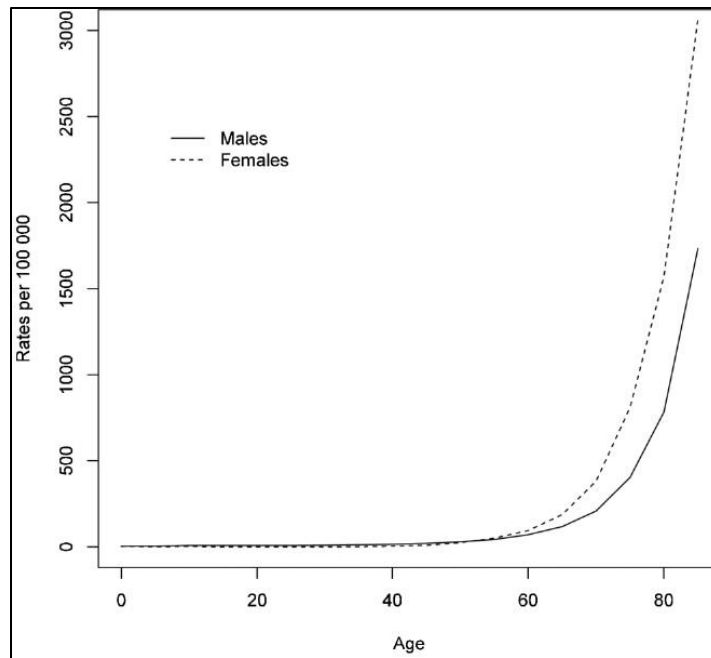


Figure 2.1: Hip fracture rates by age (years) in males and females in Canada, 1985 to 2005 (Jean et al., 2013)

Looking past the societal burden of hip fractures, these injuries pose an equally large economic burden. In fact, a study looking at all hip fracture cases between 1995 and 1996 in the Hamilton-Wentworth region (of Ontario) found that the average one year cost of a hip fracture was 26 527 dollars, but could raise to 44 156 dollars if the individual was moved to a long term care facility (Wiktorowicz et al., 2001). By combining both the average one year cost of a hip fracture with the total number of hip fractures in Canada (in 1995/6), the authors estimate a total annual cost of 650 million dollars for hip fractures in Canada.

In 2009/2010, there were 256 011 self-reported injurious falls sustained by older Canadians, and of the 78 330 that resulted in hospitalization, approximately 50% of the falls occurred at home and 17% occurred at residential institutions (Canadian Institute for Health Information, Hospital Morbidity Database). Though exact numbers of non-injurious falls are unknown for the older adult population of Canada, it is estimated that, worldwide, approximately

one third of older adults (30-35%) fall at least once per year (Blake et al., 1988; Campbell et al., 1989; Tinetti et al., 1992). Therefore, roughly 2.4 million older adults will fall at least once per year, with even higher numbers if we were to attempt to estimate the total number of individual falls. If we compare this 2.4 million falls estimate to the 25 495 hip fracture hospitalizations reported in 2010/2011, approximately 1.06% of all falls in this population result in a hip fracture. And while an estimated 95% of all hip fractures result from falls (Stevens and Olson, 2000; Wolinsky et al., 2009), the term “falls” itself is broad term, as falls can vary in many different ways, such as the direction of the fall (falling forwards, backwards, or sideways), the height of the fall (and the velocity of the impact), body configuration during the fall, impact surface, or the use of other limbs to break fall. These factors, and many more, are all risk factors and potential modulators of fracture outcome in the occurrence of a fall.

2.1.2 Associated Risk Factors

Previous studies have found many risk factors associated with hip fractures. Figure 1 (from Jean et al., 2013) depicts two very clear risk factors, the first of which is sex. More specifically, females are at increased risk of sustaining hip fractures (Blake et al., 1988; Campbell et al., 1989; Jean et al., 2013), and this sex disparity only increases as age, the second risk factor, also increases. While age is associated with increased risk of falling (Campbell et al., 1989) and sustaining a fall-related hip fracture, age itself is not the cause of increased hip fractures. Instead, it is the other factors that change with increased age that are risk factors for falling, and ultimately, hip fractures. One of these age-associated risk factors includes changes in balance, which can include changes in gait patterns (Winter et al., 1990), altered or reduced function of sensory systems (Lord et al., 1996), increased mediolateral instability (Rogers et al., 2001) as well as increased number of compensatory steps after a perturbation (McIlroy and Maki, 1996). Beyond the age-related risk of

falling, there are other relevant factors that are influenced by age. One such example is Bone Mineral Density (BMD), a key factor that is directly linked to bone strength. Although the concept of BMD, and how it relates to bone strength, will be further explored in section 2.2.2, previous studies have shown a link between decreasing BMD with increased age (Akdeniz et al., 2009; Fatayerji et al., 1999).

Additionally, low BMD (specifically of the pelvis and femur) is a risk factor in itself. In fact, a recent study, which used patient specific finite element models to study hip fractures, found that areal BMD of the proximal femur was a key factor in determining whether or not a fracture would occur from a lateral fall (Ferdous and Luo, 2015). This study also determined that body weight is also a key factor in determining fracture outcome during a lateral fall; a finding which is also supported by the link between body weight and peak impact force of lateral falls to the hip (Robinovitch et al., 1991). Although, it should be noted that more factors than weight affect peak impact force, such as height (which in turn affects impact velocity) and fall direction; these factors relate more to the mechanics of hip fractures and will be discussed in more detail in the following section.

Finally, there are other non-anthropometric risk factors for falls and fall-related hip fractures. Some of these risk factors include polypharmacy (i.e. prescription of multiple medications) and the use of assistive devices (such as canes) (Blake et al., 1988; Campbell et al., 1989), as well as family history of hip fractures, smoking and drinking status, oral glucocorticoid intake, presence of rheumatoid arthritis and previous fragility/osteoporotic fractures (Kanis et al., 2008). While these latter six risk factors are currently used in the World Health Organization Fracture Risk Assessment tool, information on these are not well defined on a population-level and are difficult to incorporate into a probabilistic model.

2.2 Mechanics of Hip Fractures

Structural failure of an object occurs when the applied load surpasses the strength, or tolerance, of the object. Similarly, bone fractures occur when they are subjected to a force or load that exceeds the bone strength (Figure 2.2). Historically, the relationship between applied load and bone strength when studying hip fractures from lateral falls has been reported as the Factor of Risk (FOR), which is a ratio of impact force to bone strength. Previous studies have shown that an elevated FOR is strongly associated with the future occurrence of hip fracture (a 1 SD increase in factor of risk was associated with roughly a 80% increase in hip fracture risk for males and a 23-41% increase for females) (Dufour et al., 2012). In the following section, I will present the mechanics of hip fractures from lateral falls, including the different factors that influence either the impact force or the bone strength, and how these factors play a crucial role in determining if a hip fracture will occur.

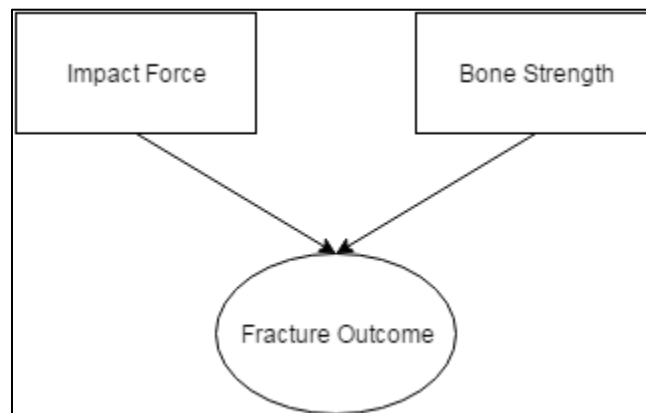


Figure 2.2: Simplified flowchart of factor of risk, where both impact force and bone strength play a role in determining whether or not a fracture occurs

2.2.1 Determinants of Impact Force

Beginning with the numerator for the Factor of Risk ratio, impact force plays a crucial role in fall-related hip fractures. The higher the impact force, the higher the risk of sustaining a hip fracture, while reductions in impact force result in a reduction of fracture risk. Of course, this is only one side of the ratio, and bone strength can also modulate fracture risk. While impact force can vary greatly with different impact scenarios, this portion of the literature review will focus on the determinants of impact force from lateral falls from the hip. The hip impact force correlates with the impact energy; an increase in the hip impact energy will lead to an increase in hip impact force. This impact energy ($E_{Impact} = \frac{1}{2}kx^2$) is driven entirely by the conversion of potential gravitational energy ($GE = mgh$) into kinetic energy ($KE = \frac{1}{2}mv^2$). Previous studies have used these equations to derive an estimate of impact force, where $F = \sqrt{2ghmk}$ predicts the impact force of an object with a mass m and stiffness k released from a height h (assuming the force of the impact is directed through a single point) (Robinovitch et al., 1991). With this in mind, impact force of an object is primarily determined by its impact velocity (which is governed by the height of the fall), mass and stiffness. And so, when observing a hip impact from a lateral fall in a human subject, impact force is primarily determined by the fall height, the subject's mass (or more specifically, the effective mass of the pelvis system) and the stiffness of the femur-pelvis system (Figure 2.3). This simplified equation has been used to predict impact force in previous studies (Bouxsein et al., 2007; Dufour et al., 2012; Van Den Kroonenberg et al., 1996), or built upon to use more complex models for the pelvis system, such as a Voigt model, which allowed the inclusion of a damping factor (Bhan et al., 2014; Laing and Robinovitch, 2010; Levine et al., 2013; Robinovitch et al., 1991).

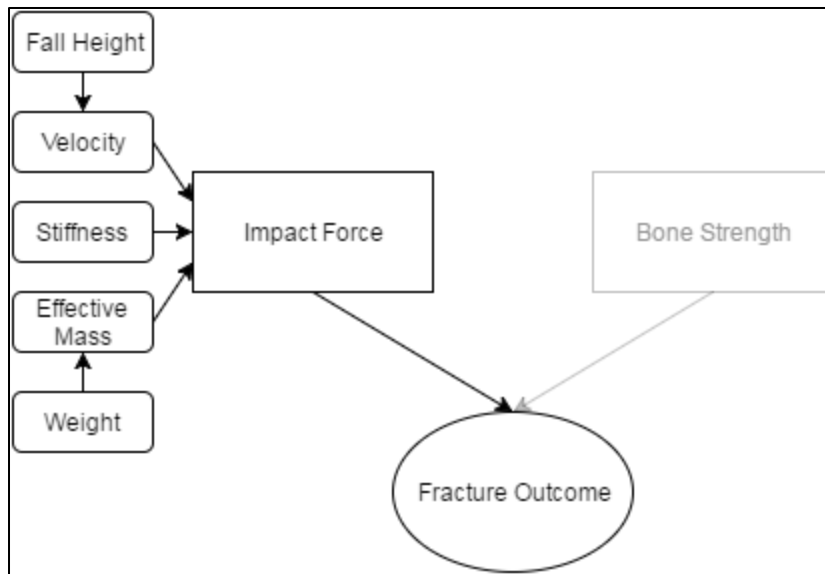


Figure 2.3: Impact Velocity, Pelvic Stiffness and Effective Mass are the primary Determinants of Impact force in a Direct Lateral Fall to the Hip

In a direct lateral fall onto the greater trochanter, the variable ‘ h ’ in the equation corresponds to the hip height of the individual (which is the height from the ground to the greater trochanter as measured when standing), or in some cases center of mass (COM) height; this has typically been calculated as 51% of the individuals height (Dufour et al., 2012). Hip impact studies that use the lateral pelvis release technique (Bhan et al., 2014; Laing and Robinovitch, 2010; Levine et al., 2013; Robinovitch et al., 1997a, 1991) adjust the release height of the participant (or height of the supporting sling) to modulate the impact velocity and ultimately change the impact force. These studies have shown that increasing the release height also increase the impact force.

Effective mass is another important driver of impact force. As mass increases, so does the potential gravitational energy, kinetic energy, and ultimately the hip impact force. Previous studies have described effective mass as the “mass of the pelvis and those portions of the trunk and lower limbs moving with a nonzero downward velocity” (Robinovitch et al., 1991). Simply put, it is the

portion of body mass that contributes to the impact force during a lateral fall to the hip. This has been measured in experimental studies using the lateral pelvis release paradigm. More specifically, effective mass has been defined as the steady state, or equilibrium, force measured by the force plate (after a lateral pelvis release trial) divided by gravity (Levine et al., 2013).

Finally, the stiffness of the pelvis system effects the peak impact force in lateral falls to the hip. In a study by Robinovitch and colleagues in 1991, a best-fit exponential function was used on the collected data from human volunteers, who were exposed to simulated lateral hip impacts, and found an average stiffness value of 90 440 N/m for males and 71 060 N/m for females. It should be noted that the r^2 values for the functions were 0.222 and 0.415, respectively, and so there is inherent variability of pelvic stiffness over the loading period. More recent studies have proposed much more conservative stiffness values, such as an average of 25 194 N/m for females and 34 271 N/m for males (Levine et al., 2013). While the human pelvis and thigh both have three-dimensional characteristics (and may be more accurately modelled with a Hertzian or volumetric contact model), and include velocity dependant damping factors (Laing and Robinovitch, 2010; Robinovitch et al., 1991), previous studies have shown that a mass spring model can accurately predict peak impact force (Robinovitch et al., 1997b).

2.2.2 Determinants of Bone Strength

While impact force plays a crucial role in determining the factor of risk, bone strength also plays an important role as it contributes equally to the factor of risk (Figure 2.4). When bone strength (typically reported as the fracture threshold, or the applied load necessary to cause the bone to fracture) is reduced, the risk of hip fracture increases. The problem is that determining that fracture threshold directly is currently difficult, and is not feasibly done *in vivo*. Traditionally, bone strength has been derived from cadaveric testing of bones. While different methods for

determining fracture threshold exist, most relevant to this thesis are simulated lateral impact to an excised cadaveric femur with the load going through the greater trochanter, as has been done in several studies. The specific goal of some of these studies was to determine the impact force necessary to fracture the excised femurs to then determine what physical characteristics of the bone correlate with this fracture threshold (Bouxsein et al., 1995; Chappard et al., 2010; Cheng et al., 1997; Dall’Ara et al., 2013). The majority of these studies observed that both Bone Mineral Density (BMD for short), and Bone Mineral Content (BMC), of the femur (of specific parts or of the whole bone) have strong positive correlations with the fracture threshold (r^2 ranging from 0.78 to 0.88 for the four studies referenced; more studies of this type exist) (Bouxsein et al., 1995; Chappard et al., 2010; Cheng et al., 1997; Dall’Ara et al., 2013). The remainder of the variance is most likely explained by geometry and micro-architecture. Nigg and Herzog 2007 summarize that bone density (and bone mass) are correlated with bone strength and stiffness (Nigg and Herzog, 2007).

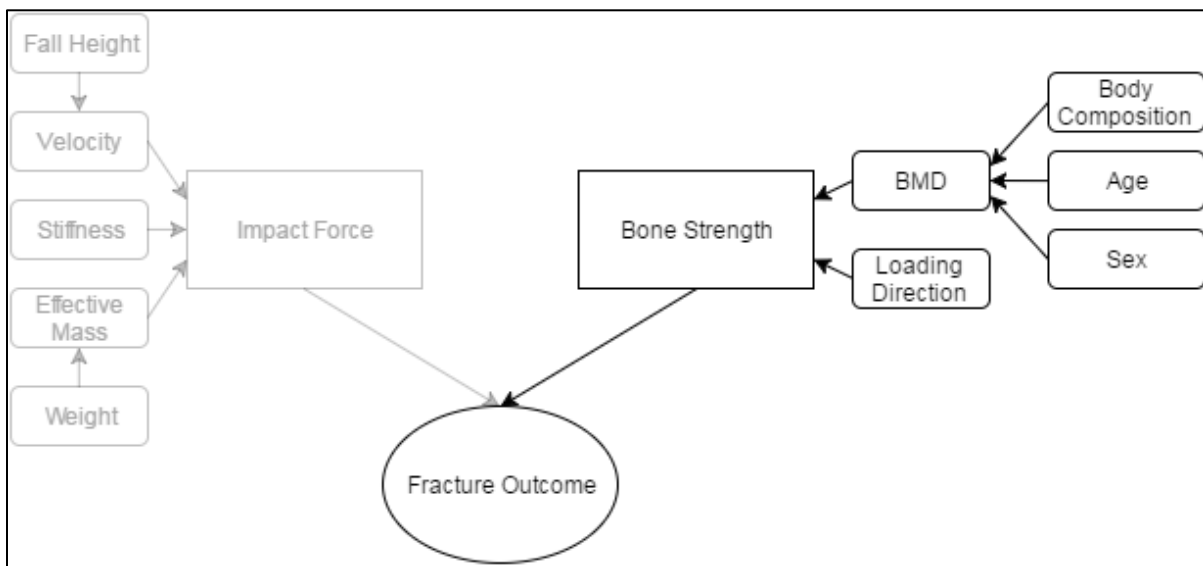


Figure 2.4: Bone Mineral Density (BMD) and Loading direction are the primary Determinants of Bone Strength

Bone mineral density is a measure of the structural mineral density within a bone, which has been shown to give insight into the strength or resilience of that bone. The importance of BMD is in its relative clinical relevance and ease to measure in vivo, which can be done with medical imaging devices such as x-rays, or with more purpose designed equipment like Dual Energy Xray Absorptiometry (DEXA, or DXA) which is most commonly used. These imaging devices allow us to image the skeletal structure and make inferences about certain characteristics of the bone (such as areal BMD) by the amount of the xray that is absorbed. Though this gives us a simple two-dimensional measure of the areal mineral density in part of a bone, this measure seems to explain a large portion of the variance when it comes to predicting fracture thresholds (Ferdous and Luo, 2015). Using this relationship, equations have been derived allowing us to predict the fracture threshold of a femur given the BMD, such as the regression equation derived by Roberts and colleagues in 2010, where:

$$\text{Femoral strength} = 8,207 \times (\text{femoral neck BMD (g/cm}^2\text{)}) - 568.62.$$

While BMD has been shown to be the primary correlate with bone strength, there are many factors that correlate or influence BMD, ultimately affecting bone strength. Firstly, there are age-dependent changes in femur BMD. While BMD fluctuates over the entire life course (increasing with growth), femoral neck BMD has been shown to decrease linearly in men between 20 and 79 years, with an approximate decrease of 21% over that time period (Fatayerji et al., 1999). Similarly, a study by Skrzek and colleagues found a pronounced decrease in femoral neck BMD of females between the ages of 40 and 75, with a noticeable and linear decrease beginning around 45 years (Skrzek et al., 2011). Even when focusing on the older adult population, a study by Hannan and colleagues in 1992 found that proximal femur BMD decreases linearly with age (between the ages

of 68 to 98 years) in both men and women, with no significant differences in the rates of decrease between sexes (Hannan et al., 1992).

While there no sex differences in the rate at which BMD decreases with age, there is a clear sex difference in rates of older adult hip fractures, with higher rates for females (Jean et al., 2013) which may be due to absolute differences in femoral BMD. While it is unclear whether or not the differences were significant, Hannan did notice that females had considerably lower femoral BMC than men in all three sites (femoral neck, greater trochanter and Ward's triangle) (Hannan et al., 1992). In fact, a study by Gong and colleagues in 2016 found a significant difference in femoral neck BMD between aged matched older adults with older adult females having significantly lower BMD than males (Gong et al., 2016). They also found significant sex differences in cross-sectional area (CSA) and cross-sectional moment of inertia (CSMI) of the femur, showing that there were differences in size and shape of the bones which will directly affect its strength.

Femoral BMD is also modulated by other physiological factors, such as body composition. Ahn and colleagues attempted to determine the relationship between different body compositions and BMD at different sites and found that increased fat mass (total, truncal, and peripheral fat mass) lead to decreased BMD (including femoral neck), and consequently, increases in lean mass (muscle mass) lead to increases in BMD (Ahn et al., 2014). As for BMI, a meta-analysis by De Laet and colleagues found that, without considering BMD, the relative risk of hip fracture seems to decrease non-linearly with increasing BMI, with the highest relative risk at the low BMI end (De Laet et al., 2005). However, when they also accounted for BMD, the relationship between BMI and fracture risk becomes a U shape, with higher risk at both the low and high ends of the BMI range, and the lowest relative risk when BMI was between 25 and 30 kg/m² (Figure 2.5). The BMI range of 25.0 to 29.9 kg/m² represents the Overweight, Pre-Obese, classification (World

Health Organization, 1995), meaning individuals with a BMI slightly higher than the range that is deemed normal, or recommended, are at a relatively lower risk of hip fracture.

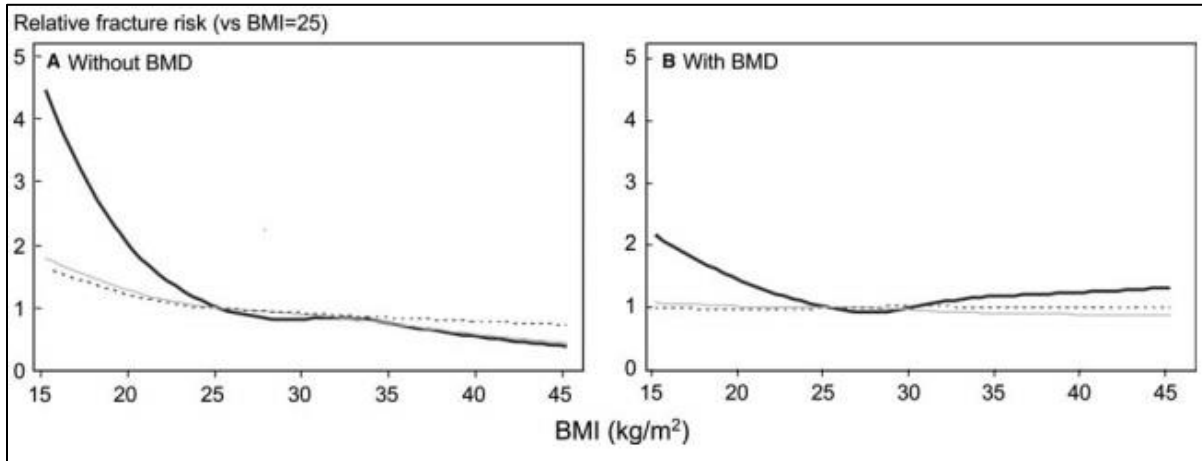


Figure 2.5: Relative risk of fractures (when compared to a BMI of 25 kg/m²). The bold black line represents hip fractures, the solid grey line represents osteoporotic fracture and the dotted line being any fracture. (De Laet et al., 2005)

Although the reduction in femoral neck BMD with age seems to be an important factor in hip fracture outcomes in older adults, what makes lateral falls onto the hip (proximal femur) a particularly common medium for hip fractures is the unique loading encountered during this event. As bones are a non-uniform material and undergo changes in size, structure and composition throughout the life course, bones have both viscoelastic and anisotropic material properties. This means that changes in either loading rate or direction will change the fracture threshold of the bone. While the loading rate is primarily determined by the impact velocity (as well as the compliance of the impact surface), the loading direction will depend on the fall direction and the body configuration during the fall. In a direct lateral fall to the hip (with the forces being primarily directed through the greater trochanter), there is compression of the superior aspect of the femoral neck and tension of the inferior aspect, as can be seen from Figure 2.6 (de Bakker et al., 2009).

Typically, the proximal femur experiences loading in the opposite direction when standing (tension of the superior aspect of the femoral neck, compression of the inferior aspect), which leads to the development of bone (proximal femur) resistant to this type of loading. Since the proximal femur is not typically loaded as it is during a direct lateral impact to the hip, the bone is “unprepared”, or not structured in a way to effectively resist these forces, meaning that the bone is more vulnerable to fracture.

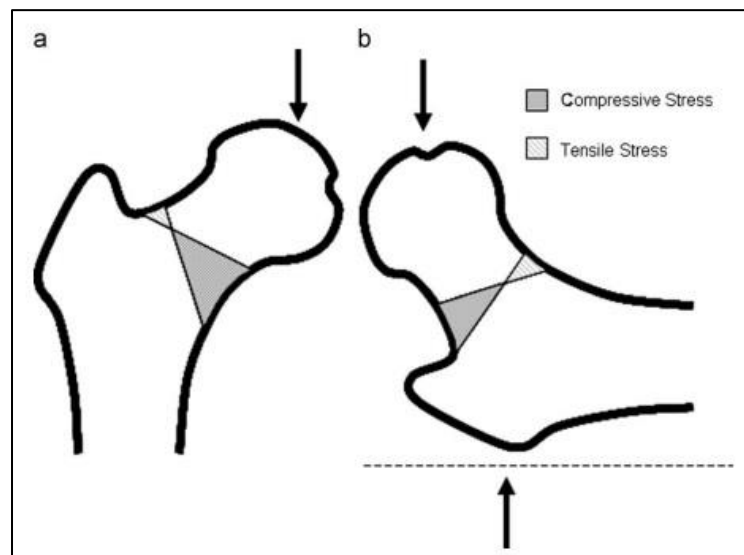


Figure 2.6: The differential and opposite loading of the proximal femur during (a) walking and (b) a lateral impact to the hip (de Bakker et al., 2009); in this figure, the arrows represent the principle loading vector in upright stance (a) and during a lateral hip impact (b)

2.2.3 Modulators of Fracture Outcome

While fracture outcome (in instances of lateral falls onto the hip) is determined by the combination of impact force and bone strength, there are other factors that may affect or modulate the outcome. These can be either internal or external modulators that affect either of the factor of risk components (impact force, or bone strength). For example, an internal modulator would be

the amount of soft tissue overlying the greater trochanter (also referred to as Trochanteric Soft Tissue Thickness, or TSTT). Robinovitch and colleagues (1995) reported that soft tissue overlying the greater trochanter can provide cushioning or energy absorption during a lateral hip impact, resulting in a reduction in peak impact force of roughly 71 N for every 1 mm of TSTT (Robinovitch et al., 1995). As an increase in BMI is positively associated with increases in TSTT (Maitland et al., 1993), we see decreases in peak force, normalized to body weight, with higher BMI (Levine et al., 2013). This relationship between increased BMI and TSTT, as well as the subsequent reductions peak force, may explain the previously mentioned reduction in hip fracture risk for the pre-obese overweight BMI group. Interestingly, increases in BMI will also lead to increases in effective mass and increased impact force (Levine et al., 2013; Robinovitch et al., 1991), which may help explain the rising risk of hip fracture with increases in BMI beyond the pre-obese classification.

An example of an external modulator of fracture outcomes would be any intervention method being applied or administered to an older adult faller. One such example would be protective hip pads (or hip protectors), which are products designed to cover the hip (covering the greater trochanter and surrounding thigh area) and absorb, or shunt, energy during a hip impact event. These products attempt to mimic the protective qualities of additional TSTT by adding an extra layer of protective padding. A previous study by Laing and Robinovitch in 2008 found that certain hip protectors can significantly reduce impact forces, but the force attenuation ability of the different hip protectors can vary greatly depending on other factors like impact velocity, the stiffness of the soft tissue underlying the hip protector and even the size or shape of the hip or pelvis (Laing and Robinovitch, 2008). Regardless of the variability in impact attenuation, the effectiveness of these products is further hindered by compliance issues (as in, older adults either

forget, or choose not, to wear these products) as this intervention requires active participation of the user (Van Schoor et al., 2002). And while an active intervention, such as hip protectors, can be effective if the compliance issues were resolved, compliance (of the user, or potential faller) is not an issue for more passive interventions such as safety flooring.

Like hip protectors, safety flooring is designed to reduce impact forces by either absorbing or shunting energy, or a combination of the two, during an impact event. This can be done through different means, such as additional foam padding beneath typical flooring surfaces (like carpet or linoleum), or with purpose-designed engineering materials that remain stable underfoot but buckle during an impact event. Although the energy absorption (or energy dissipation) provided by safety flooring will depend on the specific type of safety flooring, certain types have been shown to absorb significantly more energy, and significantly reduce peak force, when compared to hip impacts onto typical flooring (Bhan et al., 2014; Glinka et al., 2013; Lachance et al., 2017; Laing and Robinovitch, 2009).

Previous studies that have investigated the force attenuation properties of safety flooring have all characterized these force attenuation properties as percent force attenuation (when compared to a similar impact on a rigid surface). While percent force attenuation has been reported as the main variable of biomechanical effectiveness, this metric doesn't provide any direct insight into hip fracture outcomes or how safety flooring may affect hip fracture risk. Furthermore, these studies are limited in terms of the generalizability of their results, as they have only been tested at low impact velocities with a cohort of young adults, or at higher impact velocities through mechanical testing with an impact simulator that attempted to mimic a lateral hip impact in an "average" older adult female. The effects, and interactions, of factors like effective mass, pelvic stiffness, or soft tissue thickness (and subsequent force attenuation) on the force attenuating

properties of safety flooring are not well studied, and so the effectiveness of safety flooring may change with these factors. These limitations in the literature could be addressed through more thorough mechanical testing, allowing for the development of force attenuation prediction algorithms for safety floors, which was conducted as part of this thesis project (see Chapter 4).

Similar to hip protectors, factors such as impact velocity can affect the force attenuation properties of safety floors, with certain floors providing greater force attenuation with increased velocities, while others provide less (Glinka et al., 2013; Laing and Robinovitch, 2009). Furthermore, the amount of energy absorbed by safety floors can be affected by the BMI of the faller, as a study by Bhan and colleagues in 2014 found that four of the five safety floors tested absorbed significantly more energy for low-BMI subjects compared to high-BMI subjects (Bhan et al., 2014). While user compliance is not an issue for this intervention method, safety flooring does require policy makers, stakeholders, and contractors to decide on installing safety flooring (which could result in increased construction costs). Regardless, if safety flooring was installed in key locations (such as locations with high incidences of hip fractures), it may help prevent hip fractures.

2.3 A Modelling Approach to Injury Prevention

Mathematical models are often applied to different systems or mechanisms to help understand them or predict outcomes. This is no different for models of human injury, where modelling concepts are applied to different injury scenarios to help quantify the mechanism, predict the outcomes, or even estimate the influence of different interventions. There are many different types of models which differ in structure, function, and purpose. This portion of the literature review will first focus on previously developed or currently used models for hip fracture

risk or hip fracture outcome. The second part of this section will focus on probabilistic models, specifically reviewing probabilistic models of human injury.

2.3.1 Models of Hip Fracture Risk

As explained previously, hip fractures are a serious health concern for the older adult population and is well researched. Many different models have resulted from this research, from models which aim to predict which older adults are at a particularly high risk of hip fracture, to models that attempt to predict the impact force subjected to the proximal femur during an impact event. One example of a model of hip fracture risk would be the factor of risk (FOR) model used by Bouxsein in 2007, and again by Dufour in 2012. While factor of risk itself is a concept, and not explicitly a model, it was first applied to fracture risk prediction by Hayes and colleagues in 1991, where fracture load was related to some measure of bone strength (Hayes et al. 1991). This concept was then used by both Bouxsein in 2007 and Dufour in 2012 as the basis for a model to predict hip fractures. They did so by incorporating several different sub-models to predict both impact force and bone strength.

Deterministic models of predicted impact force (Robinovitch et al., 1991), force attenuation (Robinovitch et al., 1995) and bone strength (Roberts et al., 2010) (based on a number of subject specific inputs) were combined to result in a deterministically-driven prediction of hip fracture risk. By comparing the model predictions of a large cohort of males and females to the actual hip fracture outcomes within this cohort, Dufour and colleagues found that group mean factor of risk was significantly different between fracture and non-fracture groups for both males and females. It should be noted that while that the mean factor of risk for the male fracture group was a value of 1 (and the male non-fracture group had a mean factor of risk value of 0.87), this was not so for the female groups (mean factor of risk value of 0.49 for female fracture group, and

0.41 for the female non-fracture group) (Dufour et al., 2012). This is most likely due to oversimplification of the model, such as relationship between TSTT and force attenuation (linear and non-limited force attenuation), and highlights that factor of risk may not be appropriate as a tool to predict potential fracture outcomes, but may be better used as a metric of hip fracture risk (acting as a baseline to compare intervened results to).

As the concept of factor of risk is derived from engineering practices, factor of risk models (like the one used by Dufour and colleagues) have a mechanical or physical basis. Another example of a mechanically driven model would be finite element models of the hip and the proximal femur, such as the two dimensional, subject specific finite element model of the proximal femur developed by Ferdous and Luo in 2015. DXA scans of the proximal femur were used to generate the subject specific finite element models, allowing the experimenters to simulate falls, or impacts with this model. From this, fracture risk was assessed through indices at different areas of the proximal femur, which are based on the stresses observed in the different elements (Ferdous and Luo, 2015).

As opposed to mechanistic models, epidemiological approaches for predict hip fracture risk exist. An example of this type of model would be the Fracture Risk Assessment Tool (or FRAX) developed by Kanis and colleagues, in collaboration with the World Health Organization, in 2008. This model computes the ten-year probability of an individual to suffer a hip fracture by using subject specific inputs for age, height and mass, as well as the presence or absence of other risk variables, which include the history of a prior fragility fracture, smoking status, presence of rheumatoid arthritis and a few other “risk variables” (Kanis et al., 2008). And so, a higher ten-year probability of hip fracture relates to an overall increased risk of sustaining a hip fracture in the future. FRAX is but one example of an epidemiological prediction tool used for hip fracture risk;

others include the Canadian Association of Radiologist and Osteoporosis Canada (CAROC) risk assessment tool, and other country/demographic-specific risk assessment tools or tables.

As highlighted above, there are many different model paradigms that can be used to assess or predict an individual's hip fracture risk. Unfortunately, these models all have a major limitation in the form of their restriction to individual, or subject specific, inputs or predictions. While these models can be used to predict the risk of each individual within a given population, they do not inherently produce a measure of the risk of hip fracture on a population-level; further steps must be taken to achieve such a measure with these models. Furthermore, some of these models are further limited by their inputs as some of these are not known on a population-level or, in some cases, require medical images. One of the main motivations for this thesis was to develop a population-level model of hip fracture risk that only uses readily available population data as its main inputs, and further derives non-available population data from known relationships (for example, the relationship between BMI and TSTT). One type of model, or model structure, that would allow for this population-level model would be a probabilistic, or stochastic, model, allowing us to use known distributions to simulate cohort of realistic individuals.

2.3.2 Probabilistic Models of Human Injury

The models presented in the previous section are all examples of deterministic models. Deterministic models assume that the inputs are exact and precise, allowing for exact and precise outputs. Although this allows us to make clear conclusions, deterministic models do not account for the variability of the human body, or the uncertainty in our measurements. Probabilistic models, on the other hand, incorporate this uncertainty in the inputs and allows for an element, or elements, of randomness when predicting the outputs and the likelihood of those outputs (Laz and Browne, 2010). To achieve this input uncertainty, distributions of each input parameter are first defined;

this then allows the model to generate a random variable (representing an input parameter) that follows the defined distribution. By running a large number of simulations of random sampling, such as Monte Carlo simulations, this method allows for a distribution of outputs to be calculated.

This model structure used in a biomechanics context allows us to capture or account for human variability in the inputs (given that the input parameter distributions properly represent the population of interest), allowing us to then account for that same human variability in our outputs. While deterministic models tend to dominate the field of injury biomechanics, probabilistic models can be logically applied to certain injury mechanisms. As there is variability within the injured individual, as well as variability in the exposure, there will always be variability in the outcomes. One example of a probabilistic model structure being applied to injury mechanisms would be the “Probabilistic orthopaedic population model to predict fatigue-related subacromial geometric variability” model developed by Chopp-Hurley and colleagues (Chopp-Hurley et al., 2016). This model uses the Monte Carlo method (as well as other probabilistic modeling approaches) to randomly sample changes in different parameters (kinematic and morphological) of the shoulder complex to then quantify their effect on the minimal subacromial space (SAS). As previous research has found that decreased SAS leads to increased risk shoulder impingement and rotator cuff injuries, this model was used to perform a sensitivity analysis on these parameters to determine which of these parameters most influence the minimum SAS. Although this is but one example, probabilistic modelling methods have been applied to other injury mechanisms, such as a probabilistic injury function for cervical spine injury (Thacker et al., 2001), or orthopaedic problems, like using probabilistic methods to test the structural integrity of cemented hip implants (Bah and Browne, 2009), or the application of probabilistic methods to a finite element model of seat belt caused rib fractures (Forman et al., 2012).

One of the injury mechanisms that hasn't been investigated using probabilistic methods are hip fractures, or more specifically, hip fractures from lateral falls to the hip. While deterministic models, such as the previously discussed factor of risk models, can help predict relative hip fracture risk in an individual, they do not take into account the individual variability present in some of the parameters (such as how their BMI relates to their TSTT, and how that then relates to force attenuation). Furthermore, the currently available models do not allow for population-level predictions or analyses. Applying probabilistic modelling methods to a mechanistic model of hip fracture (using the factor of risk principle) would allow for both of these limitations to be overcome by accounting for uncertainty in the input parameters, as well as simulating a realistic population of individuals.

2.4 Literature Review Summary

In summary, this review has highlighted some key gaps in the hip fracture risk literature, most notably:

1. While subject specific models for hip fracture risk prediction exist, there are no population-level models for hip fracture risk prediction
2. Though probabilistic methods have previously been applied to injury mechanisms, these methods have yet to be applied to fall-related hip fracture mechanisms
3. The effect and interactions of impact velocity, effective mass, pelvic stiffness, BMI and TSTT on the impact attenuating properties of safety flooring has not properly been investigated, preventing the inclusion of this potential intervention into hip fracture risk prediction models

4. The effectiveness of safety flooring as a population-level intervention has yet to be investigated

This thesis intended to fill these gaps in the literature by developing a population-level model for hip fracture risk prediction using probabilistic methods to capture the inherent variability between subjects. This model defined the distribution of factor of risk for fall-related hip fracture risk of the Canadian older adult population. Furthermore, this thesis investigated the effect of anthropometrics and fall parameters on the force attenuating properties of safety flooring and successfully developed a safety flooring force reduction algorithm. This algorithm was then included into the probabilistic model structure to evaluate the effectiveness of safety flooring as an intervention for fall-related hip fractures. This was done by analyzing the change in the distribution of factor of risk in the older adult population of Canada for falls with and without safety flooring present.

Chapter 3

Predicting Population-level Hip Fracture Risk: A Novel Probabilistic Modelling Approach Incorporating Factor of Risk Principles

3.1 Introduction

Fall-related injuries are a serious concern in the older adult population. While this is a broad category of injuries, a significant portion of fall-related injuries in older adults are fall-related hip fractures. In fact, out of the 256 011 documented fall-related injuries sustained by older adult Canadians (65 years or older) between the year 2009/2010, 7% were hip fractures (Canadian Community Health Survey, 2012). The gravity of this problem is further highlighted by the fact that in the year 2010/11, the 25 495 documented hip fractures in older adult Canadians made up over one third of all fall-related hospitalizations in Canada (Canadian Community Health Survey, 2012). While age itself is a risk factor for falling (Campbell et al., 1989), and by extension, fall-related injuries, age is also associated with other factors that influence hip fracture risk, such as reduced bone quality (Akdeniz et al., 2009; Fatayerji et al., 1999) and altered or impaired balance (Pavol et al., 2002; Rogers et al., 2001).

The large number of fall-related hip fractures in the older adult population of Canada comes with an equally large economic burden on the healthcare system, with an average annual year cost of 26 527 dollars per fracture, and an estimated overall cost of 650 million dollars per year (Wiktorowicz et al., 2001). While there is a substantial societal burden, a significant burden is also placed on the injured individual, as the fracture itself is debilitating and severely impedes mobility. With restricted or impeded mobility, quality of life may also diminish. Furthermore, long term outcomes aren't favorable, with approximately 20% of older adult hip fracture cases leading to death in the first year of the injury (Ioannidis et al., 2009, Jiang et al., 2005).

Fortunately, these exact factors have also sparked interest for research in this area. By researching how these injuries occur, as well as what puts a person at risk, we can better understand why they happen and how to better prevent them. As this is a common goal for almost all other injuries, a large body of literature has already been established for this specific injury in the older adult population. The mechanics of hip impacts and proximal femur fractures are still being investigated, with past research finding that impact force and bone strength are two important factors that can influence whether or not a hip impact results in a hip fracture (Dufour et al., 2012). And yet, there are many other factors that can directly influence either of these two main factors; or both in some special cases. Factors such as bone mineral density (BMD) will directly affect bone strength, while BMD itself may be modulated by age, height, mass or a host of other factors. Many of these contributing factors have been established as “risk factors”; the sum of the risk posed by these risk factors is directly associated with the ultimate risk for hip fracture. Using this concept as a framework, different models have been developed to assess hip fracture risk in individuals. An example of one of these models is FRAX (Fracture Risk Assessment Tool), which uses the presence or absence of certain risk factors to determine a level at which an individual is at risk of sustaining a hip fracture (Kanis et al., 2008).

While these models are useful and can help us take preventative measures before the fall, and ultimately hip fracture, occurs, they are limited by the fact that an individual’s medical history, as well as risk factor information, must be available. Even if this data is available, these models are also limited by scope, as they are restricted to an individual, case by case, basis; they do not provide any estimates of hip fracture risk at a population-level. Although there is clear value in individual risk assessment, population-level estimates on hip fracture risk could be a valuable tool

for policy decision makers, helping to develop and enforce prevention methods to reduce the rates of hip fracture.

An example of a model that addresses all of the previously mentioned limitations would be a stochastic or probabilistic model. With such a model, a fictional individual is generated with characteristics (such as age, height, mass, sex) being pseudo-randomly assigned based on population-derived distributions. This process is repeated, with each iteration representing a randomly generated 'person', resulting in a large sample of virtual individuals. Using the assigned characteristics of the virtual individuals as inputs, previously defined models can be used to estimate both impact force and bone strength. The ratio between impact force and bone strength results in a Factor of Risk (FOR), which is a concept adopted from mechanical engineering. When FOR is greater or equal to one, which results when the applied load (impact force) surpasses the material tolerance (bone strength), structural failure (hip fracture) is expected. Factor of Risk principles have previously been applied to the context of hip fracture risk assessment (Bouxsein et al, 2007; Dufour et al, 2012), and therefore can be implemented within the model to predict risk hip fracture following a lateral fall to the hip. Accordingly, by incorporating population-specific data, a model of this type could theoretically generate population estimates for population-level hip fracture risk. While probabilistic models have been used to gain insights into cervical spine injuries (Thacker et al., 2001), seat belt caused rib fractures (Forman et al.2011). or to explore subacromial space changes with muscle fatigue (Chopp-Hurley et al., 2016), such approaches have never been applied to hip fractures.

The goal of this study was to develop and validate a probabilistic model to predict population-level hip fracture risk in older adults using factor of risk principles. To do so, the model was designed to use probabilistic methods to generate virtual individuals and assign parameters to

each virtual individual. Factor of Risk was then calculated for each virtual individual. The model was then validated by comparing model output group mean FOR to the 4 groups reported by Dufour et al, 2012. We hypothesized that the model estimates would mimic the results reported by Dufour et al, 2012, with model estimate group mean FOR values within 0.05 of the reported values for the respective groups. Additionally, we hypothesized that there would be significant differences between group mean FOR for the fracture and no fracture groups, for both females and males. Secondly, a virtual sample representative of the older adult population of Canada was generated and population-level risk was predicted using the model. We hypothesized that the mean FOR would be higher for males when compared to females, and that the male distribution of FOR would be more right shifted than the female distribution. Although this is contrary to what has been reported, we expect that the model estimates would reflect the trends reported by Dufour et al 2012. A regression analysis of FOR by age was conducted for both males and females to assess the influence of age on FOR. It was hypothesized that a positive linear correlation would be observed in the mean FOR of 5-year age groups (with FOR increasing with age), reflecting the increase in hip fracture rates observed as age increases (Jean et al., 2013). Finally, a sensitivity analysis was conducted to determine the relative influence of each individual parameter on FOR.

3.2: Methods

3.2.1: Model Development

The model was structured into two levels, with an upper-level ‘subject characterization’ portion, and a lower-level ‘mechanistic model’ portion. A general overview of the model structure can be seen in figure 3.1. The subject characterization portion of the model consists of generating virtual individuals (VI), and assigning physical characteristics of interest (such as age, height, mass, and sex). These characteristics were pseudo-randomly assigned along the probability distribution of that characteristic in the population, or sample, of interest. Monte Carlo simulations are conducted during this process, generating the desired number of VIs. These VIs (or more specifically their assigned characteristics) were used as the inputs for the lower-level mechanistic model. Using previously defined models for predicting fall-related impact force and estimated femur fracture threshold (bone strength), Factor of Risk (FOR) was calculated for each VI, where:

$$\mathbf{Factor\ of\ Risk} = \frac{\mathbf{Impact\ force}}{\mathbf{Bone\ Strength}} \quad [\text{Equation 3.1}]$$

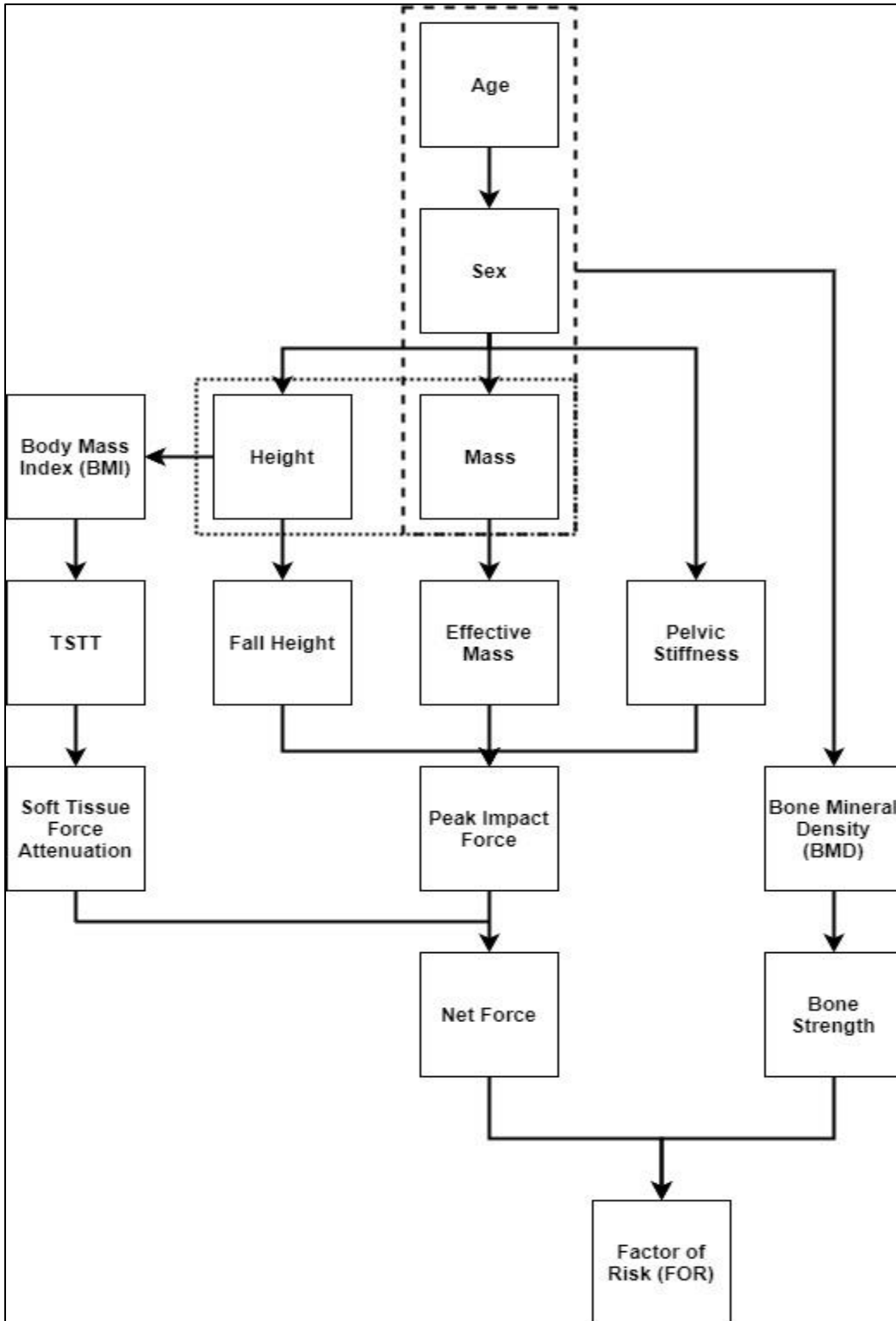


Figure 3.1: Simplified Model Structure: this figure represents the flow (from assigning physical characteristics to the VI, through calculating FOR) for one individual VI; this process is repeated for each VI generated

Probabilistic models incorporate an element of uncertainty, which is included as input uncertainty or uncertainty in outputs of predictive equations. This thesis project's model was no different, and incorporated uncertainty when pseudo-randomly assigning the characteristics to the VIs, as well as in the outputs of predictive equations used in the mechanistic model portion of the model. While this increased the variability, it helped better represent the variability observed in the population.

3.2.1.1: Subject Characterization

The upper-level portion of the model generated virtual individuals (VI) by randomly assigning physical characteristics sequentially. The physical characteristics of interest are age, sex, height, mass, and pelvic stiffness; these physical characteristics are the necessary inputs into the later sub-models used in the mechanistic modelling portion which are used to ultimately calculate factor of risk (FOR). As the end goal of this model was to assess the population-level hip fracture risk of the older adult population of Canada, the model structure was influenced by the format in which the available population data was presented. For this reason, physical characteristics were assigned sequentially (age, sex, height, mass, and pelvic stiffness, in that order).

3.2.1.1.1: Age Assignment

The method used to assign age to the VIs depended entirely on the format in which a sample's or population's age was presented and subsequently characterized. In the event that age of the population of interest was presented as a mean and standard deviation (as was the case for validation purposes), it was characterized as normal distribution with the same mean and standard deviation; generating a random variable along that normal distribution would yield a random age. In order to predict hip fracture risk at the national level, the Canadian Annual Demographic Estimates (which lists the number of female and males citizens in 5 year ages bins

between ages 60-100, as seen in Figure 3.2) was used to generate a polynomial function was used to extrapolate the probability density for each 1 year age increment. From this, a cumulative density function was defined (see Figure 3.3), where the probability density associated with each age (a) in years between 60 and 100 was calculated by

$$\hat{p} = -0.000127 * a^2 - 0.027456 * a + 1.475331. \text{ [Equation 3.2].}$$

By generating a uniformly distributed random variable between 0 and 1, age was assigned to the VI by comparing the random variable to the CDF to find the age associated with that cumulative probability density.

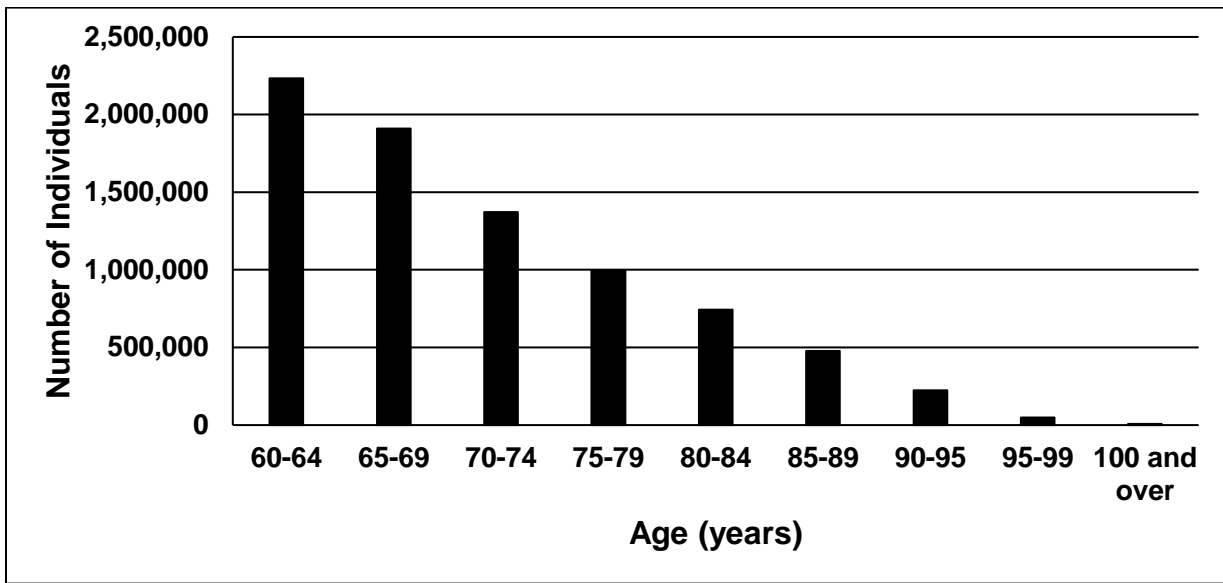


Figure 3.2: Bar graph of the older adult population of Canada divided by 5 year age groups

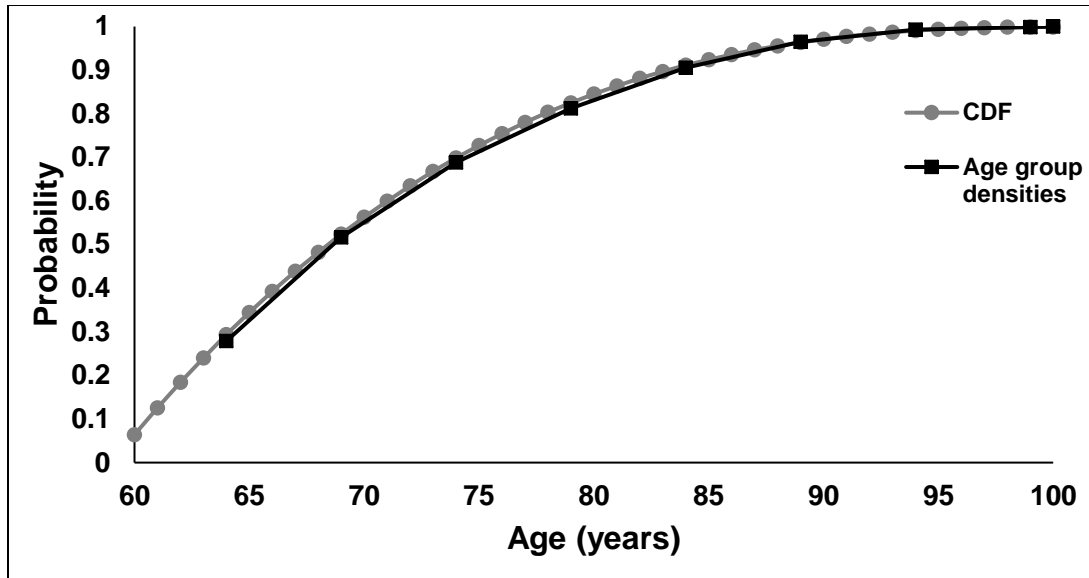


Figure 3.3: CDF of Canadian older adult age by years compared to the cumulative probability densities of the age groups presented in the CCHS. The squares and bold black line represent these age groups, with the squares being anchored at the upper-limit

3.2.1.1.2: Sex Assignment

The model allows for both a specific number of females and males VIs to be set (which was done for the model pseudo-validation), or to set a total number of desired VI, which was split between females and males (which was done when the model was applied to the Canadian older adult population). When the age specific number of females and males are available, such as in the Canadian Annual Demographic Estimates, sex ratios (proportion of males from the total number of citizens in that age strata) are defined. By generating a uniformly distributed random variable between 0 and 1, sex (“1” for males, “2” for females) was assigned to the VI by comparing the random variable; if the variable was less than the male ratio for that age strata, that VI was defined as a male, else the VI was defined as female.

3.2.1.1.3: Height and Mass Assignment

For the pseudo-validation of the model, the mean and standard deviations for height and mass of the reported samples were used to define normal distributions. Generating a random variable along the normal distribution for height yielded random height; this was done similarly with mass. When applied to the Canadian older adult population, the Canadian Health Measures Survey (which lists the average, and 95% confidence interval, heights and masses for the 5th, 10th, 25th, 50, 75th, 90th and 95th percentile female and male Canadians) was used to develop a polynomial function (as was done for age). More specifically, the average values (for the seven listed percentiles) for the oldest age group (60 to 79 years) were used to develop a polynomial function to represent the Canadian older adult population. To properly characterize the population distributions, a second order polynomial was developed for height (allowing extrapolation of the probability density for each 0.5 cm increment), where the probability density of each height increment for females was calculated by

$$p(h) = -25.9947 \cdot h^2 + 82.7646 \cdot h - 65.5944 \text{ [Equation 3.3]}$$

and for males was calculated by

$$p(h) = -24.6223 \cdot h^2 + 84.6544 \cdot h - 72.4768 \text{ [Equation 3.4].}$$

This method was also employed for mass, instead using a third order polynomial (allowing extrapolation of the probability density for each 0.5 kg increment), where the probability density of each mass increment for females was calculated by

$$p(m) = 0.0001786 \cdot m^3 - 0.0045 \cdot m^2 - 0.3663 \cdot m - 9.3676 \text{ [Equation 3.5]}$$

and for males was calculated by

$$p(m) = 0.00010730 \cdot m^3 - 0.0032 \cdot m^2 - 0.3101 \cdot m - 9.4198 \text{ [Equation 3.6].}$$

From these, sex-specific cumulative density functions were defined for both height and mass (by adding the probability density of each subsequent height or mass increment). As done for Age, a uniformly distributed random variable between 0 and 1 was generated, allowing for height and mass to be assigned to the VI by comparing the newly generated randomly variable to the CDF to find the height or mass associated with that cumulative probability.

3.2.1.1.4: Pelvic Stiffness Assignment

For the model validation portion, a set pelvic stiffness value was used for males and females (90440 N/m and 71060 N/m, respectively) as was used by Dufour et al, 2012. More recently published data (based on observed pelvic deflection during simulated lateral falls to the hip) have reported much lower pelvic stiffness values. One such example is a study published in 2013 by Levine and colleagues, where mean and standard deviation values of 34271 (9464) N/m reported for males, and values of 25194 (6126) N/m for females. To better represent the variance observed in the population, as well as align with current literature, these mean and standard deviation values were used to define sex specific normal distributions pelvic stiffness and a random variable (K) can be generated, where

$$K \sim N(34271, 9464^2) \text{ for males}$$

$$\text{and } K \sim N(25194, 6126^2) \text{ for females.}$$

3.2.1.2: Mechanistic Model

The mechanistic model portion was comprised of the 11 sub-models required to calculate estimated impact force and femoral bone strength. The model used to predict fall-related impact

force was first used in the context of fall-related hip impacts by Robinovitch and colleagues in 1991, where

$$\mathbf{Impact\ Force} = \sqrt{2ghmk} \quad [\text{Equation 3.7}].$$

More recently, Dufour et al. (2012) used this equation to retrospectively estimate fall-related hip impact when quantifying Factor of Risk in a cohort of older adult males and females (Dufour et al, 2012). Force attenuation provided by the soft tissue overlying the greater trochanter (trochanteric soft tissue thickness, TSTT) was also accounted for, where,

$$\mathbf{Soft\ Tissue\ Force\ Attenuation\ (N)} = 71 \left(\frac{N}{mm} \right) * \mathbf{TSTT\ (mm)} \quad [\text{Equation 3.8}];$$

Net Impact Force was then calculated;

$$\mathbf{Net\ Impact\ Force\ (N)} = \mathbf{Impact\ Force} - \mathbf{Soft\ Tissue\ Force\ Attenuation} \quad [\text{Equation 3.9}].$$

The model used to estimate femoral bone strength was the same used by Dufour and colleagues (2012) derived from Roberts (2010), where

$$\mathbf{Femoral\ Strength\ (N)} = 8207 * \mathbf{femoral\ neck\ BMD} \left(\frac{g}{cm^2} \right) - 568.62 \quad [\text{Equation 3.10}].$$

During the model validation phase fall height (h) was calculated as 0.51* the height if the VI to align with the approaches in Dufour et al. (2012). For the model application phase, h was assigned based on a normal distribution of fall height ratios (hr) as a proportion of total body height, where

$$HR \sim N(0.5857, 6.24 * 10^{-5}).$$

This distribution was based on the mean, and standard deviation, ratio of COM height to total body height reported by Chandler and colleagues (1975).

For the mass (m) input, values of 39 kg for males and 31 kg for females, which were first established by Robinovitch et al, 1991, were used during the model validation (to replicate the

approach used in Dufour et al (2012). In the model application phase, normal distributions (male and female) of effective mass ratios (*em*) as a proportion of total body mass were employed, where

$$\text{Male: } EM \sim N(0.467, 0.043),$$

$$\text{Female: } EM \sim N(0.553, 0.029).$$

This distribution was based on the mean, and standard deviation, ratio of effective mass to total body mass of subjects measured by Martel and colleagues (2017).

To estimate TSTT for the model validation phase, two separate regression equations estimating TSTT from BMI were used, where

$$\text{Male: } TSTT (mm) = 2.3415 * BMI - 33.444 \text{ (Nielsen 2009)} \quad [\text{Equation 3.11}],$$

$$\text{Female: } TSTT (mm) = 3.4795 * BMI - 38.015 \text{ (Bouxsein 2007)} \quad [\text{Equation 3.12}].$$

An alternative approach was employed in the model application phase utilizing data collected in our lab (Lafleur, 2016), where

$$TSTT (mm) = s * -2.218 + BMI * 0.313 - 3.312 \text{ (R}^2 = 0.734) \quad [\text{Equation 3.13}].$$

In this equation, *s* was a binary variable for sex (males = 1, females = 0). Additionally, uncertainty was included in this input, where the result of this equation for a given VI was as the mean of a normal distribution (with the square of the standard error of this equation being used as the variance), where

$$T \sim N(TSTT, 1.12015^2).$$

A random variable generated along this distribution was then assigned to that particular VI as their TSTT.

To estimate femoral neck BMD for the model validation portion, 4 normal distributions with the means and standard deviations of each of the 4 reported groups were generated. BMD was assigned to the VI by generating a random variable along the distribution that corresponded

with their group allocation. An alternative regression approach was used for model application based on data from our lab (Lafleur 2016), where

$$BMD (mm) = a * -0.006 + s * 0.058 + m * 0.005 + 0.818 (R^2 = 0.340) \text{ [Equation 3.14].}$$

In this equation, s was a binary variable for sex as in the estimate for TSTT, a was the age of the VI, and m was their total body mass. Additionally, uncertainty was included in this input, where the result of this equation for a given VI was used as the mean of a normal distribution (with the square of the standard error of this equation being used as the variance), where

$$B \sim N(BMD, 0.13438^2).$$

A random variable generated along this distribution was then assigned to that particular VI as their femoral neck BMD.

With these variables defined, Net Impact Force (Equation 3.9) and Femoral Bone Strength (3.10) were calculated and Factor of Risk (FOR) (Equation 3.1) were quantified in both the Model Validation and Application phases.

3.2.2: Model Validation

To validate the model, model outputs (in the form of group mean FOR) were compared to values reported by Dufour et al, 2012. To do so, 4 separate groups of VIs ($N = 1000$, for each group) were generated. In all instances, the same sub-models and equations used in Dufour et al's 2012 study were used in this model. Once the VI's were generated, FOR was calculated and group mean FORs were compiled. An objective threshold (maximum difference of 0.05 FOR between model and reported group mean FOR) was set a-priori to indicate successful model validation. This process was conducted a total of 10 times in order to assess variability in the model. The average difference between reported group mean FOR and the 10 model group mean FOR values were calculated and again, a threshold (maximum difference of 0.05 FOR) was set for model

variability as well.

3.2.3: Model Application

The model was applied to the older adult population of Canada. As mentioned in section 3.2.1.1 of the Methods, population data was used to generate representative distributions of age, sex, height and mass. Furthermore, certain sub-models were updated to better reflect current literature as well as include elements of uncertainty. One complete simulation of the model was conducted with a sample of 100 000 virtual individuals being generated. Mean (SD) FOR was compiled both for males and females. To better represent the population distribution of hip fracture risk, FOR distributions were characterized for males and females.

3.2.4: Sensitivity Analysis

To conduct a sensitivity analysis, model parameters (aligning with physical characteristics of interest) were independently varied to assess the influence of that parameter of FOR, independent of changes in other parameters. With the exceptions of age, all parameters were held to their mean value (based on the Canadian older adult population) while the parameter of interest was considered at seven values (-3 to +3 standard deviations of that parameter's mean. For age, it was considered between ages 60-100 in 5-year increments. The sensitivity analyses were performed separately for females and males; in both cases one VI was generated (with the set parameters assigned) and FOR was calculated.

For both male and female sensitivity analyses, 54 VIs were generated, each assigned with a unique set of parameters. The first VI for both sexes, referred to as the baseline, were assigned the sex specific mean values for each parameter, which are height, mass, pelvic stiffness (which was not assessed in this analysis), fall height ratio, effective mass ratio. For the baseline, values for TSTT and BMD were assigned based on the outputs of both regression equations used

previously in the model application portion; unlike in the model application portion, these equations were used deterministically to remove uncertainty. Each of the following VI's generated maintained all but one of the same parameter values as the baseline; the unique parameter that was assigned was either +/-1, +/-2, +/-3 SD of the mean value of that parameter.

When the unique parameter was either TSTT or BMD, uncertainty was reintroduced and values assigned were done so using probabilistic methods (finding a mean and +/- 3 standard deviations). To include uncertainty, the deterministic values for TSTT and BMD that were defined previously for the baseline were then used as the mean to define a normal distribution. One thousand random variables were generated along each of these distributions, from which the mean and standard deviation were calculated; these values (mean and +/- 3 SD) were assigned to 14 new VIs (7 for each TSTT and BMD).

3.2.5: Fracture Point Analysis

While theoretically fractures should occur in instances where the FOR is greater or equal to one, the results presented in Dufour et al, 2012 show that fractures can occur at values below 1 (using their proposed model and assumptions). Although the goal of this study (and the overall goal of this thesis project) wasn't to develop a model to predict fracture outcomes, but instead attempt to quantify risk, determining some sort of threshold (Fracture Point) value of FOR that determines whether a fracture was more likely to occur or not (or the opposite, if below the threshold) could be valuable to put a FOR value in context. To do so, the data presented in Dufour et al, 2012 was once again used to help determine sex-specific Fracture Point values that differentiate between the reported fracture groups (non-fracture and fracture). The model structure used in the pseudo-validation was modified to replace the non-measured parameters (effective mass, pelvic stiffness, TSTT, and fall height) with the sub-models that were used in the model

application experiment for those parameters. Performing 50 simulations (of 10 000 VI in each group), group mean FOR was computed at each simulation, and the grand mean FOR values for the 4 groups were calculated (mean across all 50 simulations). For each sex, the Fracture Point was determined as the FOR value directly between the two group mean values (non-fracture and fracture group), which we called the Midpoint method. This value was then compared to the data generated in the model application experiment to determine the number (and percentage) of VI who had a FOR value greater than the Fracture Point. A secondary method of determining the Fracture Point is presented in Appendix A.

3.2.6: Statistics and data interpretation

3.2.6.1: Pseudo-Validation

The pseudo-validation of the model was conducted in such a manner to pseudo-validate the model on a per-simulation basis, and on an overall basis (to demonstrate the repeatability of the model estimates). To pseudo-validate the model on a per-simulation basis, the model estimate group mean FOR of all four groups were compared to the respective group mean FOR values reported by Dufour et al, 2012. The model estimate was deemed valid if the absolute difference between the model estimate and reported group mean FOR was less than or equal to 0.05. This comparison was performed for all 4 groups in each of the 10 simulations (resulting in a total of 40 comparisons, 10 for each group). To pseudo-validate the model on an overall basis, the grand group mean FOR (combining the mean FOR estimates of the 10 simulations for each group, separately) was calculated for all 4 groups; these values were compared to the difference threshold of 0.05. To further evaluate the validity of the model, the grand mean was computed for age, height, mass and BMD for all 4 groups; these values were compared to the respective mean values reported in Dufour et al, 2012. This was performed as a form of verification of the model, testing

the ability of the model to generate a properly representative sample of VI. Additionally, T-tests (two-tailed) were performed on group mean FOR between fracture groups (fracture vs no fracture) within sex (similar to the analyses performed by Dufour et al, 2012). As was observed by Dufour et al, 2012, we hypothesize that there would be a significant difference between the group mean FOR values of the fracture groups, for both females and males. T-tests were performed using the SPSS statistical processing software package (SPSS Version 21, SPSS Inc., Chicago, IL, USA) using an α of 0.05

3.5.6.2 Model Application

As stated above in section 3.2.3, the mean (SD) FOR was computed for both females and males, and the values compared between sexes. Furthermore, the distributions of FOR were characterized for both female and males, allowing us to visually represent the range of risk for both sexes. To assess the influence of age on FOR, a univariate ANOVA was performed for both female and male FOR. Additionally, group mean (SD) FOR was compiled for males and females at each 5-year age interval between 60 and 100 years. This compiled data was used to further analyse the effect of age on FOR with a linear regression model on the age-group mean FOR values for males and females (using mean FOR data of all 5-year age groups, which are: 60-64 years, 65-69 years, 70-74 years, 75-79 years, 80-84 years, 85-89 years, 90-94 years, and 95-100 years). All ANOVA statistical analyses were performed using the SPSS statistical processing software package (SPSS Version 21, SPSS Inc., Chicago, IL, USA) using an α of 0.05, and the linear regression analysis was performed in the RStudio software package (RStudio Version 1.0.136, RStudio Inc., Boston, MA, USA) using the R statistical programming language (R Core Team, 2015).

3.2.6.3 Sensitivity Analysis

Changes in FOR (due to changes in a given parameter) were assessed using linear regression, with the seven data points (baseline and +/- 3 SD) of each parameter being characterised as a regression. To assess which factors had the greatest potential effect on FOR, we assessed the slopes (or correlation coefficients) of the regression line; theoretically, the higher the slope of the line of best fit, the larger the effect of changes in that parameter on FOR. While the influence of all factors were reported, we highlighted the two parameters with the greatest observed effect on FOR. All linear regression analyses were performed in the RStudio software package (RStudio Version 1.0.136, RStudio Inc., Boston, MA, USA) using the R statistical programming language (R Core Team, 2015).

3.2.6.4 Fracture Point Analysis

The FOR distributions (list of FOR values for each VI) for both females and males were compared to their sex-specific *Fracture Point* values, determining VI who's predicted FOR value was greater than their respective *Fracture Point*. The total number of such cases was computed for both sexes; these values were also reported as a percentage of the total number of VI for the respective sexes. Additional analyses used a secondary method of determining the Fracture Point are outlined and is presented in Appendix A.

3.3: Results

3.3.1: Model Validation

After 10 iterations of the model validation process, mean and standard deviations of all randomly generated input variables (age, height, mass, BMD) were compiled to compare to group mean reported by Dufour et al, 2012. When compiled over the 10 iterations, the group means for all input variables had less than 1% difference when compared to the reported means, though group

means of individual iterations ranged as high as a 5.7% difference (Table 3.1).

When examining model FOR outputs, variability was observed across the 10 iterations, with some of the model estimated group mean FOR values differing from the reported values by more than the 0.05 threshold (Figure 3.4). However, the overall mean difference between reported and model FOR were all below or equal to the 0.05 threshold for all 4 groups (Table 3.1).

During these simulations, there were instances where a VI had an estimated FOR of less than 0 (a negative FOR value), which were due to negative net force values. As a negative net force is not theoretically possible (in the specific context presented), and by extension a negative FOR is not possible, instances where a negative FOR occurred were noted. In a secondary analysis, these negative FOR values were corrected to a value of 0, and the overall group means were computed for FOR. While the grand mean FOR values changed very little for the male fracture and no fracture groups, noticeable changes were observed in the both female groups (most notably the female non-fracture group). The results of this secondary analysis are included in Table 3.1, and can be seen in Figure 3.5.

Estimates of FOR were significantly influenced by sex ($t = 183.248$, $p < 0.001$), with male values (on average) 2.19-fold greater than females. FOR was also significantly different between control (no fracture) and hip fracture groups, when compared within sex. For males, there was a significant difference in mean FOR between the fracture groups ($t = -38.014$, $p < 0.001$), with a 13% difference in mean FOR. Likewise for females, a significant difference in mean FOR was observed between fracture groups ($t = -30.335$, $p < 0.001$), with a 26% difference in mean FOR.

Table 3.1: Comparison of mean values (Dufour 2012 vs mean of 10 model simulation). The absolute difference was calculated, as well as the percent difference (absolute difference/reported mean value). The “Adjusted FOR” row represents the data after converting negative FOR values

Parameters	Male, No Fracture			Male, Fracture			Female, No Fracture			Female, Fracture		
	Dufour (2012)	Model Estimate	Difference (%)	Dufour (2012)	Model Estimate	Difference (%)	Dufour (2012)	Model Estimate	Difference (%)	Dufour (2012)	Model Estimate	Difference (%)
Age (year)	75.0	75.04	0.04 (0.06)	78.4	78.36	0.04 (0.05)	75.4	75.46	0.06 (0.08)	77.1	77.11	0.01 (0.01)
Height (m)	1.704	1.703	0.00 (0.04)	1.712	1.711	0.00 (0.06)	1.562	1.562	0.00 (0.00)	1.562	1.562	0.00 (0.01)
Mass (kg)	78.9	78.88	0.00 (0.00)	78.7	78.8	0.13 (0.16)	65.5	65.37	0.13 (0.20)	61.4	61.42	0.02 (0.03)
BMD (g/cm²)	0.878	0.876	0.00 (0.23)	0.778	0.778	0.00 (0.02)	0.730	0.731	0.00 (0.18)	0.665	0.664	0.00 (0.09)
FOR	0.87	0.872	0.00 (0.22)	1.00	0.999	0.00 (0.15)	0.41	0.362	0.05 (11.6)	0.49	0.491	0.00 (0.26)
Adjusted FOR	0.84	0.872	0.00 (0.22)	1.00	0.999	0.00 (0.15)	0.41	0.415	0.01 (1.29)	0.49	0.527	0.04 (7.49)

to 0

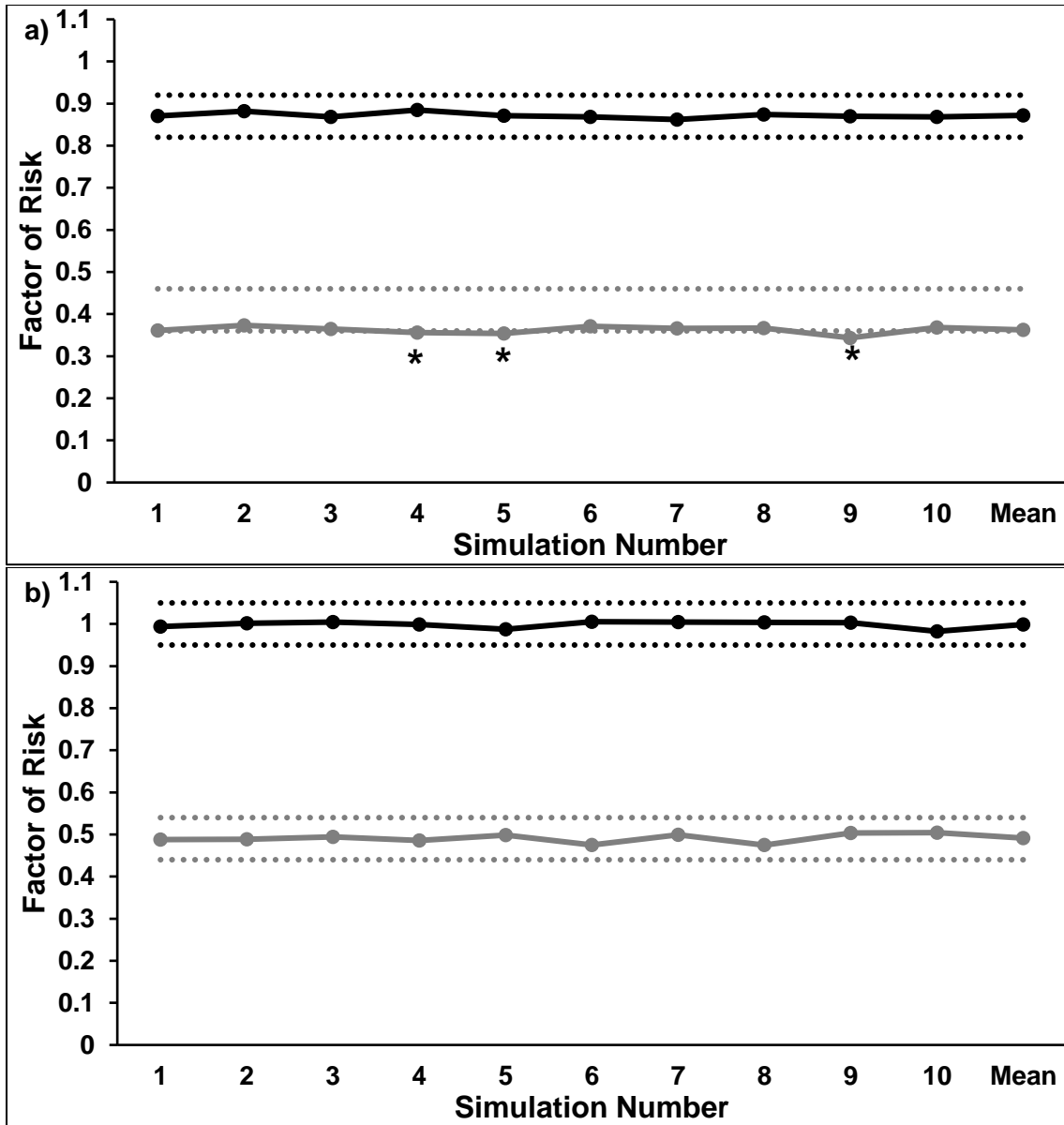


Figure 3.4: Model group mean FOR of females (solid grey line) and males (solid black line) over 10 simulations, compared to a ± 0.05 FOR corridor (dotted lines), for both no-fracture (a) and fracture (b) groups; asterisk (*) denote instances when the model group mean surpassed the threshold for validity (for that given simulation)

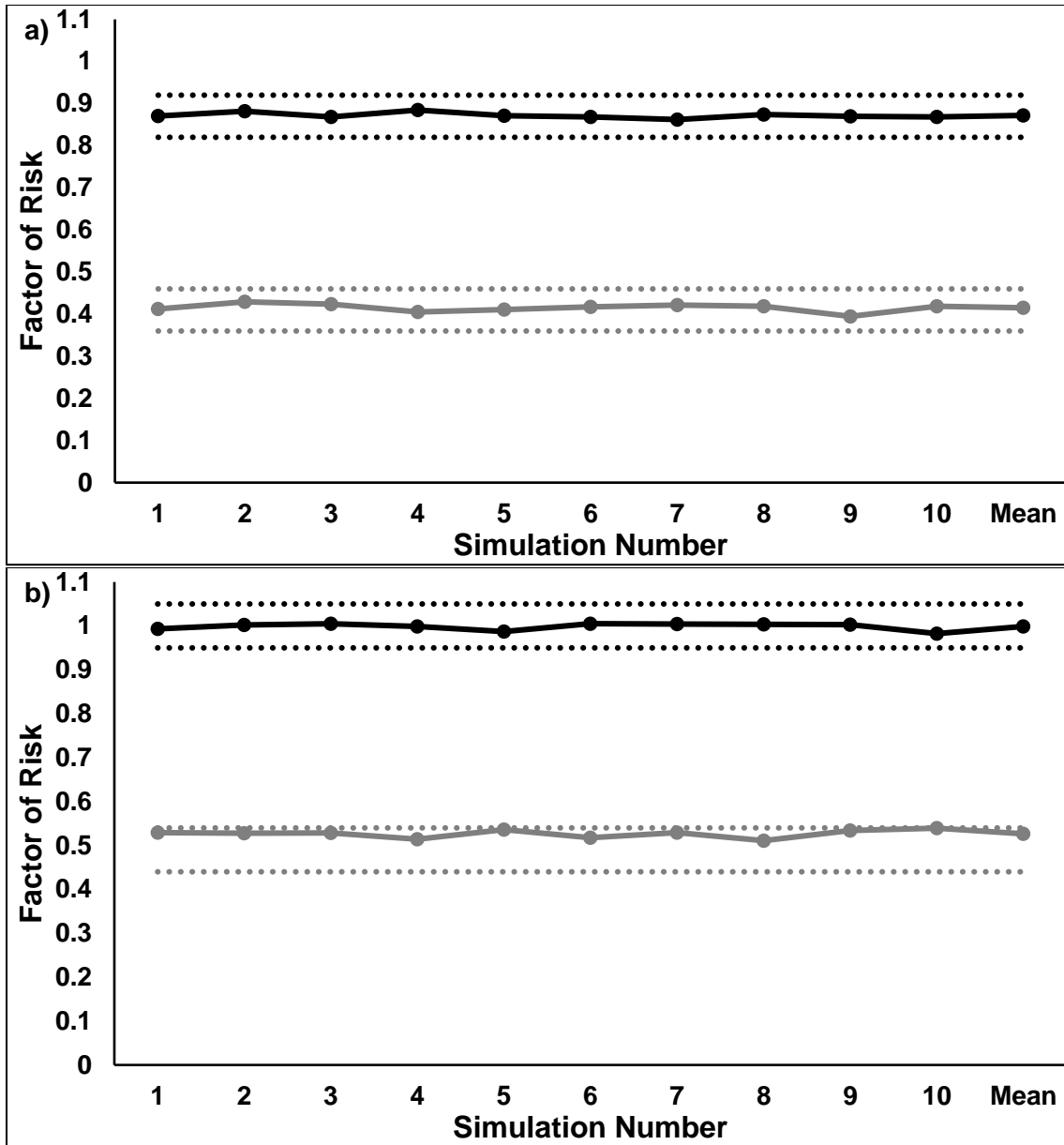


Figure 3.5: Adjusted (negative FOR values changed to 0) model group mean FOR of females (solid grey line) and males (solid black line) over 10 simulations, compared to a +/-0.05 FOR corridor (dotted lines), for both no-fracture (a) and fracture (b) groups

3.3.2: Model Application

When applied to the Canadian population using a representative sample of 100 000 Virtual Individuals, 46955 males and 53045 females were generated. The mean age of each group was 69.13 for males and 70.31 for females, with the mean heights and masses being 1.718 m and 83.8 kg for males, and 1.590 m and 70.9 kg for females. For BMD, the group mean values were 0.881 g/cm² for males, and 0.751 g/cm² for females.

The univariate ANOVA revealed a significant effect of age on FOR for both females ($F = 2.468$, $p > 0.001$) and for males ($F = 22.693$, $p > 0.001$), with mean FOR (SD) values significantly higher for males (0.422[0.231]) compared to females (0.067[0.238]). Additionally, the linear regression analysis of the effect of age on FOR revealed strong positive correlations for both females (Multiple $R^2 = 0.8122$, Adjusted $R^2 = 0.7809$, $F = 25.95$, $p = 0.002$) and males (Multiple $R^2 = 0.9108$, Adjusted $R^2 = 0.8959$, $F = 61.26$, $p > 0.001$), as can be seen in Figure 3.6.

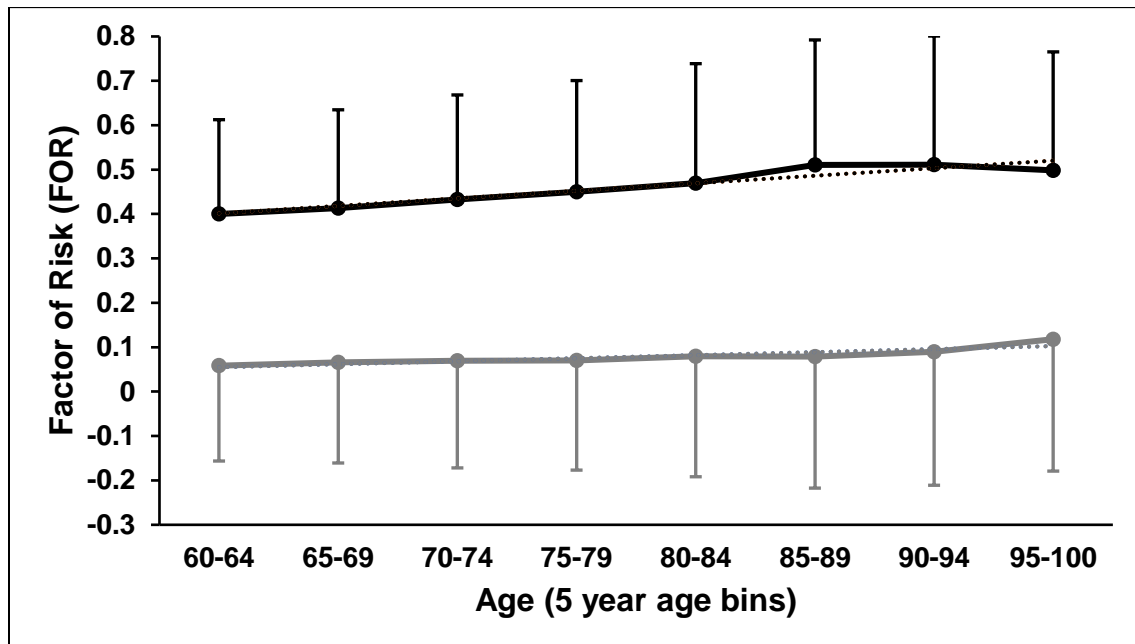


Figure 3.6: Mean Factor of Risk for females (solid grey line) and males (solid black line) when grouped into 5-year age bins. Both female and male data presented with 1 standard deviation error bars, and a line of best fit (dotted lines, respective colours)

The predicted mean FOR for both females (0.067) and males (0.422) were significantly lower than the values reported from Dufour et al. 2012 study. Compared to the reported group mean FOR values for no fracture groups (female = 0.41, male = 0.87), the model predicted mean FOR for females was 83.7% lower, and was 51.5% lower for males. While these values offer some information on population-level risk of hip fracture, further detail can be seen in the sex specific FOR as distributions (Figure 3.7). While the two distributions overlapped, the majority of each distribution was distinct from the other.

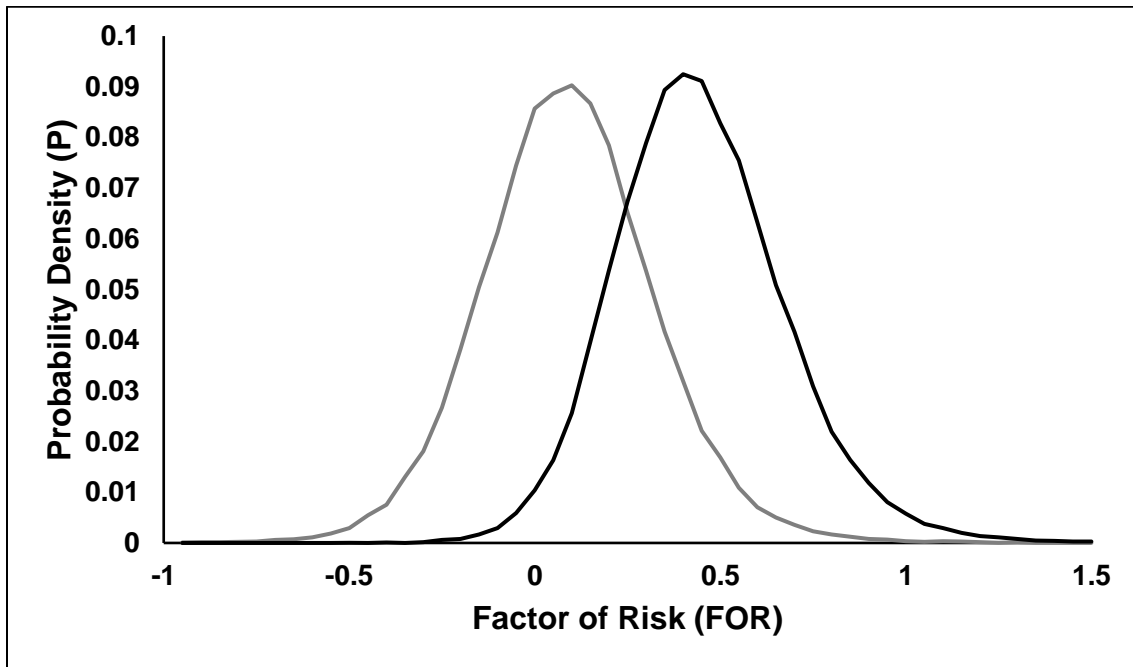


Figure 3.7: Factor of Risk Distributions for Females (grey line) and Males (black line) (100 000 samples)

3.3.3: Sensitivity Analysis

To analyse the effects of changes in all parameters, the outcome FOR values calculated for each of these VIs were plotted (Males Figure 8, Females Figure 9). Lines of best fit were assigned to each parameter of interest and characterized with regression equations. As males and females were assessed separately, their results would be discussed in the same manner.

All parameters were characterized by linear relationships for both males and females (Table 3.2, Figure 3.8). For males, increases in height, pelvic stiffness, fall height ratio, and effective mass ratio lead to increases in FOR when the parameters increased from -3 to +3 SD (increases in mass, TSTT, and BMD lead to decreases in FOR). Of these, pelvic stiffness had the strongest influence, with a slope (correlation coefficient, c) of 0.117, followed by mass ($c = -0.097$), BMD ($c = -0.086$), height ($c = 0.077$), effective mass ($c = 0.036$), TSTT ($c = -0.012$), and fall height ratio ($c = 0.005$). For females, increases in height, pelvic stiffness, fall height ratio, and effective mass lead to increases in FOR when the parameters increased from -3 to +3 SD (increases in mass, TSTT, and BMD lead to decreases in FOR). Of these, pelvic stiffness had the strongest influence, with a slope of 0.098, followed by mass ($c = -0.095$), height ($c = 0.084$), effective mass ratio ($c = 0.020$), BMD ($c = -0.017$), TSTT ($c = -0.014$) and fall height ratio ($c = 0.005$). For both males and females, pelvic stiffness and mass lead to the largest changes in FOR.

A strong positive correlation was found between age and FOR for both females and males (female adjusted $R^2=0.9859$, male adjusted $R^2=0.9904$). The results revealed that FOR increased by 0.150 from age 60 to 100 for males, and 0.028 for females. This aligns with the trends of increasing FOR with age that was observed for females and males during the model application portion of this study (Figure 3.9)

Table 3.2: Linear Regression Results for FOR changes as the parameter of interest cycles through +/- 3 SD and mean value (with the exception of age which cycles through the age range of 60 to 100 in 5 year.

(F statistics presented on 1 and 5 df for all factors (1 on 7 df for age)

a) Female

Factor	Multiple R ²	Adjusted R ²	F	p	Coefficient
Age	0.9876	0.9859	559.4	6.14E-08	6.88E-04
Height	0.9946	0.9935	924.1	7.23E-07	0.0844
Mass	0.9931	0.9917	717.2	1.36E-06	-0.0947
K	0.9841	0.9809	309.2	1.09E-05	0.0983
FH	1	1	1.27E+05	3.27E-12	5.10E-03
EMR	0.9995	0.9994	9456	2.18E-09	0.0199
TSTT	0.9738	0.9685	1.86E+02	3.82E-05	-0.0139
BMD	0.8701	0.8441	33.5	2.17E-03	-0.0172

b) Male

Factor	Multiple R ²	Adjusted R ²	F	p	Coefficient
Age	0.9916	0.9904	827.7	1.58E-08	0.0037
Height	0.9943	0.9932	875.8	8.26E-07	0.0773
Mass	0.9930	0.9917	714.4	1.37E-06	-0.0968
K	0.9759	0.9711	202.5	3.09E-05	0.1168
FH	1	1	1.33E+05	2.97E-12	5.20E-03
EMR	0.9984	0.9980	3040	3.71E-08	0.0357
TSTT	0.9722	0.9667	1.75E+02	4.41E-05	-0.0124
BMD	0.9050	0.8860	47.65	9.77E-04	-0.0859

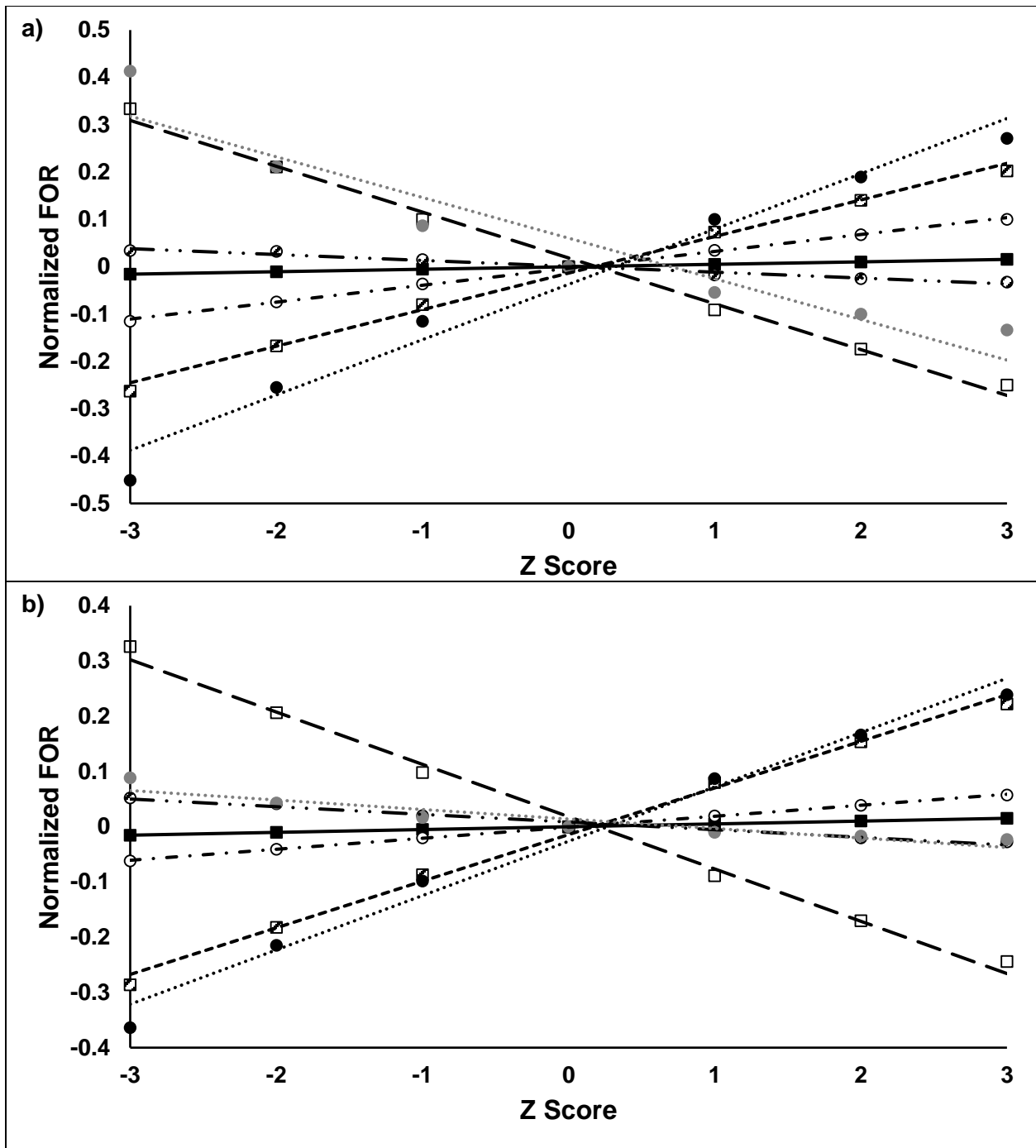


Figure 3.8: Factor of Risk sensitivity analysis assessing changes in FOR as parameters changed between ± 3 SD, for males (a) and females (b): parameters include height (striped square), mass (empty square), pelvic stiffness (black circle), fall height ratio (black square) effective mass (empty circle), TSTT (striped circle), and BMD (grey circle)

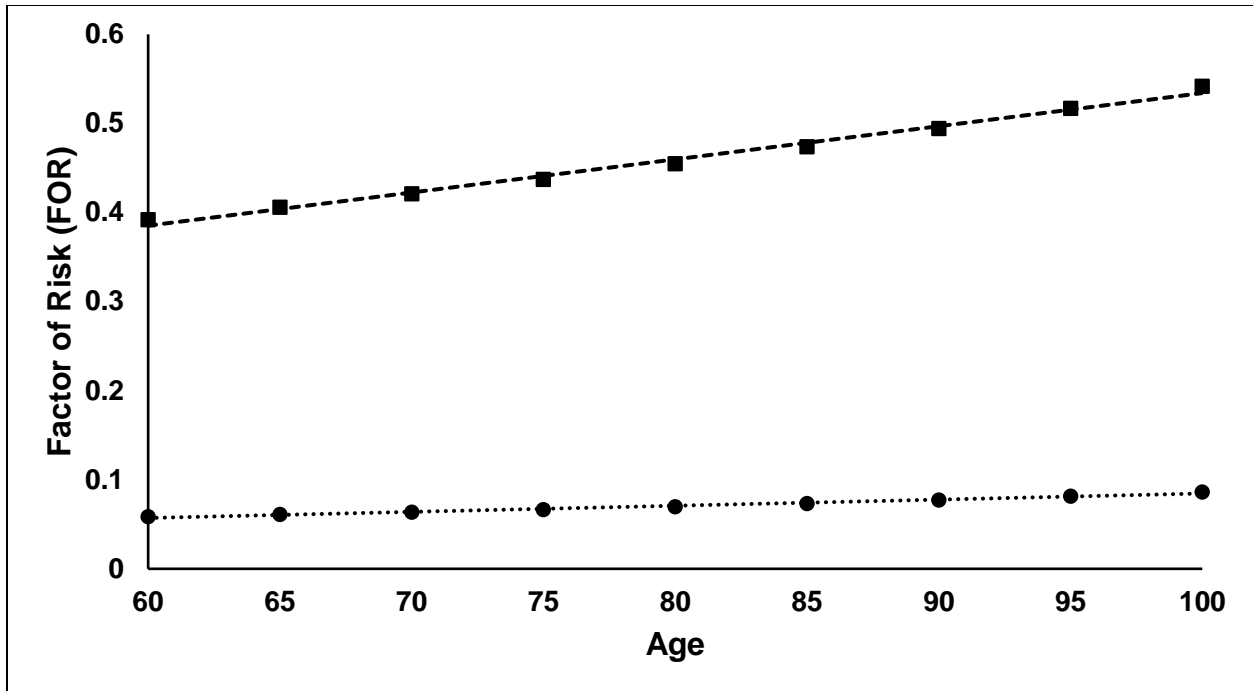


Figure 3.9: Female (black circles) and Male (black squares) changes in FOR with age, with trendlines included

3.3.4: Fracture Point Analysis

The mean FOR of the female non-fracture group was 0.0148, and was 0.0715 for the fracture group; for males, the mean FOR was 0.3725 for the non-fracture group, and 0.4373 for the fracture group. Using these group mean FOR values, the Fracture Point was determined to be 0.0432 for females, and 0.405 for males (Figures 3.1). When this value was compared to the mean FOR values of females and males from the sample of VI generated for the model application experiment, 28339 (53.4%) of the 53045 female VI, and 23722 (50.5%) of the 46955 male VI, are predicted to be more likely to suffer a hip fracture than not in the event of a fall (Table 3.3). Results using the secondary method of determining Fracture Point are presented in Appendix A.

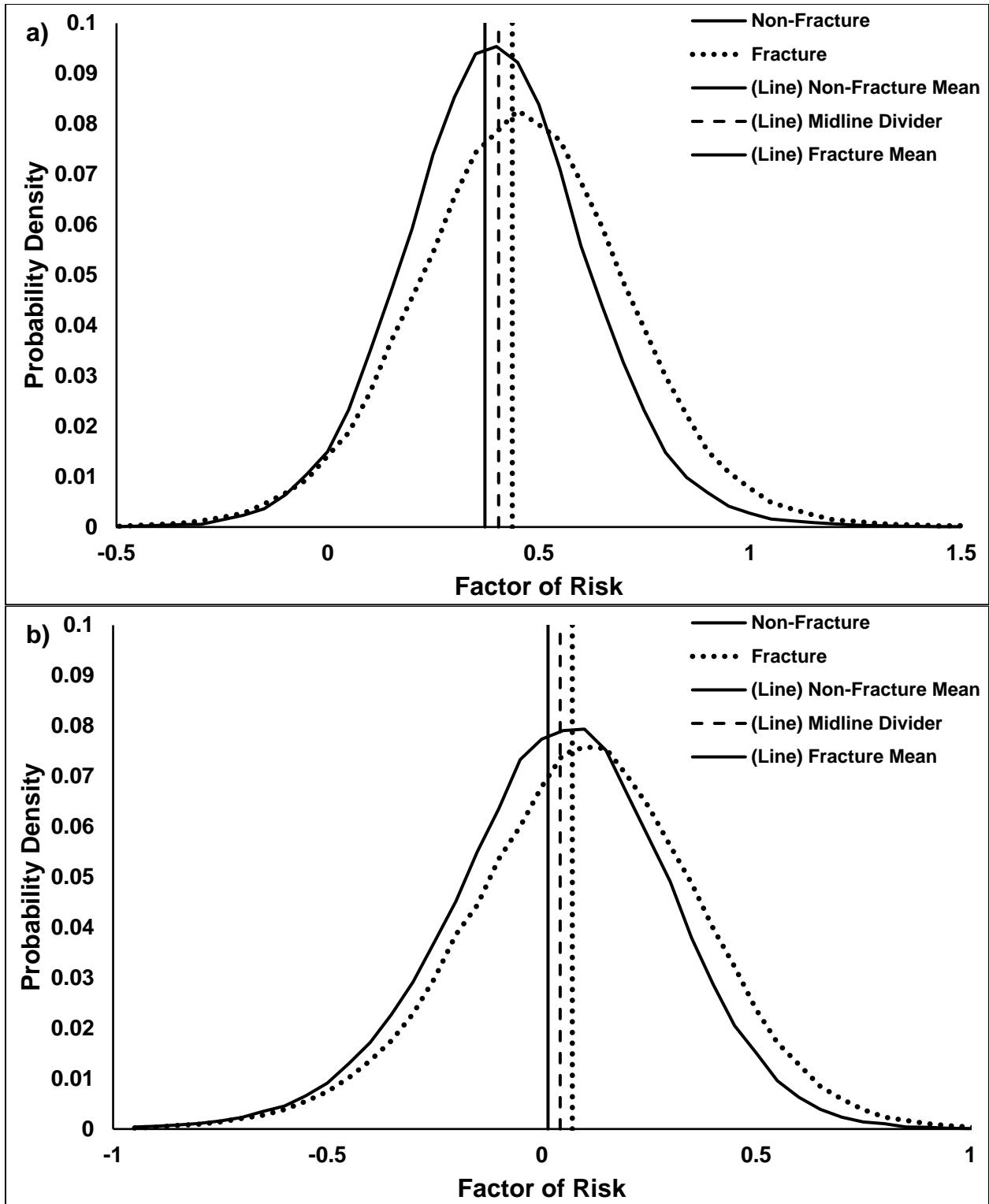


Figure 3.10: Probability Distributions for male (a) and female (b) non-fracture (solid curve) and fracture (dotted curve) groups. The vertical lines represent the group mean FOR values (solid line for non-fracture, dotted line for fracture) and the midpoint method Fracture Point (dashed line)

Table 3.3: Results Summary for Fracture Threshold Analysis; Analysis was performed on the same dataset that was generated for the model application experiment

Metric	Female	Male
N	53045	46955
Mean FOR	0.067	0.422
Fracture Point	0.0432	0.405
N FOR > Fracture Point	28339	23722
Percent > Fracture Point	53.4%	50.5%

3.4: Discussion

The goal of this study was to develop and pseudo-validate a mechanistic, probabilistic model of hip fracture risk in the older adult population using factor of risk (FOR) principles. The pseudo-validation portion of this study demonstrated that the model predicts FOR values similar to those published in literature, and can equally differentiate between groups of differing fracture risk. First, the overall model estimates of group mean FOR were within the error threshold (maximum difference of 0.05 in FOR value between model estimates and values reported by Dufour et al, 2012). Second, the model was able to differentiate between groups at different levels of hip fracture risk. Specifically, there was a significant difference in mean FOR between sexes. Also, within each sex, there were significant differences between the fracture groups, as was found in Dufour et al, 2012. Accordingly, the validation process confirmed that the model has the potential to be a tool with the sensitivity to explore the potential of clinical effectiveness of interventions targeting reductions in hip fracture risk.

The application portion of this study provides important insights into hip fracture risk at the population-level. First, the model output suggests that hip fracture risk increases with age. This corresponds to clinical evidence, but does not increase at the rate expected. This potential

discrepancy likely relates to the fact that the current model does not take fall-risk into account, and assumes that every VI was at equal risk of suffering a fall-related hip impact. Second, the model predicts different hip fracture risks across sex. However, the model predictions are different than expected, with the model estimates for FOR being higher for males, the opposite of what is observed in the population (Gryfe et al., 1977; Jean et al., 2013). This could be explained by the associations between TSTT and the force attenuation it provides (reducing FOR). In the model, the amount of force attenuation provided by TSTT was based on work by Robinovitch and colleagues in 1995, where a linear relationship between TSTT and force attenuation was found (with 71 N of force attenuation for every mm of TSTT). While this finding provides insight into the role that TSTT plays in hip impacts, it is extremely limited in applicability as it was based on a small sample of cadaveric specimen. It is possible that the range of specimens tested did not cover the entire range of TSTT observed in the population, making it possible that this linear trend does not remain linear at the high or low end of the spectrum of TSTT. And so, using this simple relationship may have led to unrealistic predictions of soft tissue force attenuation, especially for females, who tend to have larger amounts of TSTT (Lafleur Thesis, 2016). Another possibility was that the structure of the model (based on Factor of Risk, calculating a simple peak impact force and fracture threshold) was too simplistic and does not include certain factors that may play an important role in hip fracture risk (for example, bone collagen quality).

There are important implications from the sensitivity analysis related to parameter identification when using this model to predict hip fracture risk. Specifically, pelvic stiffness and mass had the largest influence on FOR, with increases in pelvic stiffness increasing FOR, whereas increases in mass lead to decreases in FOR. While pelvic stiffness had the largest degree of variability (standard deviation of 24% of the mean for females, 27% for males), which may explain

why this factor had the largest effect, the order of factors based on their influence did not reflect the order of variance in those factors. Regardless, the results of the sensitivity analysis confirm that it was imperative that these parameters be accurately measured, or estimated, and allocated in order to improve the value of model output.

While changing the parameter inputs for the application portion compared to the pseudo-validation study significantly lowered FOR values, there was evidence to support this approach. Firstly, many of the parameters used in the model during the pseudo-validation study (pelvic stiffness, fall height, effective mass) were single sex-specific value (mean values reported by Robinovitch et al, 1991), meaning that every VI of a given sex had those parameters. These single values do not properly represent the variance we see on a population-level. To counter this, a combination of previously published values and recently collected data were used to determine appropriate mean values and their standard deviation: doing so allowed us to characterize these parameters as normal distributions. Additionally, the predictive equations used to estimate TSTT from BMI were updated, as these equations were based on TSTT measured during a supine DXA scan. Previous work (most notably Lafleur Thesis, 2016) has found that TSTT measurements in a supine position are larger when compared to measurements made from a person in either a side-lying or standing position, postulating that posterior tissue was compressed in a supine position, causing it to then protrude laterally (potentially artificially increasing TSTT measures). To counter this, and use more current data, a previously developed regression equation for estimating TSTT in a standing position (based on sex and BMI) was used instead (Lafleur Thesis, 2016). Uncertainty was also included in the estimates of TSTT (as detailed in section 3.2.1.2). Finally, the BMD parameter used in the pseudo-validation study could not be confidently applied to the Canadian population, as the values represented the mean (and standard deviation) measured BMD for the

four groups. As we currently have no population estimates of BMD, we implemented a previously developed predictive equation for estimating BMD from age, sex, and mass (Lafleur Thesis, 2016), as well as including an element of uncertainty (as detailed in section 3.2.1.2). By updating these parameters, we believe that the model generated VIs (and subsequent model estimates of population risk) would better reflect the distribution of parameters present in the population, resulting in a better population-level estimate of fall-related hip fracture risk.

While the overall goal of this study wasn't to provide an estimate of population-level hip fracture rates, but instead provide insight into the risk of hip fracture, the fracture point analysis is nevertheless a promising example of a method to put the FOR metric of hip fracture risk into the context of fracture outcomes. While this method was limited in its ability to determine whether a fracture would occur, and merely presents the *Fracture Point* as a threshold of likelihood of fracture outcome (with FOR values above the Fracture Point more likely than not to result in a hip fracture, in the event of a fall), the results of this study are promising. In general, the results of this analysis agree with current epidemiological findings that older adult females are at a higher risk of hip fractures than males, even though the mean FOR of females was much lower than that of males. Regardless, this analysis was limited as more of a proof of concept, and requires certain assumptions to be made, most notably that the age data reported by Dufour et al, 2012 was truly normally distributed, unlike what is seen in the Canadian older adult population.

There were several other limitations with this study. Firstly, there is no currently available assessment of population-level risk (in terms of Factor of Risk, or similar metrics) of fall-related hip fractures. It was for this reason that a pseudo-validation method was conducted in this study. We believe that the methods used to pseudo-validate the model, and the subsequent results, support the notion that the model can achieve accurate estimates. Furthermore, the fact that a stringent

threshold of maximum difference of 0.05 in group mean FOR was achieved when averaging over 10 trials lends some credence to the precision of the model, even with relatively small samples (N=1000, per group). Secondly, the predictive strength of the model as a whole depends largely on the individual strength of each of the sub-models employed. More specifically, some of the regression equations used in this model had moderate to low R^2 values, while some were based on a small cohort, which can make extending the predictive equations to the older adult population difficult. Regardless, the model employs the best available data, and now that the framework of the model is established, it provides a solid foundation of which we can build, allowing us to use more recent or robust sub-models, which could help with the precision and accuracy of the model's predictions. Thirdly, the group mean FOR values for both males and females were lower than the group mean values for both fracture groups reported in the Dufour et al, 2012 study. As mentioned previously, this was most likely due to the changes in sub-models from the model validation to the model application portion of this study. This does not necessarily mean that the Canadian older adult population is at an even lower risk than the fracture groups reported in Dufour et al's 2012 study. Fourthly, the fact that the model predicted the male population FOR was higher than females was intriguing, as all previous epidemiological studies, such as Gryfe et al, 1977 and Jean et al, 2013, found rates of hip fractures are higher in female older adults than males. While our results disagree with those of Jean and colleagues at face value, this could very well be explained by the fact that this model does not currently include any aspect of fall risk; every VI generated by the model was assumed to have fallen. If future this limitation could be addressed by incorporating a fall risk sub-model based on previously reported rates of falls in an older adult cohort (such as Blake et al, 1988 and Campbell 1989, or more recently Stevens & Sogolow, 2005, and Tromp et al., 2001), which would dictate whether the VI was expected to fall in this instance. Additionally,

the model could be further bolstered by determining an FOR value that is related to a threshold for fracture outcomes, as we attempted to perform in the Fracture Point analysis. Fifthly, the fact that pelvic stiffness and mass were the parameters that most influenced FOR during the sensitivity analysis does not prove that they are the biggest factors in determining actual fracture outcomes during a fall to the hip. Instead, these factors (pelvic stiffness and mass) have been shown to most strongly affect the Factor of Risk (of fall-related hip fractures), when calculated in this specific manner. While the influence of these factors might be partially explained by large variance (especially in the case of pelvic stiffness), the descending order of factor influence did not follow the descending order of the variance of the factors, meaning that there was some other mechanism by which these factors so largely influenced FOR. As for the effect of mass on FOR, the direction and magnitude of this parameter's effect may be explained by the effect of mass on BMI, and in turn the effect of BMI on TSTT and the associated force attenuation, which relates to the final limitation of this study. As mentioned earlier, the sub-model used to predict soft tissue force attenuation was taken from a 1995 study by Robinovitch and colleagues, was quite limiting. The narrow range of data used to characterize the relationship necessitates extrapolation for large levels of TSTT, which can result in estimated force attenuation larger than the predicted peak impact force. It is possible that this relationship plateaus at a certain level of TSTT, which we would expect based on results presented by De Laet and colleagues in 2005, where they observed an initial decrease in relative risk of fracture as BMI (which closely relates to TSTT) increase, followed by an increase after BMI values of 30 kg/m². Following that logic, we would expect that the influence of soft tissue on force attenuation would eventually lessen as TSTT increases. Therefore, the use of this simple TSTT-force attenuation relationship may be disguising elevated

risk in VI with high BMI values and larger amounts of TSTT, for whom the model estimates lower FOR values due to a great deal of soft tissue force attenuation.

3.5: Conclusion

This was the first example of a model using probabilistic methods to estimate population-level risk for fall-related hip fractures. Furthermore, the basis for the risk estimate was entirely mechanical and all parameters can be obtained or derived from readily accessible population data. Updating the sub-models used to better reflect recent literature, or including more complex fall impact force models could help improve the robustness and accuracy of the model. However, in its current state, the model predicted mean hip fracture FOR values within 0.05 of those reported in the literature (Dufour et al., 2012), and effectively differentiated between groups at different levels of hip fracture risk. In conclusion, this model provides a solid foundation on which to predict population-level risks of fall-related hip fractures. Furthermore, this model can become a valuable tool to policy makers interested in hip fracture prevention, as this model could lend itself to estimating the influence of large-scale interventions (such as safety flooring) prior to their actual implementation.

Chapter 4

Safety flooring – Investigations of Biomechanical Effectiveness and Effects on Population-level Hip Fracture Risk

4.1 Introduction

Fall-related hip fractures are a substantial public health issue, especially in the older adult population. In fact, 7% of all documented fall-related injuries sustained by older adults, and over one-third of all fall-related hospitalizations, are hip fractures (Canadian Community Health Survey, 2012). The risk of these hip fractures increases drastically after age 60 (Jean et al, 2013), and previous research has found that one of the primary determinants of fracture risk is the applied load to the femur during the fall scenario (Robinovitch et al, 1991, Bouxsein et al, 2007, Roberts et al, 2010). Accordingly, interventions that reduce impact forces have the potential to reduce the risk of hip fractures. One type of intervention that aims to reduce impact forces are safety floors, which are purpose-designed engineering materials which are designed to absorb, or dissipate, energy during an impact.

Safety floors are a promising intervention approach for reducing the risk of hip fractures as biomechanical studies have demonstrated their force attenuating properties (Bhan et al., 2014; Laing and Robinovitch, 2009). During low energy falls with human volunteers, the force attenuation properties of safety floors have been shown to change based on faller characteristics such as sex and body mass index. However, higher energy fall simulations with mechanical test systems tend to ignore these potential influences, and instead simulate a single ‘representative’ older adult impact scenario. This limits the ability of biomechanical test results to accurately predict population-based effects of safety flooring on hip fracture risk. To this point, little has been reported on the effects of fall and faller-specific factors (height or velocity of the fall, mass of the

faller, the amount of soft tissue the faller has over their greater trochanter, or the pelvic stiffness of the faller) on the force attenuating properties of safety flooring, along with any potential interactions between these factors and force attenuation.

Accordingly, the objectives of this study were two-fold. The first objective was to use a mechanical test system (drop tower with an instrumented surrogate pelvis) to investigate the influence of several fall and faller-specific characteristics on the force attenuation offered by a safety flooring system. More specifically, this study tested the hypotheses that the femoral neck force attenuation provided by safety flooring would:

1. increase with increasing impact velocity
2. Be insensitive to effective mass
3. Decrease with increasing TSTT
4. Increase with increasing effective pelvic stiffness

The study's second objective was to use regression analysis on the experimental data to develop an algorithm to predict the force attenuation provided from the safety floors as a function of relevant main and interaction effects.

4.2 Materials and Methods

4.2.1 Test System

Simulated lateral hip impacts were conducted using a vertical drop tower along with a surrogate human pelvis (Figure 4.1 and 4.2). The drop tower was made up of a steel frame which houses two high-precision linear shafts (guide bars). A steel load carriage was mounted around the guide bars using four pillow block bearings, allowing for near frictionless vertical movement of the load carriage (Figure 4.1). Attached to the load carriage was the surrogate pelvis system, which

was made up of a leaf spring system (to simulate effective pelvic stiffness) attached to a Sawbones® simulated femur which was encompassed in foam (meant to replicate the stiffness and geometry of the soft tissue overlying the greater trochanter) (Figure 4.2). This design was first developed by Robinovitch and colleagues in 1997, and has been further modified since. By raising the load carriage (through a combination of electromagnet, turnbuckle and electric winch), it can be released at a given height, allowing the surrogate pelvis (and load carriage) to drop and impact onto an impact surface with a given velocity. This setup allows for a great degree of control over the independent variables, as the load carriage/surrogate pelvis system can be modified by changing the stiffness of the leaf springs, changing the thickness of the foam shell, adding mass to the system, as well as adjusting the impact velocity by changing the release height of the load carriage. Furthermore, the force plate used as the impact surface can be covered with the safety flooring sample to then compare the impact force of the system with and without the safety flooring present. With this setup, impact force can be measured at two different locations; the first being at the force plate impact surface (Model OR6-6-200, AMTI, Massachusetts, USA), and the second being at the load cell mounted in the proximal femur at the femoral neck (1051V6, Dytran Instruments Inc., California, USA). Both instruments were sampled at 20 000 Hz using the NIAD 3.0 software (NIAD 3.0, University of Waterloo, Waterloo, Canada). Each foam shell underwent 10 pre-preconditioning trials prior to data collection, which has previously been shown to assure trial to trial repeatability after the preconditioning (Goh Thesis, 2017). Furthermore, repeatability was also assured by a mandatory three-minute rest for the foam (uncompressed, test system raised) (Goh Thesis, 2017).

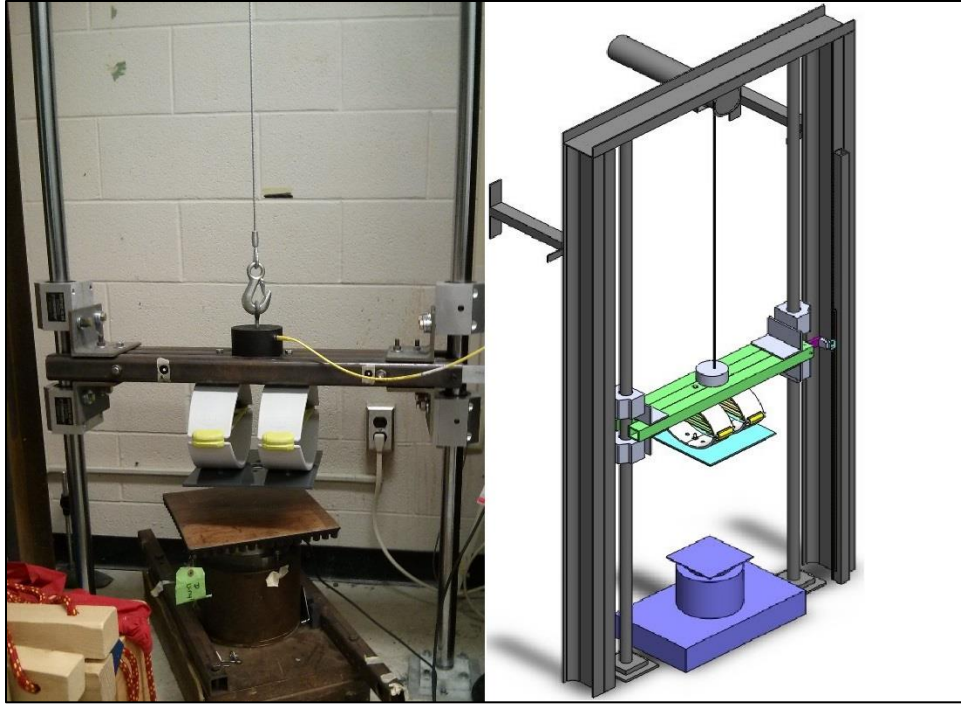


Figure 4.1: Picture and CAD rendering of the Injury Biomechanics and Aging Laboratory's drop tower system (both pictured without the femur and simulated soft tissue portions). Photos courtesy of Frederick Goh; CAD by Frederick Goh

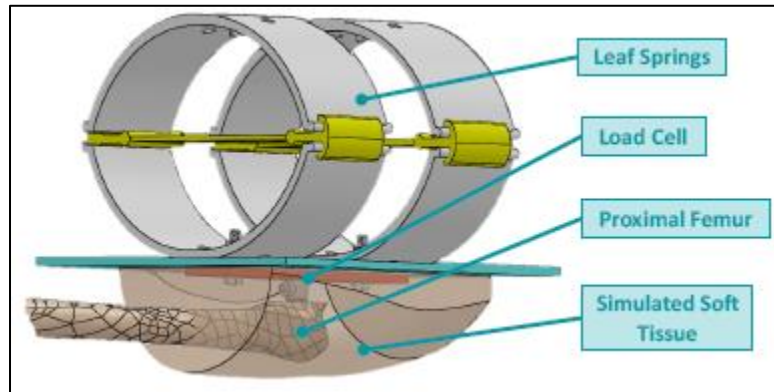


Figure 4.2: CAD rendering of the surrogate pelvis system used in the drop tower; CAD drawing courtesy of Frederick Goh

The independent variables of interest were impact velocity (v), effective mass (m), effective pelvic stiffness (k) and simulated TSTT (t_{stt}) (Table 4.1). Levels of independent variables included three impact velocities (2.1, 2.8 and 3.4 m/s), three effective mass levels (36.3, 41.4 and 46.4 Kg), two effective stiffness levels (22 650 N/m and 33 370 N/m), and three TSTT levels (2, 3 and 4 cm) (Table 4.1). In addition, two flooring conditions (control condition onto rigid force plate, and a SmartCells™ safety flooring sample [Figure 4.3]) were included, as can be seen from Figure 4.4. Impact velocity was controlled indirectly by adjusting the drop height of the surrogate pelvis system and resulting impact velocity was measured with a velocimeter (VS300, GHI systems Inc., California, USA).



Figure 4.3: The Square sample of SmartCells™ safety flooring used (Left); a cross-section image of the SmartCells™ sample, displaying the rubber columns found underneath the top surface (Right)

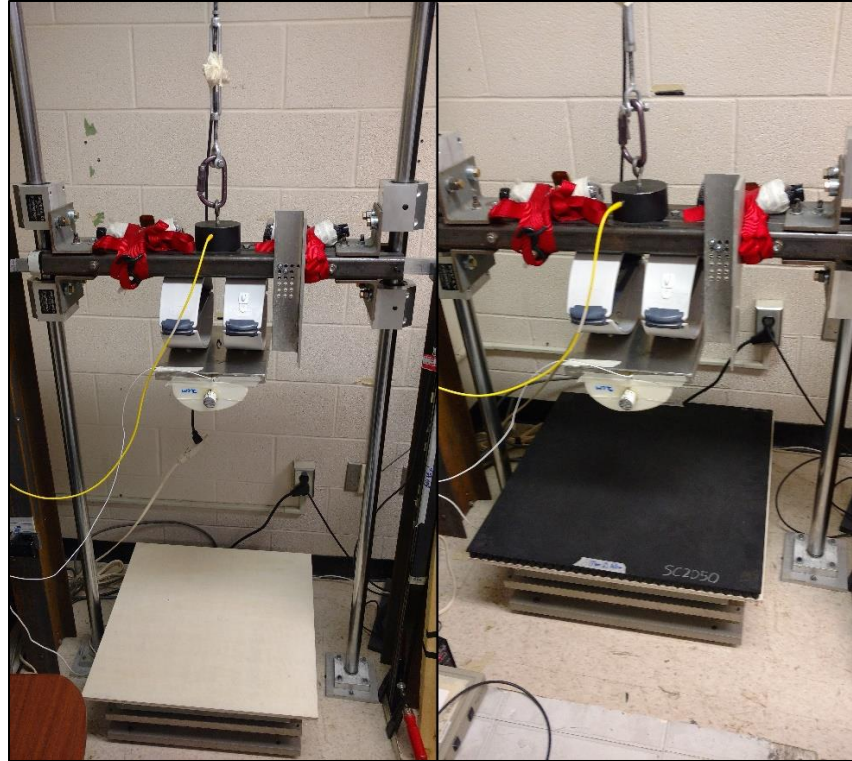


Figure 4.4: Test system in a pre-impact state for the control trial (Left) and safety floor trial (Right)

Table 4.1: Independent variables and levels for simulated lateral hip impacts using the drop-tower paradigm. *Mean and +/- 0.5 SD of effective mass (based on a ratio between mass and effective mass cohort of young adults during pelvis-release experiments; this mean ratio and SD was applied to the mean mass of the older adult population). **Based on Levine et al, 2013, closest possible with Kangoo Springs available. ***Mean and +/- 1 SD of standing TSTT (measured with ultrasound as part of Benoit Lafleur's MSc Thesis project).

Variable Name (symbol)	Levels
Flooring Surface (s)	Control (rigid surface) Safety floor
Impact Velocity (v)	2.1, 2.8 and 3.4 m/s
Effective Mass (m)	36.3, 41.4, 46.4 kg*
Effective Stiffness (k)	Low (22 650 N/m)** High (33 370 N/m)**
Trochanteric soft tissue thickness ($tstt$)	2 cm, 3 cm, 4 cm ***

As for dependent variables, impact force (in N) was measured using a force plate mounted on a rigid concrete floor (Model OR6-6-200, AMTI, Massachusetts, USA). Additionally, an in-line load cell (1051V6, Dytran Instruments Inc., California, USA) incorporated into the simulated femur measured femoral neck forces. The force plate and load cell data was sampled at 20 000 Hz

4.2.2 Quantifying safety flooring force attenuation

The peak impact force measured by the force plate (F_{max}) and the peak force measured by the femoral neck load cell (F_{neck}) were used to derive other outcome variables of interest. The primary outcome variable of interest was safety flooring force attenuation (A_{floor}), which was calculated as the difference between F_{neck} of the control trial and the safety flooring trial. This difference was converted to a percentage of F_{neck} of the respective control trial, as has been done previously in studies of hip protector force attenuation (Robinovitch et al., 2010), where

$$\mathbf{Force\ Attenuation} = \mathbf{100} * \left(\mathbf{1} - \frac{\mathbf{Safety\ Floor\ trial\ } F_{neck}}{\mathbf{Control\ Trial\ } F_{neck}} \right). \text{ [Equation 4.4.1]}$$

The highly controlled nature of the mechanical drop tower test systems results in little to no trial to trial difference; this allowed us to conduct one trial per condition. One impact trial was conducted for every combination of independent variable in addition to “control” conditions where no safety flooring was present (each impact onto the safety floor had a matched control trial). This results in a 2 (floor) x 3 (velocity) x 3 (effective mass) x 2 (pelvic stiffness) x 3 (TSTT) testing matrix, for a total of 108 trials. As stated above, F_{max} and F_{neck} were recorded for each trial, and A_{floor} was calculated for the safety floor trials. It should be noted that impact velocity was measured for each trial to confirm that the appropriate velocity was achieved; if the appropriate velocity was not achieved, the trial was redone. For the purposes of certain analyses (ANOVAs), trials were

grouped by target velocity, and not by measured impact velocity, whereas the measured impact velocity was used during the regression analysis.

4.2.3 Data Analysis

Both the force plate and load cell signals were processed using a customized MATLAB (MATLAB R2013b, Mathworks, Natick, Massachusetts, USA) script, wherein the data was filtered using a dual-pass 2nd order I(resultant 4th order) Butterworth filter with an initial cutoff frequency of 50 Hz (normalized cutoff frequency of 0.04 Hz); these filtering parameters follow the International Hip Protector Research Group's (IHPRG) recommendations for mechanical testing of hip protectors, as outlined in both Robinovitch et al, 2010, and the 2017 CSA Express document (EXP08-17).

4.2.4 Statistical Analysis

To analyze these results, two different types of statistical analyses were performed. Firstly, 4 separate one-way univariate ANOVAs were conducted (one for each factor, with the exception of flooring condition) where A_{floor} was the dependent variable. A 2x3x3x3 ANOVA was not conducted, as we only collected one trial per condition, which prevented analysis of interaction effects via ANOVA methods. These main effects were investigated in order to determine which factors had the greatest effect on A_{floor} , as well as determine factors that may be excluded in future experiments of this type. Bonferroni post-hoc tests were performed to determine significant difference within factors, if a significant main effect was found. Additional statistical analyses were performed on the collected data; these results are presented in Appendix B.

Interaction effects were investigated through a second statistical approach, namely a multiple linear regression model. The explicit goal of this analysis was to find the best fitting model (highest possible adjusted R^2), and so stepwise regression methods were used (backwards

elimination and forward selection) achieve this goal. All ANOVA statistical analyses were performed using the SPSS statistical processing software package (SPSS Version 21, SPSS Inc., Chicago, IL, USA) using an α of 0.05, and the regression models were generated in the RStudio software package (RStudio Version 1.0.136, RStudio Inc., Boston, MA, USA) using the R statistical programming language (R Core Team, 2015).

4.3 Results

4.3.1 Group Means and ANOVA Results

While F_{max} and F_{neck} of the control trials varied between conditions, the mean (SD) values for F_{max} and F_{neck} were 3449.28 N (570.54 N) and 2267.43 N (497.79 N), respectively. For the safety floor trials, the mean (SD) values for F_{max} and F_{neck} were 3414.28 N (564.14 N) and 1665.05 N (243.04 N). The mean (SD) value of A_{floor} across all trials was 25.2 % (8.1%).

Significant main effects on A_{floor} were observed for velocity ($F = 6.887$, $p = 0.002$), mass ($F = 3.587$, $p = 0.035$), and TSTT ($F = 22.846$, $p < 0.001$) (Table 4.2). We observed an increase in A_{floor} as target velocity increase, as the mean (SD) values for the three levels of velocity (2.1, 2.8, and 3.4 m/s) were 20.84 (7.64), 24.76 (7.47) and 29.84 (6.74)%. Post hoc analyses revealed that there was a significant difference in A_{floor} between the 2.1 and 3.4 m/s trials, but not between the 2.1 and 2.8 m/s trials or the 2.8 and 3.4 m/s trials (Figure 4.5). Similarly, A_{floor} increased with the three levels of mass (35, 40, 45 kg) with values of 21.60 (7.59), 25.39 (7.71), and 28.46 (7.79)%, respectively. Post hoc analyses revealed that there was a significant difference only between the 35 and 40 kg trials (Figure 4.6). A_{floor} decreased as TSTT increased, as the mean (SD) values for the three levels of TSTT (2, 3, and 4 cm) were 32.58 (3.46), 23.39 (6.96), and 19.48 (6.82)%, respectively. Post hoc analyses revealed that there were significant differences in A_{floor} between the 2 and 3 cm, and 2 and 4 cm, trials (Figure 4.7). The effect of pelvic stiffness on A_{floor} did not

reach significance (pelvic stiffness: $F = 3.256$, $p = 0.077$). For the two levels of pelvic stiffness (22 650 N/m, and 33 370 N/m), the mean (SD) values were 23.21 (9.53), and 27.09 (5.82)% (Figure 4.8).

Table 4.2: Univariate ANOVA results for the effects of Velocity, Effective Mass, TSTT, and Pelvic Stiffness on A_{floor} (* denotes significant difference, at $\alpha = 0.05$)

	Main Effect		Post Hoc		95% CI	
Factor	F	p	Level	p	Lower Bound	Upper Bound
Velocity	6.887	0.002*	2.1 m/s - 2.8 m/s	0.339	-9.94	2.099
			2.1 m/s - 3.4 m/s	0.002*	-15.018	-2.98
			2.8 m/s - 3.4 m/s	0.125	-11.098	0.94
Mass	3.587	0.035*	36.3 kg - 41.4 kg	0.437	-10.1423	2.5606
			36.3 kg - 46.4 kg	0.03*	-13.2103	-0.5075
			41.4 kg - 46.4 kg	0.712	-9.4195	3.2834
TSTT	22.846	<0.001*	2 cm - 3 cm	<0.001*	4.2674	14.1204
			2 cm - 4 cm	<0.001*	8.1748	18.0278
			3 cm - 4 cm	0.165	-1.0191	8.8339
Pelvic Stiffness	3.256	0.077				

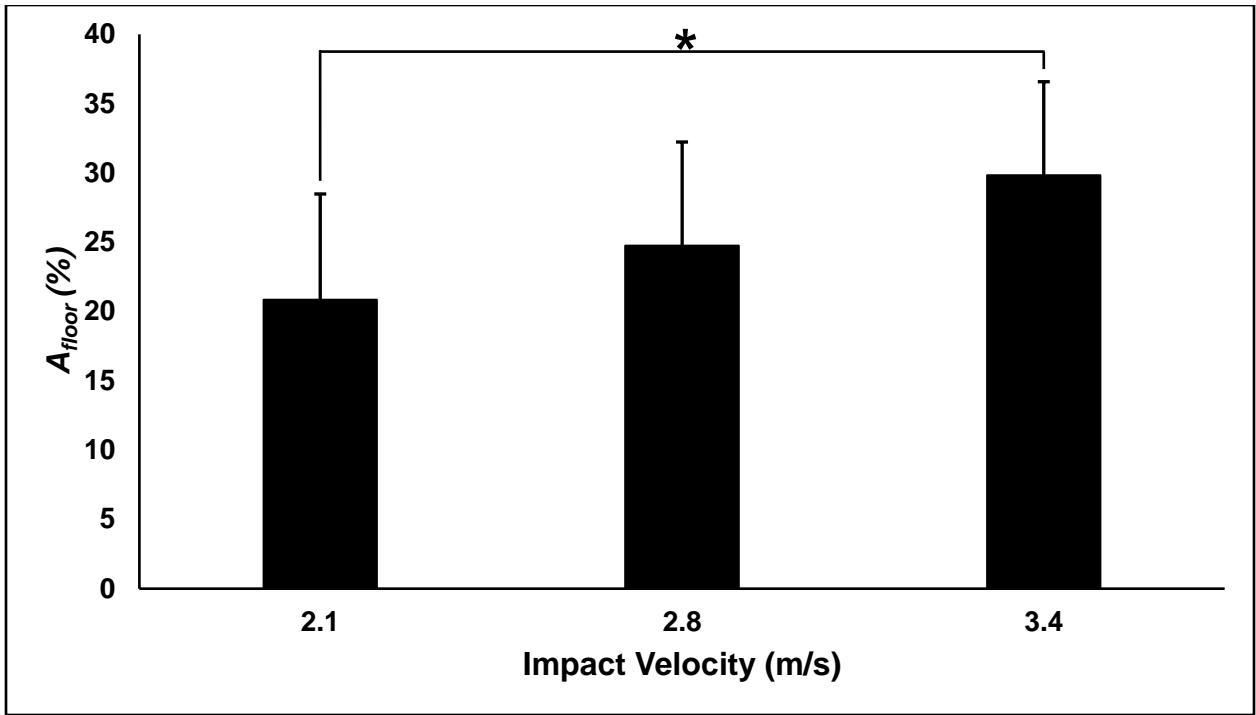


Figure 4.5: Mean differences between the three levels of Impact Velocity. Post-Hoc analyses revealed a significant difference between 2.1 and 3.4 m/s ($p < 0.05$)

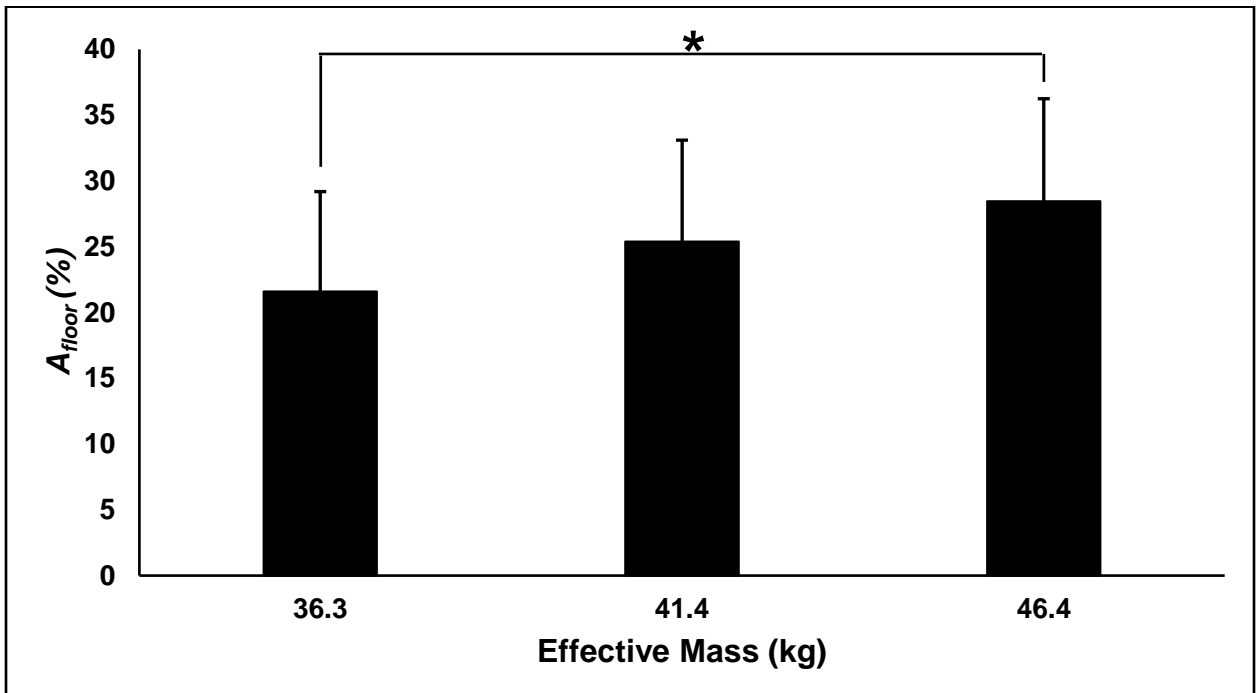


Figure 4.6: Mean differences between the three levels of Effective Mass. Post-Hoc analyses revealed a significant difference between 36.3 and 46.4 kg ($p < 0.05$)

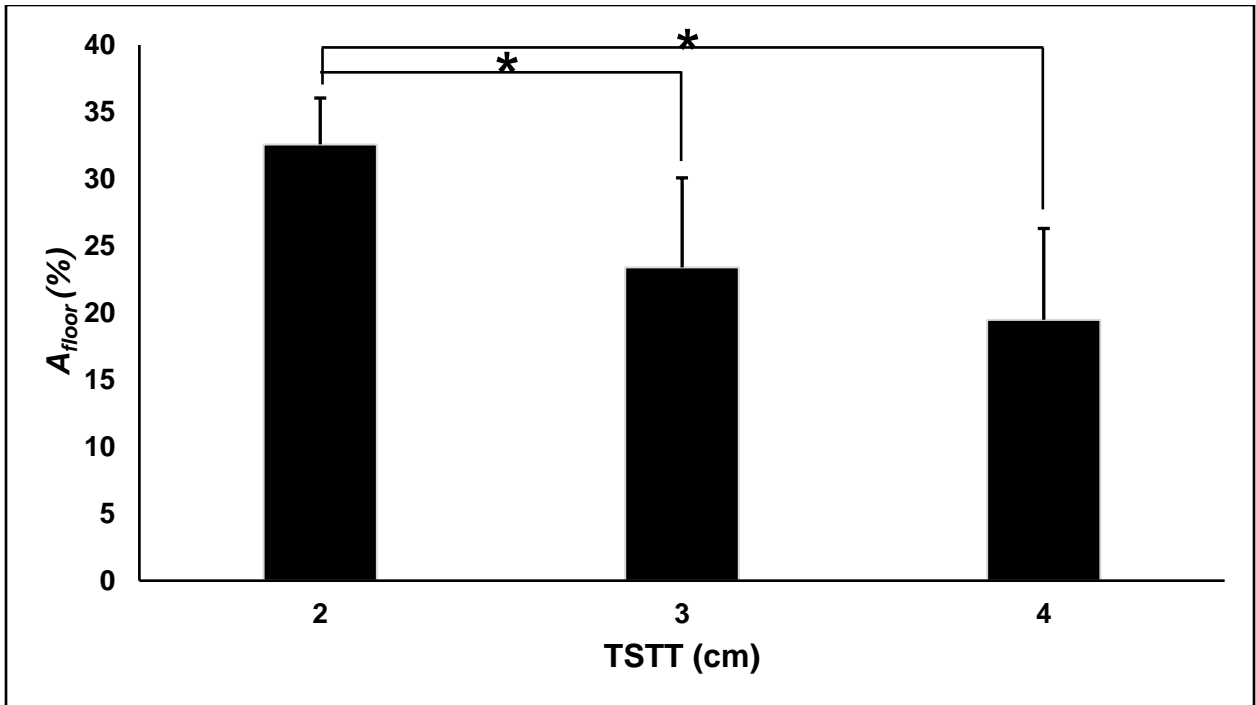


Figure 4.7: Mean differences between the three levels of TSTT. Post-Hoc analyses revealed a significant difference between 2 and 3 cm, as well as 2 and 4 cm ($p < 0.05$)

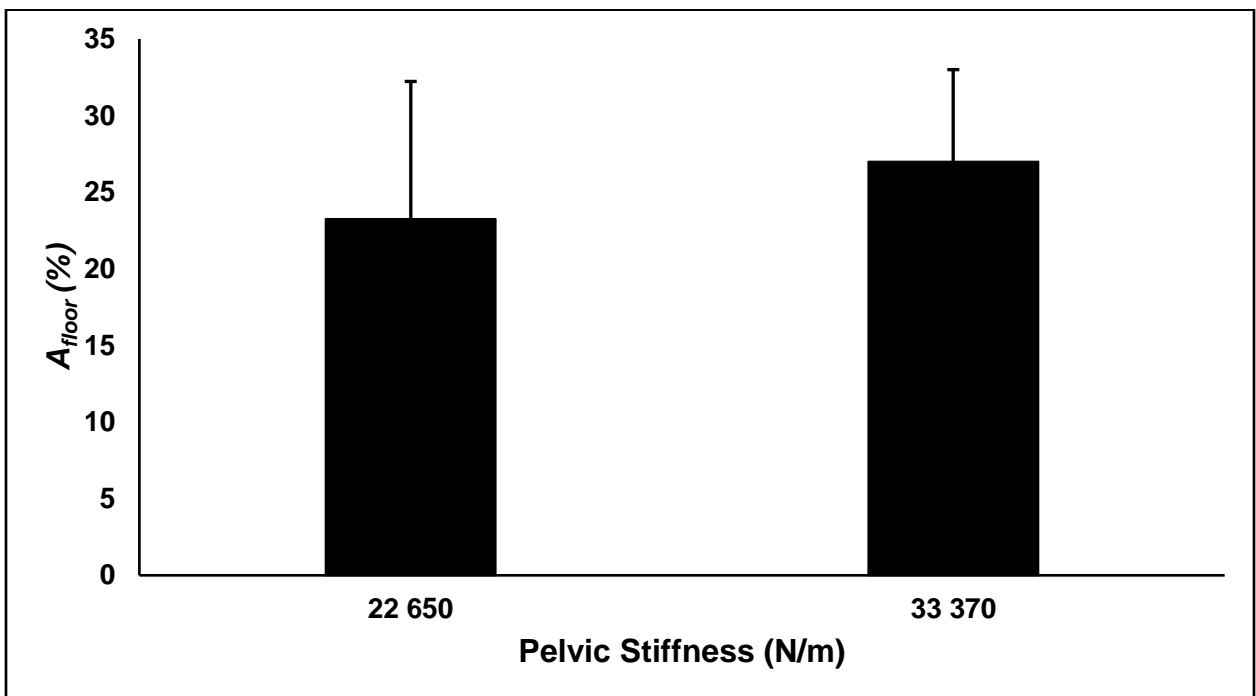


Figure 4.8: Mean differences between the two levels of Pelvic Stiffness

4.3.2 Multiple Linear Regression Analysis

In both the forward and backward stepwise direction, the same model was generated. This model included all main effects, all two-way interactions, and two three-way interaction (velocity*mass*pelvic stiffness; velocity*TSTT*pelvic stiffness), and resulted in an adjusted R² of 0.8992, and a residual standard error of 2.561. The model equation was as follows:

$$A_{floor} = 296.8 - 109.2v - 5772m - 3.80t - 0.007968k + 0.003393vk + 2.544vm + 0.7787vt + 0.000178mk + 0.000073tk + 0.01359mt - 0.000078vmk - 0.00002105vtk \quad [\text{Equation 4.2}]$$

where v represents impact velocity of the test system (in m/s), m represents mass of the load carriage and surrogate pelvis system (in kg), t represents the TSTT of the foam covering (in cm), and k represents the stiffness of the surrogate pelvis system (in N/m). Below is a table of all the coefficients, with their estimates, standard errors, t values and p values (Table 4.3). This table also includes results of single factor linear regression models for the 4 main factors. As can be seen in Table 4.3, there were 3 significant two-way interaction effects, which were Velocity*Stiffness, Velocity*Mass, and Mass*Stiffness; consequently, the three-way interaction effect of Velocity*Mass*Stiffness was also significant.

Table 4.3: Stepwise Regression Analysis results summary for forward selection (and backwards elimination) (Adjusted $R^2 = 0.8992$, $F = 40.39$ [on 12 and 42 df], $p < 0.001$). * denotes significance at $\alpha = 0.05$. Table also includes multiple R^2 ("Separate R^2 ") and p values of single factor models for Velocity, Mass, TSTT, and Pelvic Stiffness.

Coefficients	Estimate	Standard Error	t value	p	Separate R^2	P
Intercept	296.80	107.60	2.758	0.009*		
Velocity	-109.20	37.86	-2.885	0.006*	0.203	0.001*
Mass	-5.77	2.44	-2.368	0.023*	0.123	0.009*
TSTT	-3.80	1.29	-2.945	0.005*	0.448	<0.001*
Stiffness	-8.00×10^{-3}	4.00	-2.119	0.040*	0.059	0.077
Velocity x Stiffness	3.00×10^{-3}	1.00×10^{-3}	2.548	0.015*		
Velocity x Mass	2.54	0.86	2.975	0.005*		
Velocity x TSTT	0.78	0.43	1.803	0.079		
Mass x Stiffness	1.80×10^{-4}	1.00×10^{-4}	2.098	0.042*		
TSTT x Stiffness	7.00×10^{-5}	4.00×10^{-5}	1.711	0.095		
Mass x TSTT	1.36×10^{-2}	0.01	1.311	0.197		
Velocity x Mass x Stiffness	-8.00×10^{-5}	3.00×10^{-5}	-2.576	0.014*		
Velocity x TSTT x Stiffness	-2.00×10^{-5}	2.00×10^{-5}	-1.39	0.172		
Sum of Separate R^2					0.833	

4.4 Discussion

The two main objectives of this study were to quantify the effects of fall and faller-specific factors on the force attenuating property of a safety floor during simulated lateral impacts with a surrogate human pelvis, as well as generate a multiple linear regression model that can predict the safety flooring force attenuation based on the factors tested. In line with the hypotheses, A_{floor} increased with impact velocity (by 9.0% from the lowest to highest condition) and effective mass (by 6.9% from the lightest to heaviest condition), and decreased by 13.1% from the thinnest to thickest TSTT condition. While there were no significant effects pelvic stiffness, there was a trend towards an effect with an average increase of 3.9% from the 22 650 N/m to 33 370 N/m pelvic

stiffness trials. The second objective (generating the multiple linear regression model for A_{floor}) was also achieved, resulting in a predictive model for A_{floor} with an adjusted R^2 of 0.8992. These data provided substantively value to the field by demonstrating the importance of standardizing mechanical test system parameters, and by robustly characterizing the force attenuation profile of a safety flooring product across a range of fall and faller characteristics.

As mentioned in the results, the model did not include the 4-way interaction of the factors, and only included two of the three-way interactions (velocity*mass*pelvic stiffness, and velocity*TSTT*pelvic stiffness). Both the forward selection and the backward elimination stepwise regression methods resulted in the same model. Additional models were also generated using forced entry methods, which included both a main effects only regression model, as well as a model that included all main and interaction effects. The model that included all factors and combinations did achieve the highest multiple R^2 , with a value of 0.9276, but the adjusted R^2 of this model ($R^2 = 0.899$) was lower than that of the stepwise regression method models. While main effects only model had the lowest multiple and adjusted R^2 values (0.8393, and 0.8261, respectively), the main effects did manage to explain a large majority of the variance; further evidence of this can be seen in Table 4.3, where the sum of the R^2 of the main effects (from individual factor models) is 0.833.

The study findings aligned with a majority of the original hypotheses. Firstly, it was hypothesized that A_{floor} would increase as the impact velocity increased, which was confirmed by the significant increase in A_{floor} observed when increasing the impact velocity from 2.1 m/s to 3.4 m/s. Our findings align with those of Laing and Robinovitch's 2009 study, where the force attenuation provided by SmartCells™ flooring increased by 16% when increasing impact velocity from 2 to 4 m/s (Laing and Robinovitch, 2009). Secondly, the hypothesis that effective mass (or

mass of the load carriage) would not significantly effect A_{floor} was not confirmed, as a significant linear increase in A_{floor} was observed as mass increased. This hypothesis was founded on the effect of increasing effective mass of a mass-spring model on the peak force attenuation provided by a hip protector, where a linear and slightly negative trend was expected (with a less than 5% decrease over a range of 60 kg) (Laing Thesis, 2008). Since the effects of increasing effective mass have not been reported for safety floors, this trend was used with the assumption that safety floors act similarly to hip protectors (and that the test system used in this study was similar to a mass-spring model); interestingly, our findings suggest otherwise. Thirdly, a decrease in A_{floor} was observed as TSTT increased, as was originally hypothesized. This was likely due to increasing TSTT leading to a decrease in overall system stiffness (a combination of TSTT stiffness and the pelvic stiffness as springs-in-series), which has been shown previously to increase force attenuation (Laing et al., 2006). The fourth hypothesis was not confirmed, as no significant increase in A_{floor} was observed with the increase in pelvic stiffness, where the average increase of 3.75% in A_{floor} from the 22 650 N/m to the 33 370 N/m pelvic stiffness trials did not reach significance. While increasing the stiffness of the surrogate pelvis stiffness should increase the loading rate (and consequently F_{max} and F_{neck}), the difference between the two stiffness levels may not have been large enough to result in significant changes.

The current results are supported by previous literature in the area. Firstly, Laing and Robinovitch (2009) the force attenuating properties of SmartCells™ safety flooring increased as impact velocity increased. Secondly, a study by Bhan et al in 2014 investigated the effects of body mass index (BMI) and flooring surface on the energy absorbed during simulated lateral hip impacts, where some of the flooring surfaces were safety floors (one of them being a SmartCells™ sample). While conducting simulated lateral hip impacts (using a lateral pelvis release paradigm

using human volunteers) at a controlled impact velocity, the authors reported that more energy was absorbed during the SmartCells™ sample trials for the low BMI group when compared to the high BMI group. While BMI is a metric that relates mass and height, it is also positively associated with TSTT (Maitland, Myers, Hipp, Hayes, & Greenspan, 1993; Lafleur Thesis, 2016). And so, it is possible that differences the authors observed between BMI groups was due to the difference in TSTT, with high BMI individuals having more TSTT and therefore less energy absorbed (by the safety floor), and the opposite for low BMI individuals. This aligns with the findings of this current experiment. Furthermore, it should be noted that in the Bhan et al 2014 article, energy absorbed was normalized to total body mass, and both high and low BMI groups had an equal number of males and females; it is likely that TSTT was a factor that explains that difference. In fact, previous studies who tested the energy absorbing properties of hip protectors found that the energy absorbed decreased as TSTT increased (van Schoor et al., 2006). As for effective mass and pelvic stiffness, little has been investigated to date. This was most likely due to the fact that both effective mass and pelvic stiffness can only be tightly controlled in mechanical test systems, and that previous studies using mechanical test systems have not investigated these factors. This study was one of the firsts to quantify the effects of both controlled effective mass pelvic stiffness on the force attenuating properties of safety floors. Overall, these results generally align with relevant literature, and add important insights about factors that should be considered (or standardized) in mechanical test systems used to test the protective capacity of safety floors.

The results indicate that safety floors may provide more benefits to certain segments of the population. Specifically, individuals with less trochanteric soft tissue would benefit greatly from these safety floors, compared to individuals with greater amounts of soft tissue. But more generally, as the mass of the faller increases, and the height (or the velocity) of the fall also

increases, so do the potential benefits (ie: force attenuation) of safety flooring. Furthermore, it should be noted that the safety flooring did not appear to bottom out, even at the highest tested impact velocity. This is promising, as the safety flooring provided more force attenuation in high velocity impacts, which relates to high energy falls where fractures are most likely to occur.

The regression equation developed in this study can provide valuable insight when estimating the effect of a safety flooring intervention of fall-related hip fracture risk. In fact, the regression equation could be applied to previously developed models of hip fracture risk, such as the population-level probabilistic model developed in Chapter 3, allowing us to estimate the risk reducing effect of a safety flooring intervention. This exact scenario will be presented in the following Chapter, where the population-level effects of a safety flooring intervention will be evaluated for hip fracture risk.

The design of this study did result in some limitations. Firstly, collecting one trial per condition limited us to investigating only main effects via ANOVA methods. This resulted in a lack of degrees of freedom to assess interaction effects. This was only partially a limitation, as a full factorial design was used, with every possible combination of factors being tested at least once, and the high reliability of the test system used lead to a high degree of confidence in the measures. Furthermore, while interaction effects were analyzed in the regression model, the primary goal of this study was to assess the main, or simple, effects of these factors (as stated in the hypotheses). A second limitation to this study was the use of only two levels for pelvic stiffness. Apart from the flooring condition, this was the only independent variable that had two levels included into the test matrix. It is possible that adding a third level (specifically a value that would increase the range of pelvic stiffness tested) could have lead to a significant main effect of pelvic stiffness being observed. The rational for using the two pelvic stiffness levels (33 370 N/m, and 22 650 N/m) was

to best replicate the male and female mean values reported by Levine and colleagues in their 2013 article (male = 34 271 N/m; female = 25 194 N/m), allowing us to simulate a “male” and “female” surrogate pelvis. The two values used were the closest total system stiffness values achievable with the current test system (pelvic stiffness was primarily adjusted by changing the “T springs” that sit beneath both sheets of the leaf spring system). In the future, there is value in assessing the effect of effective stiffness within a sex (e.g. one + and – 1 SD of the average values measures for females). Thirdly, the range of TSTT included in this study was not representative of the range observable in the Canadian older adult population of Canada, where the average measured TSTT is typically higher for females (males = 2.96 cm; females = 5.14), and can range up to over 9 cm, or higher in special cases (Lafleur Masters Thesis, 2016). While the range chosen for this study adequately represents the average for the male population, this range was primarily chosen based the IHPRG recommendations for a minimum value of 18 mm of soft tissue covering the greater trochanter to simulate higher-risk females. Regardless, a significant main effect was observed even with the small range tested – future work to better characterize the relationship across a greater range of TSTT would be of merit. Fourthly, the a-priori criteria set for the multiple linear regression model (achieve the best possible adjusted R^2 value) could have resulted in a model that over fits the data. While this can be a limitation in some cases, this was the explicit purpose of this model, as it was to be used as a sub-model within a probabilistic model. Since the probabilistic model already includes elements of uncertainty, the goal was to minimize the residual error and account for as much uncertainty possible. The final limitation was that only one type of safety flooring was tested. While this does prevent the generalization of the findings to other types of safety floors, one of the goals of this study was to develop a safety flooring specific regression equation to predict A_{floor} , which was to be used in a larger predictive model.

4.5 Conclusion

This study successfully quantified the effects of fall and faller-specific characteristics (impact velocity, effective mass, TSTT, and pelvic stiffness) on the force attenuation provided by a sample of SmartCells™ safety flooring (A_{floor}). More specifically, we observed that impact velocity, effective mass and TSTT all have significant effects on A_{floor} , with increasing velocity and effective mass increasing A_{floor} , and TSTT having the opposite effect. Increases in pelvic stiffness however, lead to non-significant increases in A_{floor} . Furthermore, this study used the data generated during the mechanical testing to develop a multiple linear regression equation that predicts the force attenuation provided by a safety floor (A_{floor}) based on both fall and faller-specific characteristics in the event of a lateral fall to the hip. The findings of this experiment could prove valuable in informing future studies involving mechanical testing of this kind, showing that impact velocity, mass and TSTT are the main influencers of A_{floor} . Additionally, the regression equation developed can be used to predict the influence of a safety flooring intervention on the risk of fall-related hip fractures in specific populations. This will be done in the following chapter by applying the regression equation developed in this study as a sub-model in the probabilistic model of hip fracture risk in the Canadian older adult population that was developed in the previous chapter of this Thesis document.

Chapter 5

The Effect of a Simulated Safety Flooring Intervention on the Population-level Hip Fracture Risk for Canadian Older Adults

5.1 Introduction

As the older adult portion of the population increases, so does the overall cost of fall-related hip fractures, were the rates increase exponentially with age after age 60 (Jean et al, 2013) (see section 2.1.1 of Chapter 2 for further details on the scope of the issue). With the elevated risk of fall-related hip fractures in older adults, there has been an equal increase in the desire to predict and prevent fall-related hip fractures in older adults.

Historically, predictive models, such as FRAX and QUORAC, have been used to predict an older individual's risk of suffering a fall-related hip fracture (see section 2.3.1 of Chapter 2 for further details on predictive models of hip fracture risk). While these models are easily implemented on an individual, or person specific, basis, they cannot provide insights into the risk of hip fracture of large groups (or populations), nor account for the effects of potential interventions. As shown in Chapter 3 of this Thesis document, probabilistic modeling is a promising approach for assessing hip fracture risk on a population-level.

The probabilistic model developed in Chapter 3 could be a viable method of assessing hip fracture risk for the Canadian older adult population (see Chapter 3 for more details on the specifics of the model, as well as results). Furthermore, the structure of the model may lend itself well as an effective method of virtually testing the potential influence of an intervention on population-level hip fracture risk, given that the mechanisms by which the interventions effect risk are properly understood.

While there are many interventions designed to reduce the risk of fall-related hip fractures, one of the most promising interventions are safety floors (see section 2.2.3 of Chapter 2 for further details on fall-related hip fracture interventions). As has been demonstrated in previous research studies (Bhan et al., 2014; Laing and Robinovitch, 2009), safety floors reduce the impact forces experienced during simulated lateral falls to the hip when compared to impacts onto rigid surfaces. These findings have been further bolstered by the findings of the experiment discussed in Chapter 4, where the force attenuation provided by safety floors was characterized as a function of both fall and faller-specific factors. With the force attenuating properties of one safety flooring sample quantified, it is possible to investigate the effects of a safety flooring intervention on population-level hip fracture risk, through means of probabilistic modeling.

The goal of this study was to combine the model developed in Chapter 3 with the safety floor force attenuation regression equation developed in Chapter 4 to virtually estimate the effect of a large-scale safety flooring intervention on the population distribution of hip fracture risk. We hypothesized that the force attenuation properties of safety flooring observed in Chapter 4 (more specifically, the influence of fall and faller-specific factors on the force attenuation provided by safety floors) would translate into substantial decreases in hip fracture risk (FOR values) for both males and females.

5.1 Methods

5.1.1 Model Modification

As described in Chapter 3, the original probabilistic model begins by assigning physical characteristics to a virtual individual (VI), which are then used to compute peak impact force and bone strength (fracture threshold). The model also estimates the force attenuation provided by the soft tissues overlying the greater trochanter of the hip (TSTT), which was then subtracted from the

peak impact force (resulting in net force). The ratio between the net force and bone strength was computed, resulting in a factor of risk (FOR). For this study, the model was modified to include additional computations. Firstly, the safety floor force attenuation regression equation developed in Chapter 4 (which predicts the attenuation of peak femoral neck force as a percentage of net impact force) was added to the model, where

$$A_{floor} = 296.8 - 109.2v - 5.772m - 3.80t - 0.007968k + 0.003393vk + 2.544vm + 0.7787vt + 0.000178mk + 0.000073tk + 0.01359mt - 0.000078vmk - 0.00002105vtk$$

[Equation 5.1],

where v represents impact velocity, m represents effective mass, t represents TSTT, and k represents pelvic stiffness. Impact velocity (v) was derived from the fall height, where

$$v = \sqrt{2gh} \text{ [Equation 5.2].}$$

Secondly, safety floor force attenuation (A_{floor}) was computed by using the same physical characteristics of the virtual individual and multiplied by the net impact force; this was then subtracted from net force, resulting in an intervened net force. This was not done for VI with a net force of 0 or less (a potential case when the estimated force attenuation provided by the TSTT surpasses the predicted peak impact force). Finally, the ratio between intervened net force and bone strength was computed to result in the intervened factor of risk (IFOR), which represents that virtual individual's factor of risk if the fall-related hip impact occurs on a safety floor. A pictographic representation of the modified model structure can be seen in Figure 5.1.

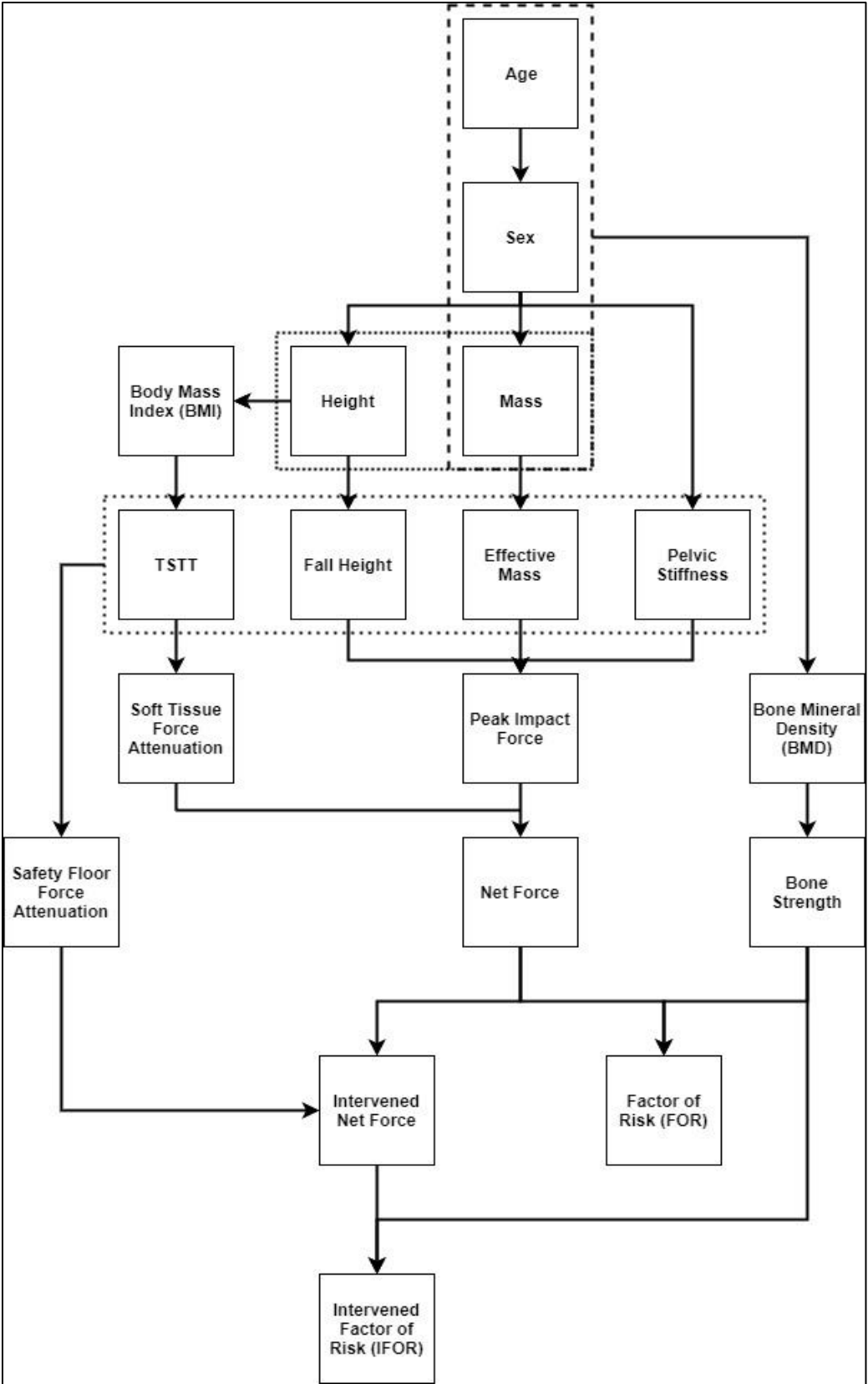


Figure 5.1: Modified Probabilistic Model including FOR and IFOR

5.1.2 Intervention Effectiveness

To assess the effectiveness of a safety flooring intervention (SmartCells™) on population-level hip fracture risk in Canadian older adults, we assessed the difference between FOR and IFOR for each simulated individual, and calculated the mean change in FOR (difference between mean FOR and IFOR) for both males and females. As was done in the model application portion of Chapter 3 (see section 3.2.3 of Chapter 3 for more details on the specifics of the simulation used), a representative sample of 100 000 VI was generated and run through the model, calculating both the FOR and IFOR for each simulated individual. This allowed us to quantify the predicted effectiveness of the safety flooring intervention at the level of an individual VI. This mean change represents the average reduction in FOR provided by a safety flooring intervention for male and female Canadian older adults. To calculate this, the difference between FOR and IFOR was calculated for each VI, and the mean difference (and standard deviation) was computed. Additionally, to better understand how the sex specific population distributions of fall-related hip fracture risk are affected by the intervention, both the FOR and IFOR distributions for both males and females were characterized as probability distribution functions (PDF) (50 bins, ranging from an FOR value of -1 to 1.5 in 0.05 value increments). We compared the FOR and IFOR PDFs by calculating the difference in probability density at each FOR bin; this allowed us to quantify the change in the population distribution of risk between an un-intervened and an intervened simulation. Furthermore, the difference between each VI's FOR and IFOR was computed, and the mean of this difference was calculated for both females and males, quantifying the average reduction in FOR due to the intervention. It should be noted that VI with an FOR value of 0 or less did not receive additional force attenuation from the safety flooring intervention, as the net force prior was less than or equal to zero.

5.1.3 Model Stability and Convergence of Variance

While the relative stability (ability to produce the same, or near same, result from one simulation to the next) was demonstrated in the validation of this model against an existing dataset (see section 3.2.2 of Chapter 3 for more details), additional analyses were conducted to quantify the stability (in variance) of the model. Firstly, to demonstrate the stability of the model with the number of VI used in the model application portion of Chapter 3 and used in the intervention effectiveness portion of Chapter 5 (100 000 VI), the model (including the intervention sub-model) was run 50 times with 100 000 VI being generated each time. Similar to what was done for testing the effectiveness of the intervention, sex specific PDFs were characterized for both FOR and IFOR; this was done for each of the 50 simulations. For both the FOR and IFOR PDFs, the mean probability density over the 50 simulations was computed for each FOR bin (for both males and females). The standard deviation of the means of each FOR bin (over 50 simulations) was also calculated.

Secondly, convergence of variance was also quantified as a function of the number of VI generated in a given simulation. To do so, the model was run with 12 different numbers of VI (100, 250, 500, 1000, 2000, 3000, 4000, 5000, 10000, 25000, 50000, 100000); at each of these 12 numbers, 50 simulations were run and the mean sex specific FOR and IFOR values were extracted (for each of the 50 simulations). Since the number of males and females vary from simulation to simulation, an equal number of males and females were generated for this test (equal to the level of VI). The grand mean and (standard deviation of the means) of the 50 simulations were computed for all 12 levels of VI. To determine the minimum number of VI (of one sex) needed to reach stability, we set an a priori stability threshold of 0.005 for standard deviation of mean FOR. Using this threshold, we determined the minimum number of VI needed as the point of the curve that intersected horizontally with the 0.005 threshold. As we compared four different curves (FOR and

IFOR for both males and females), we determined the overall minimum number of VI (to the nearest 5 VI) required to achieve stability as the highest of these 4 values; this allows for all four values (sex-specific mean FOR and IFOR) to achieve our desired level of stability. With this number found, at least twice that number of total VI (males and females combined) were assumed to be required to achieve the desired variance stability. As an additional validation of the number of VI used in previous simulations (100 000 VI), we also determined the percent variance that intersected with the curve at the VI level of 100 000.

5.1.4 Fracture Point Analysis

As was done in section 3.2.5 of Chapter 3, the *Fracture Point* values determined in the Fracture Point analysis (0.0148 for females, 0.3725 for males) were compared to the data generated in the intervention effectiveness experiment (in this Chapter) to determine the number (and percentage) of VI who had a FOR value greater than the *Fracture Point*, as well as the number (and percentage) of VI who had a IFOR value greater than the *Fracture Point*. The difference between these percentages (percent reduction of likely fractures outcomes) was also quantified.

5.2 Results

5.2.1 Intervention Effectiveness

A model simulation of 100000 VI was computed, resulting in sample with a mean (SD) age of 69.8 (8.4) years. The sample was split by sex, with 52968 females and 47032 males being generated, with the mean (SD) age of those groups being 70.3 (8.8) and 69.1 (8.0) years, respectively. The mean (SD) mass, height, and pelvic stiffness was 71.0 (9.4) kg, 1.59 (0.05) m and 25173 (6113.5) N/m for females, and 83.4 (10.7) kg, 1.72 (0.05) m, and 34246 (9439.9) N/m for males. Further detail is summarized in table 5.1 below.

Table 5.1: Results Summary for 1 simulation of the model, including the safety flooring module

Variable	Female		Male		Units
	Mean	SD	Mean	SD	
Number of VI	52968		47032		Number
Age	70.3	8.8	69.1	8.0	Years
Height	1.59	0.05	1.72	0.05	Meters (m)
Mass	71.0	9.4	83.8	10.7	Kilograms (kg)
Pelvic Stiffness	25173	6113.5	34246	9439.9	Stiffness (N/m)
BMI	28.14	4.13	28.46	3.99	kg/m ²
TSTT	54.94	17.10	33.90	16.46	Millimeters (mm)
Fall Height	0.932	0.031	1.007	0.031	Metres (m)
Effective Mass	39.26	5.63	39.10	6.19	Kilograms (kg)
BMD	0.752	0.152	0.880	0.143	g/cm ²
Bone Strength	5603.0	1244.6	6651.7	1250.1	Newtons (N)
Peak Impact Force	4205.9	614.7	5073	843.7	Newtons (N)
Soft Tissue Force Attenuation	3900.6	1214.3	2407	1168.6	Newtons (N)
Net Force	305.2	1201.8	2666.0	1265.0	Newtons (N)
Factor of Risk (FOR)	0.067	0.337	0.422	0.231	Ratio
Non-Negative Factor of Risk	0.128	0.291	0.424	0.227	Ratio
Safety Floor Force Attenuation	117.4	189.6	758.1	572.2	Newtons (N)
Intervened Force	187.9	1059.7	1907.9	800.4	Newtons (N)
Intervened Factor of Risk (IFOR)	0.044	0.298	0.301	0.145	Ratio
Non-Negative Intervened Factor of Risk	0.105	0.250	0.302	0.140	Ratio
FOR – IFOR	0.023	0.039	0.121	0.086	Ratio
FOR – IFOR (% decrease)	34.3	11.6	28.9	37.2	Percentage

The addition of the safety flooring module to the model resulted in a downward (leftward) shift of the distribution of hip fracture risk for both females and males (Figure 5.2). More specifically, the intervention led to the probability density decreasing for FOR values greater than 0.3 for females and 0.45 for males, with concomitant increases in the lower risk spectrum (Figure 5.3). The largest increase in probability density was observed at FOR values of 0.15 for females and 0.3 for males, with the largest decreases at FOR values of 0.4 and 0.6 for females and males, respectively.

Overall, the safety flooring intervention decreased mean risk by 34.3% for females (from a FOR of 0.067 to 0.044) and 28.9% for males (from a FOR of 0.422 to 0.301). Furthermore, the addition of the safety flooring module decreased the variance about the mean as characterized by a 11.6% decrease in standard deviation for females, and a 37.2% decrease for males. (Figure 5.2, Table 5.1). When viewed at the individual VI level (comparing IFOR to FOR for each VI), we observed an average reduction of risk of 8.87% for female VI, and 24.56% for male VI.

Using a simple threshold FOR value of 1.0 as the dividing line between non-fractures and fractures, approximately 0.13% of the female VI are at risk of suffering a hip fracture in the event of a fall (N = 68), compared to 1.41% of male VI (N = 665). When applying the same threshold to IFOR values, ~0.02% of the female VI are still at risk of suffering a hip fracture in the event of a fall (N = 13), resulting in 55 (80.9%) of the 68 potential hip fractures being prevented (if the fall was intervened by a safety floor). For male VI, approximately 0.05% are still at risk of suffering a hip fracture (N = 24), meaning that 641 (96.4%) of the 665 potential hip fractures would be prevented with a safety flooring intervention.

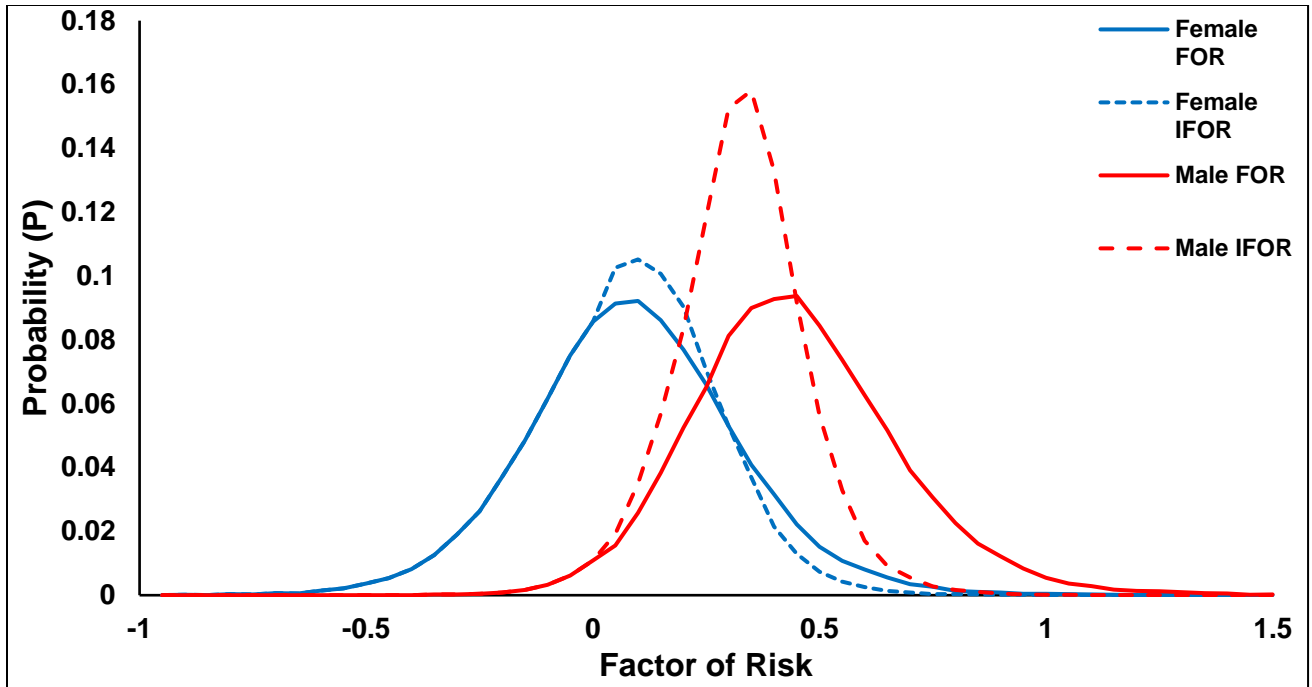


Figure 5.2: The probability distribution functions (PDF) of female (blue) and male (red) FOR (solid line) and IFOR (dashed line); the data was distributed across 50 bins of FOR (ranging from -1 to 1.5), each bin representing a width of 0.05

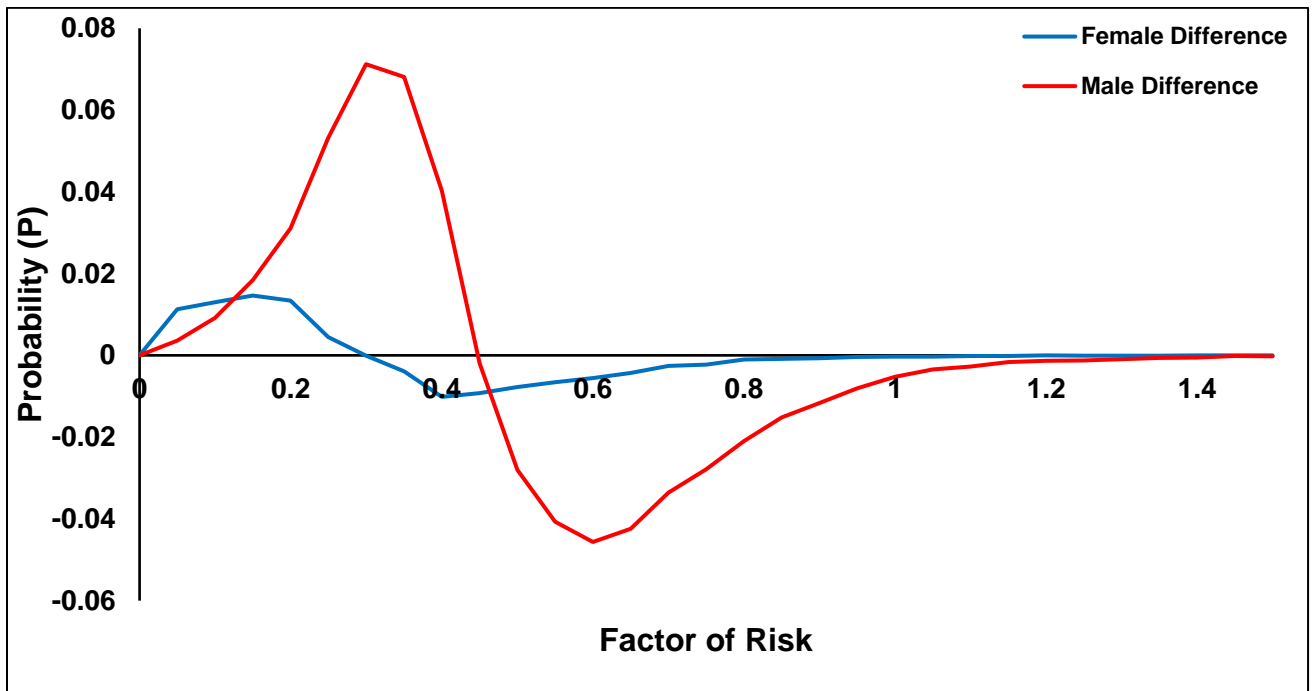


Figure 5.3: The difference between the IFOR and FOR PDFs at each FOR bin

5.2.2 Model Stability

When assessing the approaches employed in the safety flooring evaluation section above were repeatedly simulated (i.e. 50 repeated simulations of 100,000 VIs), very limited variance was observed in the probability densities of hip fracture risk across the four distributions (male and female, baseline [FOR] and safety flooring intervened [IFOR]; Figure 5.4). The maximum SD of mean FOR probability density occurred for the male IFOR curve with a value of 1.63×10^{-3} , which equated to a 1.2% of the mean value.

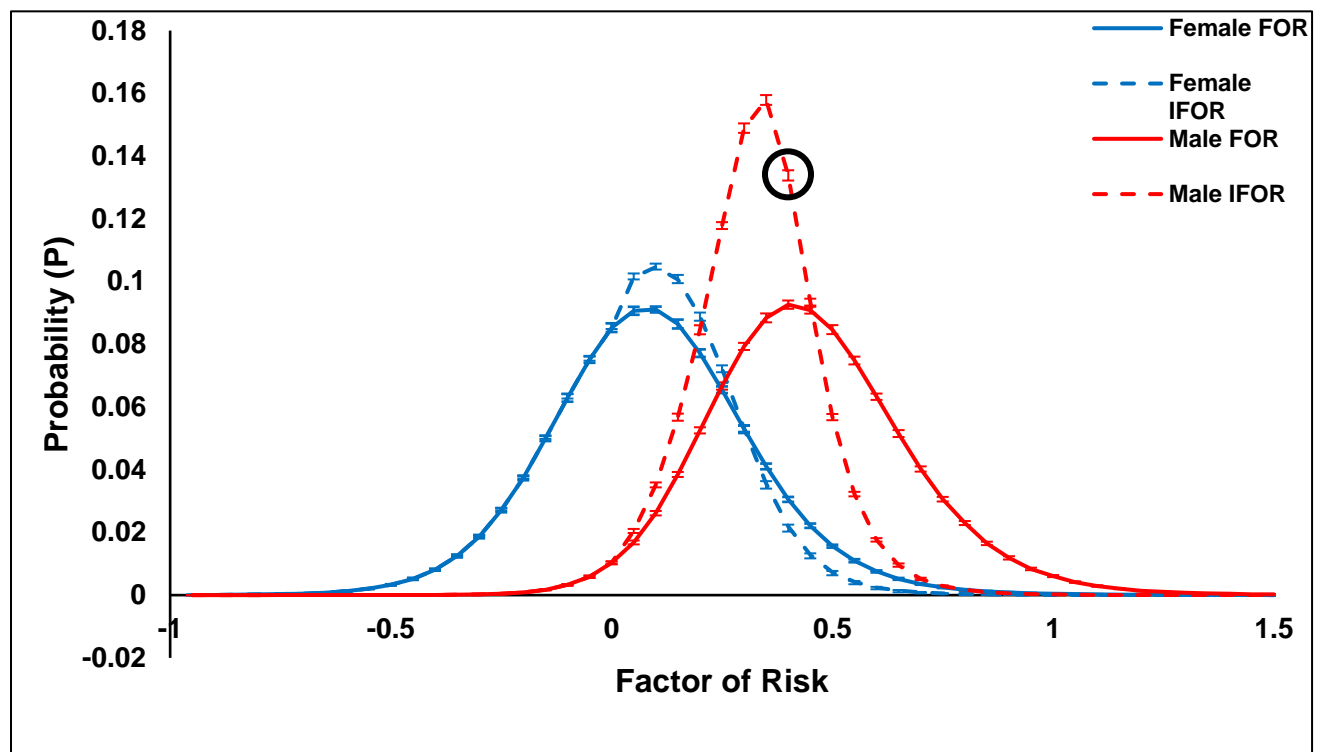


Figure 5.4: Compiled FOR and IFOR sex-specific PDFs (10 simulations of 100 000 VI); grand mean of mean FOR and IFOR at each FOR bin over 50 simulations. Circle denotes point with highest overall SD in the mean FOR probability density

For the analysis used to determine the minimum number of VIs required to produce stable model predictions, the variance in hip fracture risk estimations decreased as the number of VIs used in the simulations increased (Figures 5.5 and 5.6). The relationships were asymptotic (asymptote at 0), with variance reducing as the number of VI simulated increased for both female and male FOR and IFOR (see Figures 5.5 and 5.6). For both males and females, there was more variance present in FOR than in IFOR (Table 5.2). The point at which the FOR curve crosses the 0.005 SD threshold was at 3090 VI for females, and at 2100 for males. According to our approach of doubling this value to ensure the desired N was achieved for males and females, these analyses indicate a total VI number of 6180 would be sufficient to achieve the minimum desirable level of simulation variance.

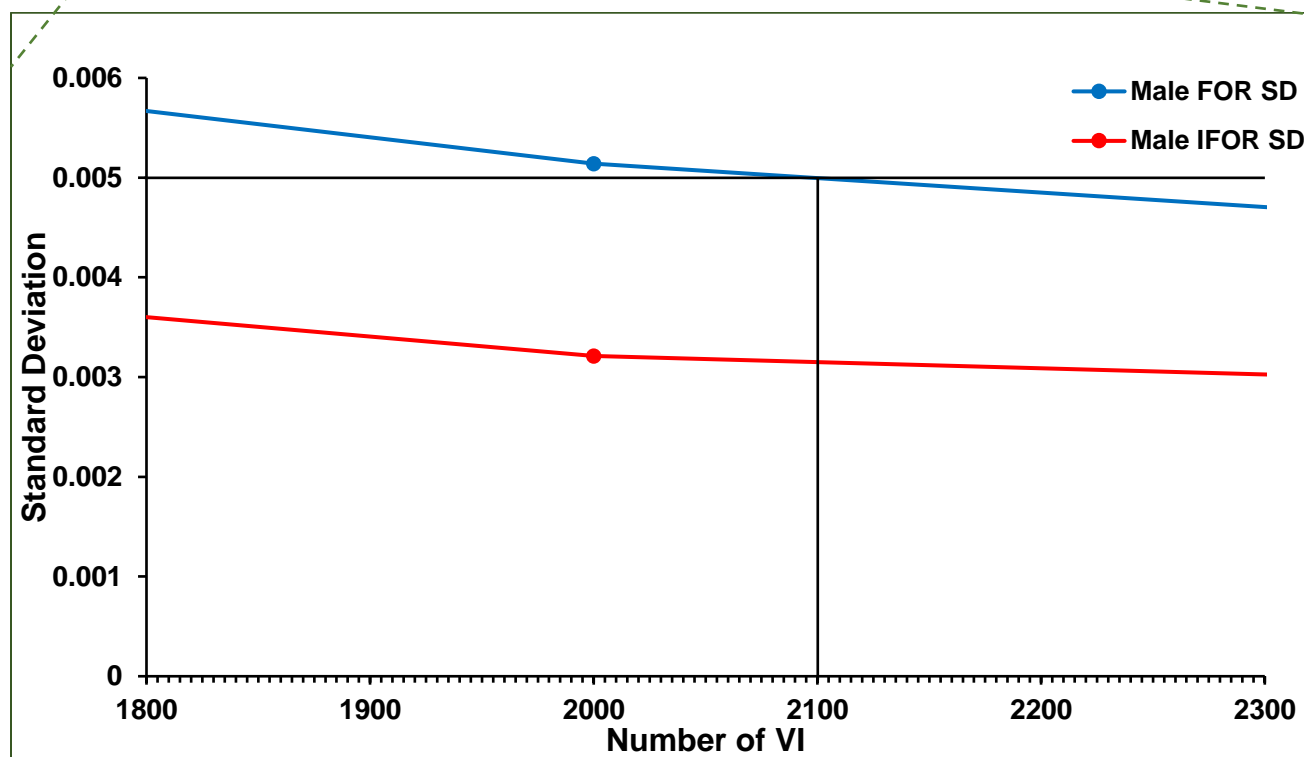
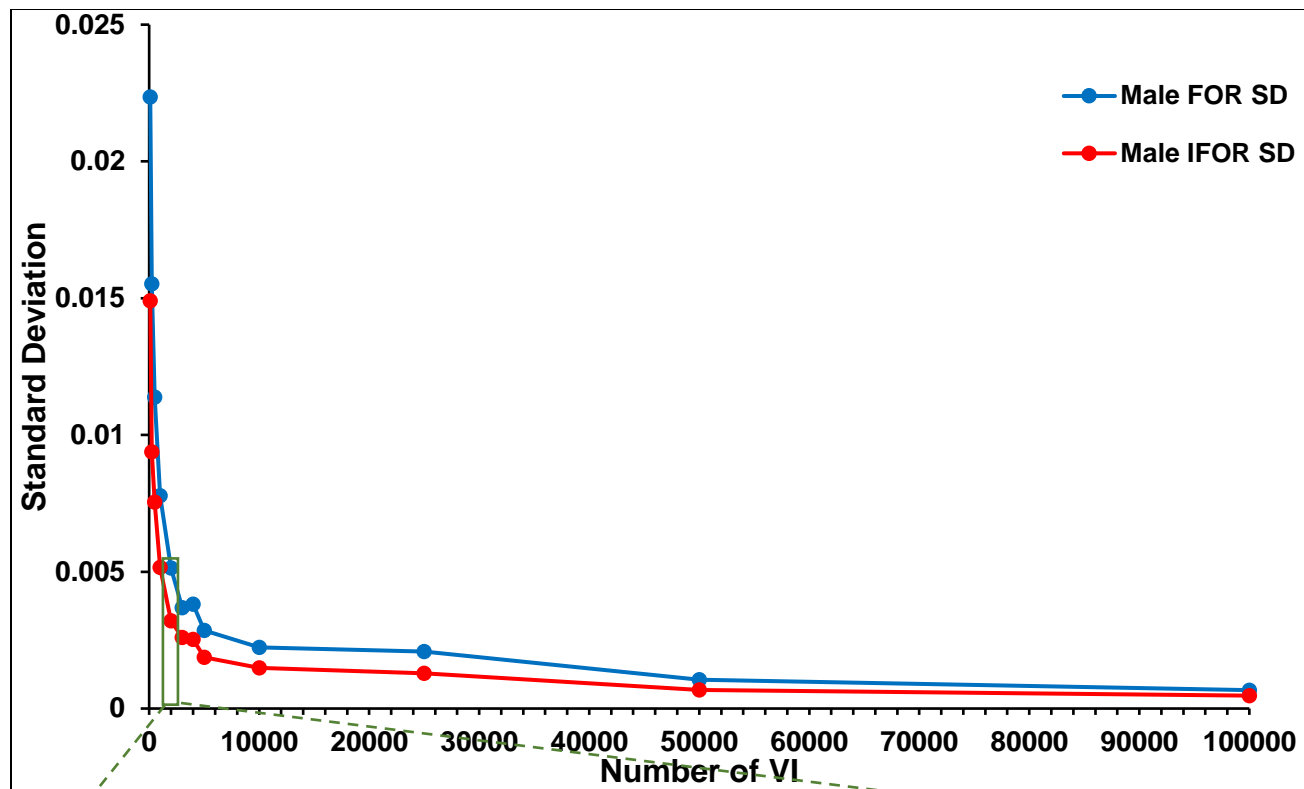


Figure 5.5: Male average SD of mean FOR of 50 simulations at various N of VI; bottom figure shows zoomed in portion of top figure

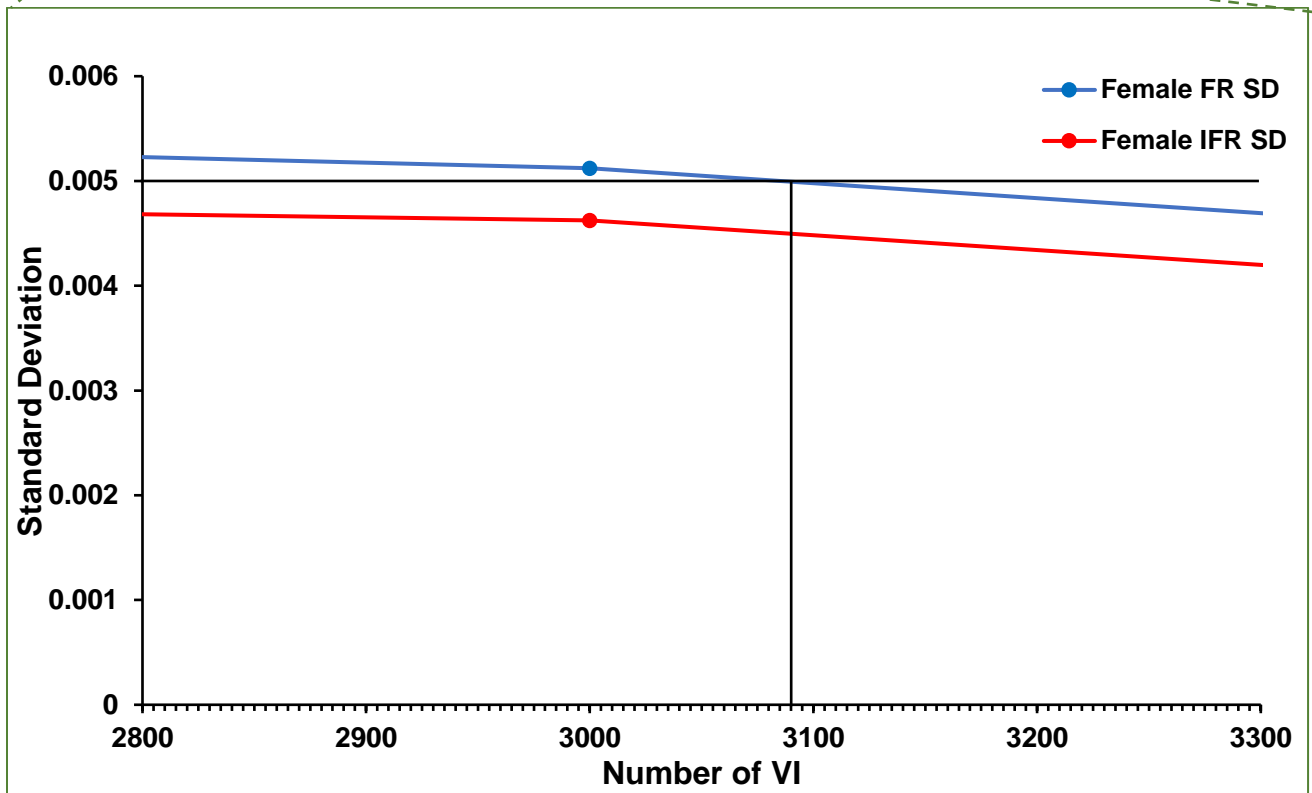
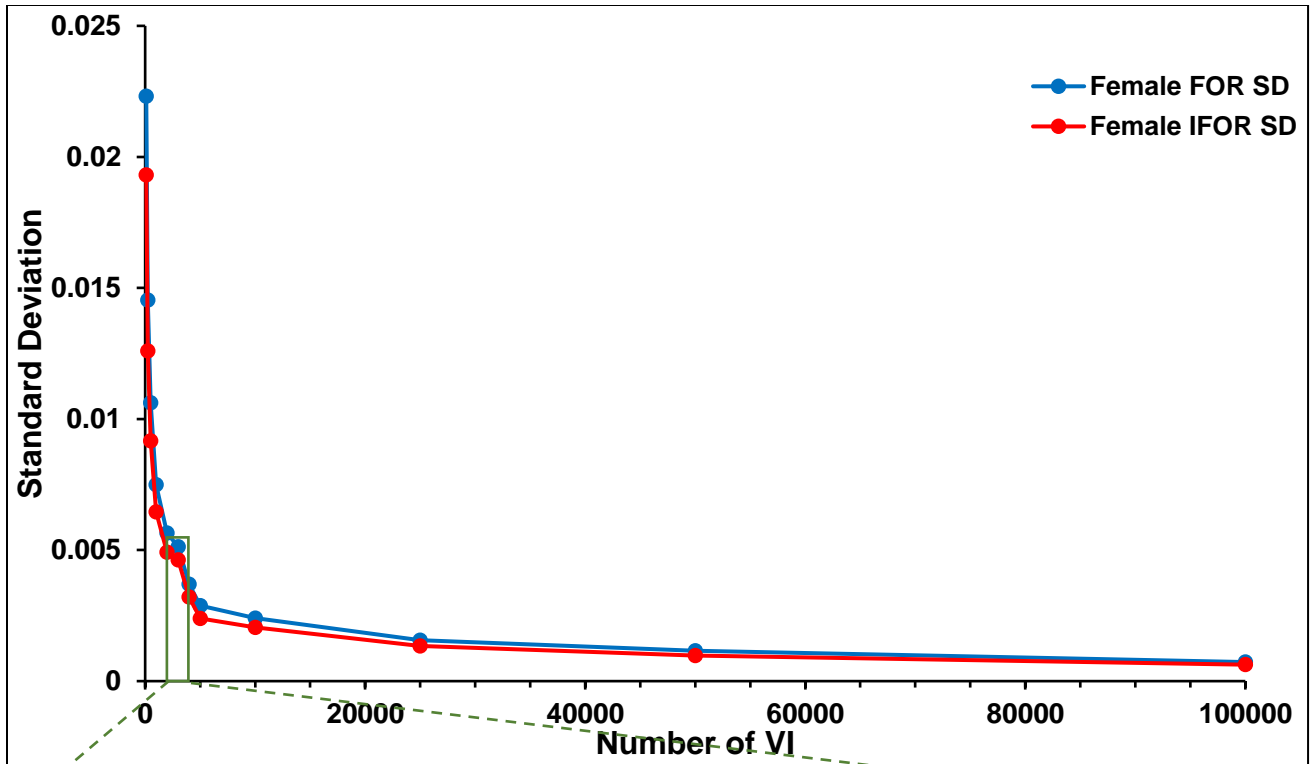


Figure 5.6: Female average SD of mean FOR of 50 simulations at various N of VI; bottom figure shows zoomed in portion of top figure

Table 5.2: Summary results of variance convergence analysis. * denotes that value was rounded to 0.000

N of VI	Male				Female			
	FOR mean	FOR SD	IFOR mean	IFOR SD	FOR mean	FOR SD	IFOR mean	IFOR SD
100	0.425	0.022	0.302	0.015	0.061	0.022	0.038	0.019
250	0.426	0.016	0.303	0.009	0.067	0.015	0.044	0.013
500	0.425	0.011	0.302	0.008	0.065	0.011	0.043	0.009
1000	0.426	0.008	0.303	0.005	0.065	0.007	0.042	0.006
2000	0.426	0.005	0.303	0.003	0.065	0.006	0.042	0.005
3000	0.425	0.004	0.302	0.003	0.064	0.005	0.042	0.005
4000	0.425	0.004	0.303	0.003	0.065	0.004	0.042	0.003
5000	0.426	0.003	0.303	0.002	0.065	0.003	0.042	0.002
10000	0.426	0.002	0.303	0.001	0.065	0.002	0.042	0.002
25000	0.425	0.002	0.303	0.001	0.065	0.002	0.042	0.001
50000	0.425	0.001	0.303	0.001	0.065	0.001	0.042	0.001
100000	0.425	0.001	0.3023	0.000*	0.065	0.000*	0.042	0.001

5.2.3 Fracture Point Analysis

Comparison of VI FOR values to the sex-specific *Fracture Point* values revealed that 28232 (53.3%) of the 52968 female VI, and 23790 (50.6%) of the 47032 male VI, are predicted to be more likely to suffer a hip fracture than not in the event of a fall. After the safety flooring intervention module, comparing female and male IFOR values to their respective sex-specific *Fracture Point* values revealed that 27754 (52.4%) of females, and 9794 (20.8%) of males, were still predicted to be likely to suffer a hip fracture in the event of a fall. This represents a 0.9% reduction (from 53.3 to 52.4%) in the predicted number of likely hip fracture cases (in the event of a fall) for females, and a 29.8% reduction (from 50.6 to 20.8%) for males (Table 5.3). Results using the secondary method of determining *Fracture Point* are presented in Appendix C.

Table 5.3: Results Summary for Fracture Threshold Analysis; Analysis was performed on the same dataset that was generated for the intervention effectiveness experiment

Metric	Female	Male
N	52968	47032
Mean FOR	0.067	0.422
Fracture Point	0.0432	0.405
N of FOR > Fracture Point	28339	23722
Percent > Fracture Point	53.4%	50.5%
Mean IFOR	0.044	0.301
N of IFOR > Fracture Point	27754	9794
Percent > Fracture Point	52.4%	20.8%
Percent Reduction	0.9%	29.8%

5.3 Discussion

The main objectives of this study were to estimate the effect of a large-scale safety flooring intervention on the population distribution of hip fracture risk, as well as evaluate the relative stability of the model from one simulation to another. By combining the probabilistic model developed in Chapter 3 with the safety floor force attenuation regression equation developed in Chapter 4, we developed a probabilistic model of hip fracture risk in the older adult population of Canada that quantifies risk with and without a safety flooring intervention. In this study, the addition of the safety flooring intervention resulted in a 34.6% reduction in mean factor of risk (when comparing mean IFOR to mean FOR) for females, and a 28.8% reduction for males. When viewed at the individual VI level (comparing IFOR to FOR for each VI), we observed an average reduction of risk of 8.87% for female VI, and 24.56% for male VI. In both tests of convergence of variance, we observed extremely little variance from simulation to simulation when generating 100000 VI per simulation (as seen in Figures 5.5 and 5.6, as well as in Table 5.2). Additionally,

we determined that a minimum of number of 6180 VI (generating at least 3090 females and 2100 males; twice the amount of the largest number should ensure that the desired number is achieved) are needed to be generated per simulation to achieve a stability threshold standard deviation of mean FOR and IFOR of 0.005.

The addition of the safety flooring sub-model into the overall probabilistic model of older adult hip fracture risk resulted in an overall reduction in the risk of suffering a fall-related hip fracture. The method in which the intervention was included in the model assumes that every VI suffers a lateral fall to the hip, and has that fall intervened by a SmartCell™ safety floor. While the studies performed in Chapter 3 reported the first estimates of population-level hip fracture risk for Canadian older adults, the study conducted in this chapter quantified the anticipated effect of a population-wide safety flooring intervention on the population-level hip fracture risk in the older adult population, and found that the average risk reduction (at the individual VI level) ranged between 8.87 and 24.56%, depending on sex. As explained in Chapter 4, this reduction was driven by the force attenuation provided by the safety floor, where the force attenuation provided was dependent on both fall and faller-specific characteristics.

The model proved robust in its ability to generate repeatable distributions of factor of risk from simulation to simulations. With as little as 3090 female VI and 2100 male VI generated per simulation, the model can achieve a standard deviation of mean FOR of 0.005 or less after 50 simulations. While the overall goal of the probabilistic model was to include elements of uncertainty to reflect the variance seen in the population (and therefore define a distribution of risk), the model should predict the same (or very similar) distribution of risk when assessing the same population. The structure of the model leads to a unique sample of VI being generated in each simulation, the general spread of risk should be similar on a population-level.

While the model predicted that a safety flooring intervention would result in substantive reductions in FOR for the older adult population of Canada, it was difficult to assess the accuracy of the predictions without large-scale clinical data. While some clinical trials have found that falls onto safety floors do not result in hip fracture outcomes (when compared to a similar number of falls onto normal, rigid flooring, where a small percentage of hip fracture outcomes were observed), it was difficult to assess the influence of the safety floors on hip fracture risk based on these small numbers (for example, 82 intervened falls) (Knoefel et al., 2013). While larger-scale clinical studies of safety flooring could provide more insight into the accuracy of the model predictions, the agreement between the model and the available clinical data lends some credence to the model.

Although the overall goal of this study, and thesis project, wasn't to develop a model that could predict population-level hip fracture rates, but instead to develop of model to predict fall-related hip fracture risk, the fracture point analysis is nevertheless a promising example of a method to put the FOR metric of hip fracture risk into the context of fracture outcomes (as discussed in section 3.4 of Chapter 3). When the Fracture Point analysis was conducted on the Intervention Effectiveness data (comparing both FOR and IFOR values of VI to their associated *Fracture Point*), it revealed some interesting results, and some areas for future development. Firstly, the percentage of females and male VI whose FOR values were greater than their respective *Fracture Point* (53.4% of female VI, 50.5% of male VI) mirrors the results presented in the Fracture Point analysis of Chapter 3 (section 3.3.4). The troubling portion of the Fracture Point analysis results are the estimates for percent reduction in likely fracture outcomes, more specifically the estimated reduction for females (0.9%). While the analysis suggests that male VI greatly benefited from the safety flooring intervention (29.8% reduction in cases of likely hip

fractures), which corresponds with the percent decrease in mean FOR observed in the Intervention Effectiveness analysis (a 28.9% reduction in FOR), the small change observed in the percent reduction in likely fractures for females (0.9%) was much lower. Although these two analyses might well be independent of each other, it does raise the question of validity for the Fracture Point analysis approaches, especially for females. Nevertheless, as discussed in Chapter 3, Fracture Point analysis is a promising example of a method to put the FOR metric of hip fracture risk into the context of fracture outcomes (albeit, with its own set of limitations).

As this was the first attempt to characterize the population-level effectiveness of a safety flooring intervention in a purely virtual environment, there were many assumptions and limitations associated with the current model design. Firstly, as was mentioned previously, the model currently assumes that every VI has suffered a lateral fall to the hip (or assesses the risk of the VI if they were to fall), and further assumes that each fall was intervened by a safety floor (or assess the risk of the VI if they were to fall onto a safety floor). The issue with these assumptions is that it does not account for the fact that different portions of the population have different risks of falling in the first place. For example, previous studies have found age associated change in balance, such as changes in gait, altered sensory system functions, decreased mediolateral stability, and increased effort needed to recover their balance following a perturbation (Lord et al., 1996; McIlroy and Maki, 1996; Rogers et al., 2001; Rubenstein, 2006; Winter et al., 1990); each of these increase the relative risk of falling. This increased risk of falling with age could explain the increase in rates of fractures with increasing age that previous epidemiological studies have observed (for example, the exponential increase in the rates of hip fractures after age 60 reported by Jean et al, 2013). And so, in its current state, the model assesses the population-level risk of hip fracture, if the simulated individuals were to suffer a lateral fall to the hip (and if the fall was

intervened by a safety floor). Another limitation of this study was the definition of stability, or convergence of variance, as there are no other predefined thresholds to meet apart from the a priori threshold defined in this study. Furthermore, the threshold set (a max standard deviation of 0.005 of mean FOR or IFOR) was subjectively chosen as an acceptable threshold of variance. Although this value was used to determine the minimum number of VI needed to be generated in any one simulation to achieve this level of stability of variance, the standard procedure used for the model (as used in Chapter 3, and in this Chapter) was to generate a sample of 100 000 VI to represent the older adult population. As our tests of stability of variance revealed, there was a low amount of variance in mean FOR and IFOR from simulation to simulation when using this N of VI, and so, we are confident in the repeatability of the findings reported in the model application portion of Chapter 3 (see section 3.2.3 of Chapter 3) and in the analysis of the effectiveness of the safety flooring intervention reported in the current chapter.

5.4 Conclusion

This study represents the first application of an intervention sub-model (person dependent safety floor force attenuation prediction) in a population model of fall-related hip fracture risk, and was the first to provide an estimate of the relative effectiveness of a safety flooring intervention on this risk. As expected, by reducing the expected impact force of a lateral fall to the hip, a safety flooring intervention leads to reduced overall risk of fall-related hip fracture on a population-level. Furthermore, a population-level safety flooring intervention leads to a narrowing of the distribution of hip fracture risk, also resulting in less variance. This study was a successful proof of concept for predicting the effects of interventions on population-level hip fracture risk in a virtual environment; as such, the model developed over the course of this thesis project can be a valuable

tool in virtual estimating the effectiveness of different interventions on population-level hip fracture risk, given that the mechanisms of the intervention in question are well understood.

Chapter 6

Thesis Synthesis and Significance

The overall purpose of this thesis two-fold. The first goal was to develop a mechanistic probabilistic model of population-level hip fracture risk for Canadian older adults. The second goal was to use this model to quantify the population distribution of hip fracture risk for Canadian older adults, as well as quantify the effects of a safety flooring intervention on this population-level risk.

6.1 Model development and Validation

The model was developed using the Factor of Risk (FOR) concept to quantify risk, with the ratio between net impact force and estimate bone strength (or fracture threshold) representing an individual's risk of suffering a fall-related hip fracture. A combination of Statistics Canada data and previously reported equations and findings were used to characterize the population distributions of factors of interest and develop (or use previously developed) equations that would use values from these distributions to calculate FOR. The model generates a Virtual Individual (VI), to which the factors of interest are pseudo-randomly assigned (along the pre-defined distributions) and FOR was calculated. Using repeated random sampling techniques, a given number of VI are generated, and the resulting distribution of FOR was characterized. Once the model was developed, it was pseudo-validated against the findings reported by Dufour and colleagues in 2012, which reported group mean FOR for four groups (female and male fracture and non-fracture groups). By using the reported values of the factors of interest for the four groups, we generated four distinct (and representative) groups of VI. When these VI were run through the model, we successfully replicated group mean FOR within 0.05 of the reported group mean FOR values for all four groups.

6.2 Safety Floor Sub-model

Mechanical testing (simulated lateral hip impacts) of a sample safety floor (SmartCells™) was conducted using a vertical drop tower and surrogate pelvis system. The experiment quantified the effects of impact velocity, effective mass, TSTT (or foam hip thickness), and pelvic stiffness on the force attenuation provided by the safety floor sample. A multiple linear regression analysis revealed that all four factors had significant effects on the force attenuation of the safety floor, with increasing impact velocity, effective mass, and pelvic stiffness resulting in greater amounts of force attenuation, and increasing TSTT resulting in less force attenuation. The results of the regression analysis were used to develop a predictive regression equation that would predict force attenuation as a percent of the net (un-intervened force).

6.3 Population-level Hip Fracture Risk

With the model validated, we attempted to apply the model to the Canadian older adult population by generating a representative sample of 100 000 VI, and characterized the population-level risk of hip fracture as sex-specific distributions. Furthermore, the regression equation developed for safety floor force attenuation was included into the model as an additional sub-model, calculating an intervened net force, allowing us to compare the intervened net force to bone strength to compute values of intervened Factor of Risk (IFOR). With both FOR and IFOR computed for all 100 000 VI, both distributions can be compared, allowing us to quantify both the population-level risk of hip fracture for Canadian older adults as well as the influence of a safety flooring intervention on that risk. Our results revealed that the safety flooring intervention lead to a substantive decrease (downward or leftward shift in the distributions of FOR) in the predicted risk of fall related hip fractures for both females and males.

6.4 Significance

As discussed throughout this thesis, hip fractures are a serious concern in the older adult population of Canada. The economic and societal burden associated with these injuries has stimulated research into the topic, both in terms of better understanding the underlying mechanics and also developing better prevention strategies. This thesis project employed what is known about the mechanics of fall-related hip fractures, to develop a population-level estimate of hip fracture risk through the use of probabilistic modelling. While other injury mechanisms have been modelled using stochastic principles, this project was the first instance of a probabilistic model being applied to hip fracture risk prediction. This framework allowed for the modelling of the population risk of hip fracture in the Canadian older adult population, and with the addition of a safety flooring sub-model, allowed quantify the effect of a safety flooring intervention on the population-level hip fracture risk. The safety flooring sub-model was developed as part of experimental study investigating the effects of fall and faller-specific parameters on the force attenuating properties of a SmartCells™ safety floor sample, the results of which were used to develop a regression equation to predict safety floor force attenuation. In summary, this thesis project combined both an experimental and computational components to develop the first probabilistic model of hip fracture risk prediction for the older adult population of Canada, as well as virtually quantify the effect of a safety flooring intervention on the population-level hip fracture risk.

6.5 Future Research

As detailed in the limitations sections of the discussion in Chapters 3 and 5, the model was limited by the sub-models (and subsequent assumptions) included in the model. And while this thesis project provides valuable insight into population-level hip fracture risk, further insight could

be gained by updating the sub-models to more recent, or more robust, versions. For example, the current model assumes a direct lateral impact to the hip, which is not entirely biofidelic; using different fall paradigms (such as an inverted pendulum fall, or change the impact to a Hertzian contact model) may result in more biofidelic model estimates. Another example of a particularly limiting sub-model was the soft tissue force attenuation model used (71 N of force attenuation for every mm of TSTT), and future research into properly characterizing the force attenuation of soft tissue could greatly improve the model predictions. Further research into the specific age associated risk of falling could add a great deal of detail and complexity into the model, allowing us to include an individual's risk of falling into their overall risk of fall-related hip fracture. Further analysis of the regression equation should be explored, with special consideration to performing a logarithmic transformation on the data (A_{floor}) before conducting the multiple linear regression; this might result in the elimination of the two- and three-way interactions, potentially clarifying the interpretation of the results. Finally, Chapter 5 is a promising proof of concept for virtually testing the effectiveness of an intervention on fall-related hip fracture risk; future research into the effects of other interventions (such as hip protectors, or pharmacological interventions) on hip fracture risk could be included into the model as a different intervention module. While there are many potential avenues for expanding and refining the model, the modular structure developed over the course of this thesis project allows for easy updating of the model (be it with updated sub-modules, or entirely new modules). Finally, as revealed in our Fracture Point Analyses in Chapter 3 and 5, finding a way to relate FOR values back to fracture outcomes could provide some context to the population-level risk in terms of fracture rates, which the current model does not provide. One method of doing this could be to convert the FOR values to related probability of hip fracture in the event of a fall. This could be accomplished using a Bayesian prior (estimated probability of

any fall resulting in a hip fracture) compared to the related FOR distributions for falls that did result in a hip fracture versus the and falls that did not result in a hip fracture.

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Appendix A

Description of alternative method to determine *Fracture Point*:

The Distribution Intercept method:

Rather than find the midpoint between the mean FOR values of the non-fracture and fracture groups, this method involves defining the distributions of FOR as probability density functions (PDFs), as was done in Figure A.1. Working on the concept of maximizing signal and reducing noise, one can define this as the point where two overlapping distributions intersect. The model (the same version used in the first *Fracture Point* analysis in Chapter 3) was run, with the results presented in Figure A.1 and Table A.1. As can be seen in Figure A.1 a), the *Fracture Point* for males was found to be 0.523, and was 0.145 for females (Figure A.1.b). This method yielded in higher *Fracture Point* values for both females and males when compared to the Midpoint method used in Chapter 3. This also resulted in a lower number of VI with FOR values greater than the *Fracture Point*, with 35.4% of females and 30.4% of males being predicted to be more likely to suffer a hip fracture than not (in the event of a fall). More so than the Midpoint method, these results suggest that a relatively larger portion of females are at a higher risk for hip fractures than males (which agrees with current epidemiological literature).

Table A.1: Results Summary for the Distribution Intercept method Fracture Threshold Analysis; Analysis was performed on the same dataset that was generated for the model application experiment

Metric	Female	Male
N	53045	46955
Mean FOR	0.067	0.422
Fracture Point	0.145	0.523
N FOR > Fracture Point	18759	14314
Percent > Fracture Point	35.4%	30.4%

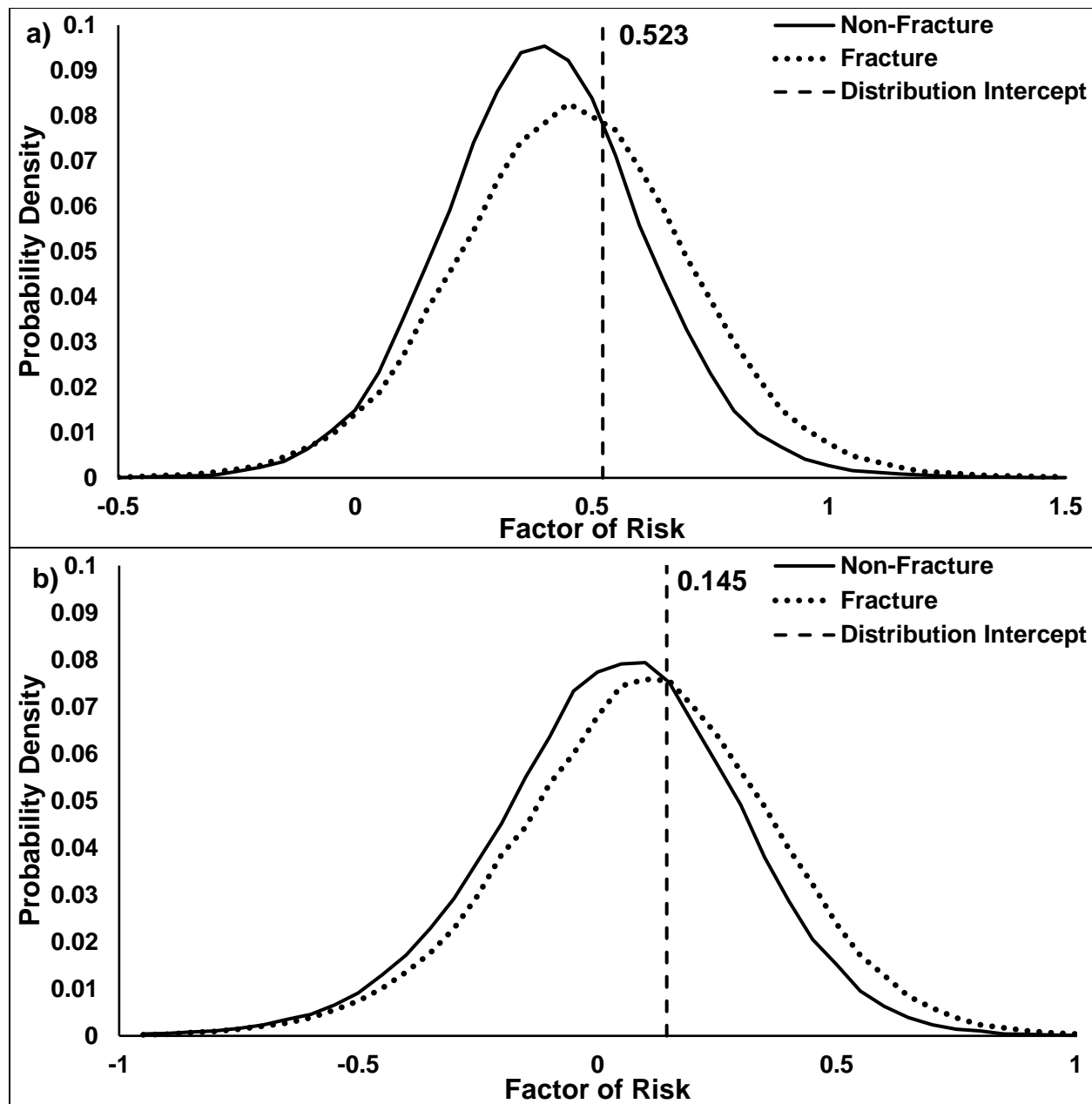


Figure A.1: Mean (50 simulations; 10 000 VI per group) Probability Distribution Functions (PDF) of male (a) and female (b) fracture (dotted line) and non-fracture (solid line) groups (VI based on group reported by Dufour et al, 2012; sub-models for Effective Mass, Fall Height, TSTT, and Pelvic Stiffness were updated to reflect current literature, and mimic what is used in the probabilistic model of this thesis). The dashed line represents the point at which the distributions cross (“Fracture Point”), relating the relative risk of a hip fracture outcome occurring; values to the right of the Fracture Point are related to a higher risk of hip fracture than non-hip fracture.

Appendix B

Presented below are additional statistical tests (Univariate ANOVAs) on F_{max} , F_{neck} , the difference between the two (F_{diff}), and a new variable, time to peak force (T_{max}). More specifically, here are the different ANOVAs that were run, and compiled in the below tables:

- F_{max} by Floor (Control vs Safety Floor)
- F_{max} by Floor and Target Velocity (used to analyze main effect of velocity, and interaction with floor)
- F_{max} by Floor and Mass (used to analyze main effect of mass, and interaction with floor)
- F_{max} by Floor and TSTT (used to analyze main effect of TSTT, and interaction with floor)
- F_{max} by Floor and Pelvic Stiffness (used to analyze main effect of velocity, and interaction with floor)
- The above 5 were repeated for F_{neck} , F_{diff} , and T_{max}

Table B.1: Summary of Univariate ANOVA statistics for F_{max} . Pairwise Comparisons are presented for significant main effects with less than 3 levels.

F_{max}	Main Effect		Post Hoc/Pairwise Comps		95% CI	
Factor	F	p	Level	p	Lower Bound	Upper Bound
Floor	0.103	0.749				
Velocity	74.323	<0.001	2.1 m/s - 2.8 m/s	<0.001	-713.292	-289.936
			2.1 m/s - 3.4 m/s	<0.001	-1271.435	-848.079
			2.8 m/s - 3.4 m/s	<0.001	-769.822	-346.466
Floor*Velocity	0.001	0.999				
Mass	5.594	0.005	36.3 kg - 41.4 kg	0.228	-547.0098	82.9646
			36.3 kg - 46.4 kg	0.003	-747.4478	-117.4734
			41.4 kg - 46.4 kg	0.374	-515.4252	114.5492
Floor*Mass	0.004	0.996				
TSTT	0.142	0.868				
Floor*TSTT	0.003	0.997				
Pelvic Stiffness	28.713	<0.001	22650 N/m - 33370 N/m	<0.001	-716.385	-329.372
Floor*Pelvic Stiffness	0.001	0.972				

Table B.2: Summary of Univariate ANOVA statistics for F_{neck} . Pairwise Comparisons are presented for significant main effects with less than 3 levels.

F_{neck}	Main Effect		Post Hoc/Pairwise Comps.		95% CI	
Factor	F	p	Level	p	Lower Bound	Upper Bound
Floor	63.856	<0.001	Control - Safety Floor	<0.001	452.930	751.838
Velocity	51.504	<0.001	2.1 m/s - 2.8 m/s	<0.001	-472.6003	-157.8810
			2.1 m/s - 3.4 m/s	<0.001	-813.3266	-498.6073
			2.8 m/s - 3.4 m/s	<0.001	-498.0859	-183.3666
Floor*Velocity	5.59	0.005				
Mass	4.505	0.013	36.3 kg - 41.4 kg	.467	-345.0998	89.6770
			36.3 kg - 46.4 kg	.010	-485.3614	-50.5846
			41.4 kg - 46.4 kg	.358	-357.6500	77.1268
Floor*Mass	1.134	0.326				
TSTT	1.2	0.305				
Floor*TSTT	2.061	0.133				
Pelvic Stiffness	8.206	0.005	22650 N/m - 33370 N/m	0.005	-354.267	-64.421
Floor*Pelvic Stiffness	0.576	0.45				

Table B.3: Summary of Univariate ANOVA statistics for F_{diff} . Pairwise Comparisons are presented for significant main effects with less than 3 levels.

F_{diff}	Main Effect		Post Hoc/Pairwise Comps.		95% CI	
Factor	F	p	Level	p	Lower Bound	Upper Bound
Floor	88.926	<0.001	Control - Safety Floor	<0.001	-686.674	-448.097
Velocity	22.857	<0.001	2.1 m/s - 2.8 m/s	0.007	-331.8861	-40.8597
			2.1 m/s - 3.4 m/s	<0.001	-549.3035	-258.2772
			2.8 m/s - 3.4 m/s	0.001	-362.9306	-71.9043
Floor*Velocity	6.675	0.002				
Mass	2.657	0.075				
Floor*Mass	1.538	0.22				
TSTT	0.953	0.389				
Floor*TSTT	3.039	0.052				
Pelvic Stiffness	36.259	<0.001	22650 N/m - 33370 N/m	<0.001	-416.789	-210.281
Floor*Pelvic Stiffness	1.281	0.26				

Table B.4: Summary of Univariate ANOVA statistics for T_{max} . Pairwise Comparisons are presented for significant main effects with less than 3 levels.

T_{max}	Main Effect		Post Hoc/Pairwise Comps.		95% CI	
Factor	F	p	Level	p	Lower Bound	Upper Bound
Floor	0.216	0.643				
Velocity	1.661	1.95				
Floor*Velocity	0.091	0.913				
Mass	22.283	<0.001	36.3 kg - 41.4 kg	<0.001	-.0110	-.0028
			36.3 kg - 46.4 kg	<0.001	-.0151	-.0070
			41.4 kg - 46.4 kg	.046	-.0082	-.0001
Floor*Mass	0.138	0.971				
TSTT	0.611	0.545				
Floor*TSTT	0.038	0.963				
Pelvic Stiffness	114.023	<0.001	22650 N/m - 33370 N/m	<0.001	.010	.014
Floor*Pelvic Stiffness	1.62	0.206				

Summary of Statistical Analyses of F_{max} , F_{neck} , F_{diff} , and T_{max} (significant effects only):

- **F_{max} Results:**
 - A significant main effect of velocity (F_{max} increasing with increasing velocity)
 - Post Hoc: all 3 levels significantly different than the others
 - A significant main effect of mass (F_{max} increasing with increasing mass)
 - Post Hoc: only the 36.3 and 46.4 kg levels were significantly different from each other
 - A significant main effect of pelvic stiffness (F_{max} increasing with increased pelvic stiffness)

- **F_{neck} Results:**

- A significant difference between floor conditions (safety floor trials significantly lower than control trials)
- A significant main effect of velocity (F_{neck} increasing with increase velocity)
 - Post Hoc: all three levels of velocity significantly different from the others
- A significant interaction between floor and velocity (F_{neck} increasing more with velocity for the control trials compared to the safety floor trials)
- A significant main effect of mass (F_{neck} increasing with increasing mass)
 - Post Hoc: only the 36.3 kg and 46.4 kg levels were significantly different than each other
- A significant main effect of pelvic stiffness (F_{neck} increasing with increased pelvic stiffness)

- **F_{diff} Results:**

- A significant difference between floor conditions (safety floor trials significantly lower than control trials)
- A significant main effect of velocity (F_{neck} increasing with increase velocity)
 - Post Hoc: all three levels of velocity significantly different from the others
- A significant interaction between floor and velocity (F_{neck} increasing more with velocity for the safety floor trials compared to the control trials)
- A significant main effect of pelvic stiffness (with F_{diff} increasing with increased pelvic stiffness)

- **T_{max} :**

- A significant main effect of mass (T_{max} increasing with increased impact velocity)
- A significant main effect of pelvic stiffness (T_{max} decreasing with increased pelvic stiffness)

Appendix C

Description of results for the Distribution Intercept method applied to the Intervention

Effectiveness results of Chapter 5:

The *Fracture Points* values obtained via the Distribution Intercept method (as described in Appendix A) were compared to the FOR and IFOR values of the VI generated for the Intervention Effectiveness experiment of Chapter 5. This Fracture Point analysis resulted in a lower number of VI with FOR values greater than the *Fracture Point* (when compared to the results presented in section 5.2.3 of Chapter 5), with 35.0% of females and 30.1% of males being predicted to be more likely to suffer a hip fracture than not (in the event of a fall). Additionally, only 31.2% of female VI, and 5.4% of male VI, were predicted to be more likely to suffer a hip fracture after the safety flooring intervention (Table C.1). This translates to a 3.7% reduction for females, and a 24.7% reduction for males. While these values may be more promising than the results presented in Chapter 5, especially for females, the estimated reduction for females is lower than the reduction seen in mean FOR by almost a factor of 10. More so than the Midpoint method, these results suggest that a relatively larger portion of females are at a higher risk for hip fractures than males (which agrees with current epidemiological literature).

Table C.1: Results Summary for the Distribution Intercept method of Fracture Threshold Analysis; Analysis was performed on the same dataset that was generated for the intervention effectiveness experiment

Metric	Female	Male
N	52968	47032
Mean FOR	0.067	0.422
Fracture Point	0.0432	0.405
N of FOR > Fracture Point	18523	14142
Percent > Fracture Point	35.0%	30.4%
Mean IFOR	0.044	0.301
N of IFOR > Fracture Point	16541	2529
Percent > Fracture Point	31.2%	5.4%
Percent Reduction	3.7%	24.7%